UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-Q

x QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For The Quarterly Period Ended March 31, 2013

OR

o TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from to

Commission File Number 001-33389

VIVUS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**94-3136179**
(State or other jurisdiction of incorporation or organization)	(IRS employer identification number)
1172 Castro Street Mountain View, California	**94040**
(Address of principal executive office)	(Zip Code)

(650) 934-5200
(Registrant's telephone number, including area code)

N/A
(Former name, former address and former fiscal year, if changed since last report)

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No o

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No o

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer x	Accelerated filer o
Non-accelerated filer o (Do not check if a smaller reporting company)	Smaller reporting company o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). o Yes x No

At April 23, 2013, 100,665,029 shares of common stock, par value $.001 per share, were outstanding.

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PART I: FINANCIAL INFORMATION

ITEM 1. CONDENSED CONSOLIDATED FINANCIAL STATEMENTS (UNAUDITED)

VIVUS, INC.

CONDENSED CONSOLIDATED BALANCE SHEETS
(In thousands, except par value)

	March 31, 2013 (Unaudited)	December 31, 2012 Note 1
ASSETS		
Current assets:		
Cash and cash equivalents	$ 90,606	$ 58,605
Available-for-sale securities	59,702	155,981
Accounts receivable, net	4,878	2,778
Inventories	27,564	25,353
Prepaid expenses and other assets	24,324	19,159
Total current assets	207,074	261,876
Property and equipment, net	2,867	1,951
Non-current assets	992	287
Total assets	$ 210,933	$ 264,114
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 18,670	$ 25,375
Accrued and other liabilities	14,656	13,777
Deferred revenue	1,546	1,150
Current liabilities of discontinued operations	506	903
Total current liabilities	35,378	41,205
Commitments and contingencies		
Stockholders' equity:		
Preferred stock; $1.00 par value; 5,000 shares authorized; no shares issued and outstanding	—	—
Common stock; $.001 par value; 200,000 shares authorized; 100,660 and 100,659 shares issued and outstanding at March 31, 2013 and December 31, 2012, respectively	101	101
Additional paid-in capital	715,162	708,921
Accumulated other comprehensive income	14	33
Accumulated deficit	(539,722)	(486,146)
Total stockholders' equity	175,555	222,909
Total liabilities and stockholders' equity	$ 210,933	$ 264,114

See accompanying notes to unaudited condensed consolidated financial statements.

VIVUS, INC.

CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(In thousands, except per share data)
(Unaudited)

	Three Months Ended March 31,	
	2013	2012
Revenue:		
Net product revenue	$ 4,112	$ —
Operating expenses:		
Cost of goods sold	390	—
Inventory charge	5,777	—
Research and development	7,046	6,291
Selling, general and administrative	44,696	12,481
Total operating expenses	57,909	18,772
Loss from operations	(53,797)	(18,772)
Interest and other income, net	35	17
Loss from continuing operations before income taxes	(53,762)	(18,755)
Provision for income taxes	(6)	(7)
Loss from continuing operations	(53,768)	(18,762)
Income (loss) from discontinued operations, net of tax	192	(16)
Net loss	$ (53,576)	$ (18,778)
Basic and diluted net loss per share:		
Continuing operations	$ (0.53)	$ (0.20)
Discontinued operations	0.00	0.00
Net loss per share	$ (0.53)	$ (0.20)
Shares used in per share computation:		
Basic and diluted	100,660	92,267

CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

(In thousands)
(Unaudited)

	Three Months Ended March 31,	
	2013	2012
Net loss	$ (53,576)	$ (18,778)
Other comprehensive loss:		
Unrealized loss on securities, net of taxes	(19)	(32)
Comprehensive loss	$ (53,595)	$ (18,810)

See accompanying notes to unaudited condensed consolidated financial statements.

VIVUS, INC.

CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)
(Unaudited)

	Three Months Ended March 31,	
	2013	2012
Cash flows from operating activities:		
Net loss from continuing operations	$ (53,768)	$ (18,762)
Adjustments to reconcile net loss to net cash used for operating activities from continuing operations:		
Provision for cash discounts	104	—
Depreciation	183	22
Amortization of discount or premium on available-for-sale securities	510	763
Share-based compensation expense	6,061	2,718
Inventory charge	5,036	—
Changes in assets and liabilities:		

Accounts receivable	(2,204)	—
Inventories	(7,071)	210
Prepaid expenses and other assets	(5,165)	(44)
Accounts payable	(6,876)	1,864
Accrued and other liabilities	879	518
Deferred revenue	396	—
Net cash used for operating activities from continuing operations	(61,915)	(12,711)
Net cash used for operating activities from discontinued operations	(204)	(316)
Net cash used for operating activities	(62,119)	(13,027)
Cash flows from investing activities:		
Property and equipment purchases	(929)	—
Purchases of available-for-sale securities	—	(48,763)
Other non-current assets	(705)	(287)
Proceeds from maturity of available-for-sale securities	95,750	13,500
Proceeds from sale of available-for-sale securities	—	9,035
Net cash provided by (used for) investing activities	94,116	(26,515)
Cash flows from financing activities:		
Net proceeds from exercise of common stock options	4	8,665
Net proceeds from issuance of common stock	—	192,005
Net cash provided by financing activities	4	200,670
Net increase in cash and cash equivalents	32,001	161,128
Cash and cash equivalents:		
Beginning of period	58,605	39,554
End of period	$ 90,606	$ 200,682

See accompanying notes to unaudited condensed consolidated financial statements.

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VIVUS, INC.

NOTES TO UNAUDITED CONDENSED CONSOLIDATED FINANCIAL STATEMENTS

MARCH 31, 2013

1. BASIS OF PRESENTATION

The accompanying unaudited condensed consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America, or U.S. GAAP, for interim financial information and with the instructions to Form 10-Q and Article 10 of Regulation S-X. Accordingly, they do not include all of the information and footnotes required by U.S. GAAP for complete financial statements. In the opinion of management, all adjustments (consisting of normal recurring adjustments) considered necessary for a fair presentation have been included. Operating results for the three months ended March 31, 2013 are not necessarily indicative of the results that may be expected for the year ending December 31, 2013. Management has evaluated all events and transactions that occurred after March 31, 2013 through the date these unaudited condensed consolidated financial statements were filed. There were no events or transactions during this period which require recognition or disclosure in these unaudited condensed consolidated financial statements, except as disclosed in Note 9. The year-end condensed consolidated balance sheet data was derived from audited financial statements, but does not include all disclosures required by U.S. GAAP. The unaudited condensed consolidated financial statements should be read in conjunction with the audited financial statements and notes thereto included in the Company's Annual Report on Form 10-K for the year ended December 31, 2012, as filed on February 26, 2013 with the Securities and Exchange Commission, or SEC. The unaudited condensed consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries. All significant intercompany accounts and transactions have been eliminated.

When we refer to "we," "our," "us," the "Company" or "VIVUS" in this document, we mean the current Delaware corporation, or VIVUS, Inc., and its California predecessor, as well as all of our consolidated subsidiaries.

Reclassifications

Certain prior year amounts in the unaudited condensed consolidated financial statements have been reclassified to conform to the current year presentation.

Use of Estimates

The preparation of these unaudited condensed consolidated financial statements requires management to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues, expenses and related disclosures. On an ongoing basis, the Company evaluates its estimates, including critical accounting policies or estimates related to available-for-sale securities, research and development expenses, income taxes, inventories, revenues, contingencies and litigation and share-based compensation. The Company bases its estimates on historical experience, information received from third-parties and on various market specific and other relevant assumptions that it believes to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results could differ significantly from those estimates under different assumptions or conditions.

Recent Accounting Pronouncements

There have been no recent accounting pronouncements or changes in accounting pronouncements during the three months ended March 31, 2013, as compared to the recent accounting pronouncements described in the Company's Form 10-K for the year ended December 31, 2012, that are of significance, or potential significance to the Company.

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2. SHARE-BASED COMPENSATION

The Company accounts for share-based compensation arrangements in accordance with the Financial Accounting Standards Board, or FASB's, Accounting Standards Codification, or ASC, topic 718, *Compensation—Stock Compensation*, or ASC 718, and ASC 505-50, *Equity — Equity Based Payments to Non-Employees*.

Total share-based compensation expense for all of the Company's share-based awards is as follows (in thousands):

	Three Months Ended March 31,	
	2013	2012
Research and development	$ 940	$ 726
Selling, general and administrative	5,121	1,992
Share-based compensation expense	$ 6,061	$ 2,718

Included in the inventory carrying value as of March 31, 2013 is $176,000 of share-based compensation expense.

3. CASH, CASH EQUIVALENTS AND AVAILABLE-FOR-SALE SECURITIES

The fair value and the amortized cost of cash, cash equivalents, and available-for-sale securities by major security type at March 31, 2013 and December 31, 2012 are presented in the tables that follow.

As of March 31, 2013 (in thousands):

Cash and cash equivalents and available-for-sale securities	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Cash and money market funds	$ 90,606	$ —	$ —	$ 90,606
U.S. Treasury securities	59,688	14	—	59,702
Total	150,294	14	—	150,308
Less amounts classified as cash equivalents	(90,606)	—	—	(90,606)
Total available-for-sale securities	$ 59,688	$ 14	$ —	$ 59,702

As of March 31, 2013, all of the Company's available-for-sale securities have a contractual maturity of less than one year.

As of December 31, 2012 (in thousands):

Cash and cash equivalents and available-for-sale securities	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Cash and money market funds	$ 58,605	$ —	$ —	$ 58,605
U.S. Treasury securities	155,948	33	—	155,981
Total	214,553	33	—	214,586
Less amounts classified as cash equivalents	(58,605)	—	—	(58,605)
Total available-for-sale securities	$ 155,948	$ 33	$ —	$ 155,981

Fair Value Measurements

As of March 31, 2013 and December 31, 2012, all of the Company's cash and cash equivalents and available-for-sale securities were measured at fair value on a recurring basis, and classified as Level 1 in the fair value hierarchy. There were no assets or liabilities where Level 2 or Level 3 valuation techniques were used and there were no assets and liabilities measured at fair value on a non-recurring basis.

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4. INVENTORIES

Inventories consist of (in thousands):

	Balance as of	
	March 31, 2013	December 31, 2012
Raw materials	$ 11,229	$ 5,139
Work in process	2,336	2,635
Finished goods	13,895	17,506
Deferred costs	104	73

Total	$ 27,564	$ 25,353

As of March 31, 2013 and December 31, 2012, the raw materials inventories consist primarily of the active pharmaceutical ingredients, or API, for the commercialization of Qsymia® (phentermine and topiramate extended-release) capsules CIV, the finished goods inventory consists of both Qsymia and STENDRA™ (avanafil) primarily for commercialization, while the work in process and deferred costs inventories relate exclusively to Qsymia. The deferred costs represent the costs of Qsymia product shipped to customers, but not yet shipped to patients through prescriptions, and for which recognition of revenue has been deferred.

Inventories are stated at the lower of cost or market. Cost is determined using the weighted average method. The Company periodically evaluates the carrying value of inventory on hand for potential excess amount over demand using the same lower of cost or market approach as that used to value the inventory. As a result of this evaluation, during the three months ended March 31, 2013, the Company recognized an inventory charge of $5.8 million, primarily to write off work-in-process and finished goods inventories on hand in excess of demand.

5. PREPAID EXPENSES AND OTHER ASSETS

Prepaid expenses and other assets consist of (in thousands):

	Balance as of	
	March 31, 2013	December 31, 2012
Interest receivable	$ 375	$ 743
Prepaid insurance	5,749	6,979
Prepaid sales and marketing expenses	10,108	5,735
Prepaid medical affairs expenses	5,224	1,782
Manufacturing capacity commitment fees	1,791	2,300
Other prepaid expenses and assets	1,077	1,620
Total	$ 24,324	$ 19,159

The amounts included in prepaid expenses and other assets consist of interest receivable, prepaid insurance, and deposits and prepayments for future services, primarily related to prepaid product commercialization costs for services relating to future periods in support of the sales and marketing of Qsymia in the U.S., prepayments related to medical affairs activities for Qsymia and STENDRA, and manufacturing capacity commitment fees. These amounts represent probable future economic benefits obtained or controlled by the Company as a result of past transactions or events, which meet the definition of an asset under FASB Concept Statement 6. As such, these costs have been deferred as prepaid expenses and other assets on the consolidated balance sheet and will be either (i) charged to expense accordingly when the related prepaid services are rendered to the Company, or (ii) converted to cash when the receivables are collected by the Company.

6. ACCRUED AND OTHER LIABILITIES

Accrued and other liabilities consist of (in thousands):

	Balance as of	
	March 31, 2013	December 31, 2012
Accrued research and clinical expenses	$ 1,576	$ 1,372
Accrued employee compensation and benefits	4,575	3,859
Accrued manufacturing costs	4,308	4,135
Accrued sales and marketing expenses	1,903	2,908
Other accrued liabilities	2,294	1,503
Total	$ 14,656	$ 13,777

The amounts included in accrued and other liabilities consist of obligations for past services, primarily related to accrued manufacturing and product commercialization costs for services relating to past periods in support of the commercial launch of Qsymia in the U.S., accrued employee compensation and benefits, and accrued research and clinical expenses.

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7. NET INCOME (LOSS) PER SHARE

The Company computes basic net income (loss) per share applicable to common stockholders based on the weighted average number of common shares outstanding during the period. Diluted net income per share is based on the weighted average number of common and common equivalent shares, which represent shares that may be issued in the future upon the exercise of outstanding stock options. Common share equivalents are excluded from the computation in periods in which they have an anti-dilutive effect. Stock options for which the price exceeds the average market price over the period have an anti-dilutive effect on net income per share and, accordingly, are excluded from the calculation. When there is a net loss, potentially dilutive common equivalent shares are not included in the calculation of net loss per share since their inclusion would be anti-dilutive.

As the Company recognized a net loss for the three months ended March 31, 2013 and 2012 all potential common equivalent shares were excluded for these periods as they were anti-dilutive. For the three months ended March 31, 2013 and 2012, 5,461,000 and 4,546,000 options outstanding, respectively, were not included in the computation of diluted net loss per share for the Company because the effect would be anti-dilutive.

8. LEGAL MATTERS

Securities Related Class Action Lawsuits

The Company and two of its officers were defendants in a putative class action lawsuit captioned *Kovtun v. Vivus, Inc., et al.*, Case No. 4:10-CV-04957-PJH, in the U.S. District Court, Northern District of California. The action, filed in November 2010, alleged violations of Section 10(b) and 20(a) of

the federal Securities Exchange Act of 1934 based on allegedly false or misleading statements made by the defendants in connection with the Company's clinical trials and New Drug Application, or NDA, for Qsymia as a treatment for obesity. Defendants filed a motion to dismiss plaintiff's Amended Class Action Complaint, and that motion was granted with leave to amend. On November 9, 2011, plaintiff filed his Second Amended Class Action Complaint, generally alleging that defendants misled investors regarding the prospects for Qsymia's NDA approval, and Qsymia's efficacy and safety. Defendants again filed a motion to dismiss. After briefing and argument, the District Court on September 27, 2012 granted the motion and dismissed the action with prejudice. The District Court entered final judgment for defendants the same day. On October 26, 2012, plaintiff filed a Notice of Appeal to the U.S. Court of Appeals for the Ninth Circuit. Plaintiff filed his opening appellate brief on February 19, 2013, and defendants filed their answering brief on April 11, 2013. Briefing is expected to continue into May 2013, after which the Court of Appeals may request oral argument.

Additionally, certain of the Company's officers and directors are defendants in a shareholder derivative lawsuit captioned *Turberg v. Logan, et al.*, Case No. CV-10-05271-PJH, pending in the same federal court. In the plaintiff's Verified Amended Shareholder Derivative Complaint filed June 3, 2011, the plaintiff largely restated the allegations of the *Kovtun* action and alleged that the directors breached fiduciary duties to the Company by purportedly permitting the Company to violate the federal securities laws as alleged in the *Kovtun* action. The parties had agreed to stay the litigation pending resolution of the appeal. The same individuals are also named defendants in consolidated shareholder derivative suits pending in the California Superior Court, Santa Clara County under the caption *In re VIVUS, Inc. Derivative Litigation*, Master File No. 11 0 CV188439. The allegations in the state court derivative suits are substantially similar to the other lawsuits. The parties have agreed to stay these consolidated actions on the same terms as the federal derivative litigation.

The Company and its directors cannot predict the outcome of the various shareholder lawsuits, but they believe the various shareholder lawsuits are without merit and intend to continue vigorously defending them.

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9. SUBSEQUENT EVENTS

The Company entered into a Purchase and Sale Agreement, or the BioPharma Agreement, effective as of March 25, 2013 between the Company and BioPharma Secured Investments III Holdings Cayman LP, a Cayman Islands exempted limited partnership, or BioPharma, which provides for the purchase of a debt-like instrument. Notwithstanding anything in the BioPharma Agreement to the contrary, the Company intends for the transactions under the BioPharma Agreement to be characterized and treated as debt for all U.S. tax and accounting purposes. Under the BioPharma Agreement, the Company received $50 million less $1.1 million in funding and facility payments, at the initial closing on April 9, 2013. Subject to the terms and conditions of the BioPharma Agreement and at the Company's sole discretion, the Company may also elect prior to December 31, 2013 to receive an additional $60 million, less $600,000 in a funding payment, at the secondary closing, which is subject to customary closing conditions and which closing shall occur, if at all, no later than January 15, 2014. The Company shall be responsible for all reasonable and documented out-of-pocket legal costs and fees incurred by BioPharma related to the BioPharma Agreement, subject to a cap of $300,000.

In return, the Company is obligated to make scheduled quarterly payments to BioPharma, as further described in the BioPharma Agreement and below, until the total amount due under the BioPharma Agreement is paid. Below is a summary of the scheduled quarterly payments:

Each Calendar Quarter Occurring	Scheduled Quarterly Amount	Total Scheduled Annual Amount
in 2014	$ 3,000,000	$ 12,000,000
in 2015	$ 5,000,000	20,000,000
in 2016	$ 5,000,000	20,000,000
in 2017	$ 5,000,000	20,000,000
in the first calendar quarter of 2018	$ 1,700,000	1,700,000
Total		**$ 73,700,000**

The scheduled quarterly payments, other than the payment(s) for the first calendar quarter of 2018, are capped at the lower of the scheduled payment amounts or 25% of the net sales of (i) Qsymia (and any derivative or improvement thereof, including Qsiva™ as it relates to the European Union), or the Product, and (ii) any other obesity agent developed or marketed by the Company or its affiliates or licensees. Accordingly, if 25% of the net sales is less than the scheduled quarterly payment, then the Company can elect to make a payment that is lower than the scheduled payment amount. The final payment, scheduled to be made in the second quarter of 2018, is not subject to this limitation. The final payment will include any unpaid scheduled quarterly payments, plus any accrued and unpaid make-whole premiums. Any quarterly payment less than the scheduled quarterly payment amount will be subject to a make-whole premium equal to the applicable scheduled quarterly payment of the preceding quarter less the actual payment made to BioPharma for the preceding quarter multiplied by 1.03. Regardless, the Company may pay scheduled quarterly payments out of any available funds notwithstanding Product net sales. The Company also has the option to prepay all scheduled quarterly payments as specified in the BioPharma Agreement. Assuming all scheduled quarterly payments are made timely and in full, the annual implied effective interest rate is 12.75% compounded quarterly, or 13.37% per annum.

To secure its obligations in connection with the BioPharma Agreement, the Company granted BioPharma a security interest to (i) the purchased receivables which are defined in the BioPharma Agreement as the scheduled quarterly payments, any underpayments of such payments based on an audit of the Company's records and any interest due on the foregoing amounts, and (ii) the Company's patents, trademarks, copyrights and regulatory filings related to the Product, or the Additional Collateral. For the purposes herein, (i) and (ii) above shall be referred to as the Collateral.

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If the Company (i) fails to deliver a payment when due and does not remedy that failure within a cure period, (ii) fails to deliver certain reports when due and does not remedy that failure within a cure period, (iii) fails to use commercially reasonable efforts in the promotion and marketing of the Product after March 25, 2015 and does not remedy that failure within a cure period, (iv) incurs certain forms of indebtedness above specified limits, (v) fails to maintain a first-priority perfected security interest in the Additional Collateral and does not remedy that failure within a cure period or (vi) becomes subject to an event of bankruptcy, then BioPharma may attempt to recover its unpaid scheduled payments, including by exercising its right to sell or otherwise dispose of all or any part of the Collateral.

During the term of the BioPharma Agreement, the Company is required to use commercially reasonable efforts, as defined in the BioPharma Agreement, to undertake certain obligations and activities to develop, market, promote and commercialize the Product and maximize net sales of the Product. Additionally, during the term of the BioPharma Agreement the Company may not (i) pay a dividend or other cash distribution on its capital stock, unless it has cash and cash equivalents in excess of a specified amount, (ii) amend or restate its certificate of incorporation or bylaws unless such amendments or restatements do not affect BioPharma's interests under the BioPharma Agreement, (iii) encumber the Collateral, or (iv) abandon certain patent rights, in each case without the consent of BioPharma. In addition, the Company may incur (i) up to $250 million in unsecured indebtedness with a maturity date after September 30, 2018, and (ii) additional unsecured indebtedness with a maturity date after December 31, 2019 in a principal amount of the lesser of (a) the net sales during the previous 12 months minus $350 million and (b) $250 million. However, the Company's total unsecured indebtedness may not exceed $450 million.

Upon the occurrence of a Company change of control transaction, as defined in the BioPharma Agreement, BioPharma will be entitled to receive an amount equal to the sum of all unpaid scheduled quarterly payments. A permitted partnering agreement and a permitted action, both as defined in the BioPharma Agreement, shall not constitute a change of control transaction under the BioPharma Agreement. A permitted partnering agreement is an agreement for promotional and/or marketing resources for the Product, where (i) the Company continues to receive 25% of the net sales of the Product and (ii) the permitted partner agrees to be subject to the same promotional and marketing covenants that apply to the Company under the BioPharma Agreement. A permitted action allows the Company to take certain actions with respect to a certain subset of the Additional Collateral as specified in the BioPharma Agreement.

On April 16, 2013, the U.S. Food and Drug Administration, or FDA, approved the Company's amendment and modification to the Risk Evaluation and Mitigation Strategy, or REMS, for Qsymia. The amendment, submitted in October 2012, allows Qsymia to be dispensed through certified retail pharmacies, in addition to the existing network of certified mail-order pharmacies. With this modification, the goals, commitments and components of the original Qsymia REMS will remain in place, including a Medication Guide, patient brochure, voluntary healthcare provider training and other educational tools.

On April 26, 2013, the European Medicines Agency's Committee for Medicinal Products for Human Use, or CHMP, adopted a positive opinion recommending the granting of a marketing authorization for avanafil, known by the trade name SPEDRA™ in the European Union, for the treatment of erectile dysfunction.

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ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

This Management's Discussion and Analysis of Financial Conditions and Results of Operations and other parts of this Form 10-Q contain "forward looking" statements that involve risks and uncertainties. These statements typically may be identified by the use of forward looking words or phrases such as "may," "believe," "expect," "forecast," "intend," "anticipate," "predict," "should," "planned," "likely," "opportunity," "estimated," and "potential," the negative use of these words or other similar words. All forward looking statements included in this document are based on our current expectations, and we assume no obligation to update any such forward looking statements. The Private Securities Litigation Reform Act of 1995 provides a "safe harbor" for such forward looking statements. In order to comply with the terms of the safe harbor, we note that a variety of factors could cause actual results and experiences to differ materially from the anticipated results or other expectations expressed in such forward looking statements. The risks and uncertainties that may affect the operations, performance, development, and results of our business include but are not limited to: (1) our limited commercial experience with Qsymia® in the United States, or U.S.; (2) the timing of initiation and completion of the clinical studies required as part of the approval of Qsymia by the U.S. Food and Drug Administration, or FDA; (3) the response from the FDA to the data that VIVUS will submit relating to post-approval clinical studies; (4) the impact of the indicated uses and contraindications contained in the Qsymia label and the Risk Evaluation and Mitigation Strategy, or REMS, requirements; (5) the impact of distribution of Qsymia through a certified home delivery pharmacy network; (6) our ability to implement the recently FDA approved amendment to the REMS for Qsymia, which, allows dispensing through certified retail pharmacies; (7) that we may be required to provide further analysis of previously submitted clinical trial data; (8) the negative opinion of the European Medicines Agency's, or EMA, Committee for Medicinal Products for Human Use, or CHMP, for the Marketing Authorization Application, or MAA, for Qsymia; (9) whether healthcare providers, payors and public policy makers will recognize the significance of the new AACE guidelines; (10) our ability to successfully commercialize Qsymia or establish partnerships for avanafil; (11) the ability of our partners to maintain regulatory approvals to manufacture and adequately supply our products to meet demand; (12) our history of losses and variable quarterly results; (13) substantial competition; (14) risks related to the failure to protect our intellectual property and litigation in which we may become involved; (15) uncertainties of government or third-party payor reimbursement; (16) our reliance on sole source suppliers; (17) our reliance on third parties and our collaborative partners; (18) our failure to continue to develop innovative investigational drug candidates and drugs; (19) risks related to the failure to obtain FDA or foreign authority clearances or approvals and noncompliance with FDA or foreign authority regulations; (20) our ability to demonstrate through clinical testing the safety and effectiveness of our investigational drug candidates; (21) the timing of initiation and completion of clinical trials and submissions to foreign authorities; (22) the results of post-marketing studies are not favorable; (23) compliance with post-marketing regulatory standards is not maintained; (24) the volatility and liquidity of the financial markets; (25) our liquidity and capital resources; (26) our expected future revenues, operations and expenditures and (27) other factors that are described from time to time in our periodic filings with the Securities and Exchange Commission, or the SEC, or the Commission, including those set forth in this filing as "Item 1A. Risk Factors."

All percentage amounts and ratios were calculated using the underlying data in thousands. Operating results for the quarter ended March 31, 2013, are not necessarily indicative of the results that may be expected for the full fiscal year or any future period.

OVERVIEW

VIVUS is a pharmaceutical company with two FDA approved therapies, Qsymia and STENDRA™. Our drug, Qsymia (phentermine and topiramate extended-release) (formerly known as Qnexa®) was approved by the U.S. Food and Drug Administration, or FDA, on July 17, 2012, as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of 30 or greater (obese), or 27 or greater (overweight) in the presence of at least one weight-related comorbidity, such as hypertension, type 2 diabetes mellitus or high cholesterol (dyslipidemia). Qsymia incorporates a proprietary formulation combining low doses of active ingredients from two previously approved drugs, phentermine and topiramate. Although the exact mechanism of action is unknown, Qsymia is believed to suppress appetite and increase satiety, or the feeling of being full, the two main mechanisms that impact eating behavior. On September 17, 2012, we announced the U.S. market availability of Qsymia. We

currently distribute Qsymia through a certified home delivery network, which includes CVS Pharmacy, Express Scripts, Walgreens, Wal-Mart Pharmacy, and, for its members only, Kaiser Permanente.

As part of the approval of Qsymia, we are committed to conducting post-marketing studies. We intend to conduct a study to assess the long-term treatment effect of Qsymia on the incidence of major adverse cardiovascular events in overweight and obese subjects with confirmed cardiovascular disease, studies to assess the safety and efficacy of Qsymia for weight management in obese pediatric and adolescent subjects, studies to assess drug utilization and pregnancy exposure and a study to assess renal function, as well as animal and in vitro studies. We anticipate beginning certain of these studies in 2013.

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On December 17, 2010, we filed a Marketing Authorization Application, or MAA, with the European Medicines Agency, or EMA, to market Qsymia in the European Union, or EU, for the treatment of obesity. The approved trade name for Qsymia in the EU is Qsiva™. On October 18, 2012, we received the formal opinion from the EMA's Committee for Medicinal Products for Human Use, or CHMP, recommending against approval of the MAA for Qsiva in the EU due to concerns over the potential cardiovascular and central nervous system effects associated with long-term use, teratogenic potential and use by patients for whom Qsiva would not have been indicated. We appealed this opinion and requested a re-examination of the decision by the CHMP. After re-examination, on February 21, 2013, the CHMP affirmed their earlier opinion. We are currently exploring options to seek approval of Qsiva in the EU, including filing on a country-by-country basis under a decentralized approval process. We also intend to seek approval for Qsymia in other territories outside the United States and EU. We intend to commercialize Qsymia in territories where we obtain approval through collaboration agreements with third-parties.

Our drug, STENDRA, or avanafil, was approved by the FDA on April 27, 2012, for the treatment of erectile dysfunction, or ED, in the United States. As part of the approval of STENDRA, we are committed to conducting post-marketing studies. In March 2012, we filed an MAA with the EMA to market avanafil in the EU for the treatment of ED. The approved trade name for STENDRA in the EU is SPEDRA™. Avanafil is an oral PDE5 inhibitor that we have licensed from Mitsubishi Tanabe Pharma Corporation, or MTPC. Through collaboration arrangements with third-parties, we intend to market and sell STENDRA in the United States and, if approved, SPEDRA in the EU and other territories outside the United States. We are currently in discussions with potential collaboration partners for all stated territories.

Foreign regulatory approvals, including approvals to market Qsiva or SPEDRA in the EU, may not be obtained on a timely basis, or at all, and the failure to receive regulatory approvals in a foreign country would prevent us from marketing our products in that market, which could have a material adverse effect on our business, financial condition and results of operations.

Recent Developments

On March 25, 2013, we entered into the BioPharma Agreement, which provides for the purchase of a debt-like instrument. At the initial closing on April 9, 2013, we received $50 million, less $1.1 million in funding and facility payments. Subject to the terms and conditions of the BioPharma Agreement and at our sole discretion, we may also elect prior to December 31, 2013 to receive an additional $60 million, less $600,000 in a funding payment, at the secondary closing, which is subject to customary closing conditions and which closing shall occur, if at all, no later than January 15, 2014. We will be responsible for all reasonable and documented out-of-pocket legal costs and fees incurred by BioPharma related to the BioPharma Agreement, subject to a cap of $300,000.

On April 16, 2013, the FDA approved an amendment to the REMS that allows for distribution of Qsymia through certified retail pharmacy locations. We intend to certify pharmacies and announce retail availability in the third quarter of 2013.

In April 2013, the CHMP adopted a positive opinion recommending the granting of a marketing authorization for SPEDRA for the treatment of erectile dysfunction in the European Union to the European Commission, or EC. A final decision from the EC regarding the SPEDRA MAA is expected to take approximately two months.

Strategy

Our goal is to build a successful pharmaceutical company through the commercialization and development of innovative proprietary drugs. We intend to achieve this by:

- successfully implementing the certified retail pharmacy distribution channel for Qsymia in the United States;
- continuing to lower out of pocket costs for patients with discount programs, increased third-party payor coverage and changes in public policy;
- establishing medical obesity treatment as a widely accepted category supported by treatment guidelines;
- increasing awareness for Qsymia through direct to consumer advertising;
- expanding our commercialization efforts for Qsymia through working with a major pharmaceutical company;
- entering into and supporting a collaboration agreement for the commercialization of STENDRA for the treatment of ED in the U.S.;

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- obtaining regulatory approval for Qsiva for the treatment of obesity and SPEDRA for the treatment of ED in the EU and other territories worldwide;
- if approved, entering into and supporting collaboration agreements for the commercialization of Qsiva for the treatment of obesity and SPEDRA for the treatment of ED in the EU and other territories worldwide; and

- continuing to identify and develop early to later stage investigational drug candidates for approval in the U.S., the EU and elsewhere, thereby providing a steady pipeline of drugs for eventual sale, partnership or commercialization.

It is our objective to continue as a successful drug development company and to become a successful commercial entity largely through the sales of Qsymia and profits from collaborations for STENDRA, SPEDRA and Qsymia outside of the U.S.

CRITICAL ACCOUNTING POLICIES AND ESTIMATES

The discussion and analysis of our financial condition and results of operations are based upon our unaudited condensed consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America, or U.S. GAAP. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues, expenses and related disclosures. On an ongoing basis, we evaluate our estimates, including those related to available-for-sale securities, research and development expenses, income taxes, inventories, revenues, contingencies and litigation and share-based compensation. We base our estimates on historical experience, information received from third-parties and on various market specific and other relevant assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ significantly from these estimates under different assumptions or conditions.

During the first three months of fiscal 2013, there were no significant changes to our critical accounting policies and estimates. Management's Discussion and Analysis of Financial Condition and Results of Operations contained in Part II, Item 7 of our Annual Report on Form 10-K for our fiscal year ended December 31, 2012 provides a more complete discussion of our critical accounting policies and estimates.

Recent Accounting Pronouncements

There have been no recent accounting pronouncements or changes in accounting pronouncements during the three months ended March 31, 2013, as compared to the recent accounting pronouncements described in our Form 10-K for the year ended December 31, 2012, that are of significance, or potential significance to the Company.

RESULTS OF OPERATIONS

For the quarter ended March 31, 2013, we reported a net loss of $53.6 million or $0.53 net loss per share, as compared to a net loss of $18.8 million or $0.20 net loss per share during the same period in 2012. The increased net loss in the quarter ended March 31, 2013, as compared to the quarter ended March 31, 2012, is primarily attributable to increased selling, general and administrative expenses related to commercialization activities for Qsymia.

We may have continued losses in future periods, depending on our success in commercializing Qsymia and STENDRA, the timing of our research and development expenditures, and our continued investment in the clinical development of our current research and investigational drug candidates, to bring those potential drugs to market.

Continuing operations

Net product revenue (Unaudited)

Net product revenue was $4.1 million for the three months ended March 31, 2013. As Qsymia was not approved until July 2012, we had no net product revenue from continuing operations for three months ended March 31, 2012. In September 2012, we began distributing Qsymia to the certified home delivery pharmacies in our network. We currently recognize revenue for Qsymia based upon prescription sell-through by our certified home delivery pharmacy services networks to patients as we do not have sufficient historical information to reliably estimate returns.

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At March 31, 2013, we have deferred revenue of $1.5 million, which represents Qsymia product shipped to our certified home delivery pharmacy services networks, but not yet shipped to patients through prescriptions, net of prompt payment discounts.

We expect Qsymia product revenue and prescriptions shipped to patients to increase in 2013 as we continue the commercialization of Qsymia.

Cost of goods sold (Unaudited)

Cost of goods sold is $390,000 for the three months ended March 31, 2013 and relates to our product shipments of Qsymia to patients and includes the inventory costs of APIs, third-party contract manufacturing and packaging and distribution costs, royalties, cargo insurance, freight, shipping, handling and storage costs, and overhead costs of the employees involved with production. The cost of goods sold associated with deferred revenue on Qsymia product shipments is recorded as deferred costs, which are included in inventories in the unaudited condensed consolidated balance sheets, until such time as the deferred revenue is recognized.

We expect cost of goods sold to increase in 2013 as product sales of Qsymia increase.

Inventory charge (Unaudited)

Inventories are stated at the lower of cost or market. Cost is determined using the weighted average method. We periodically evaluate the carrying value of inventory on hand for potential excess amount over demand using the same lower of cost or market approach as that used to value the inventory. As a result of this evaluation, during the three months ended March 31, 2013, we recognized an inventory charge of $5.8 million, primarily to write off work-in-process and finished goods inventories on hand in excess of demand. A substantial portion of the excess amount relates to the initial production of Qsymia, which has a shelf life of 24 months. With additional stability data to support a longer shelf life, we have submitted an application to the FDA to extend the shelf life to 36 months for current and future production. We will continue to evaluate our inventories on a periodic basis and we may incur additional inventory write-downs in future periods if actual events differ materially from our current assumptions.

Research and development expenses (Unaudited)

Drug Indication/Description	Three Months Ended March 31, 2013	2012	2013 vs. 2012 Increase/(Decrease)
	(In thousands, except percentages)		
Qsymia for obesity	$ 605	$ 2,703	(78)%
STENDRA for ED	2,938	639	360%
Other projects	186	405	(54)%
Share-based compensation	790	726	9%
Overhead costs*	2,527	1,818	39%
Total research and development expenses	$ 7,046	$ 6,291	12%

*Overhead costs include compensation and related expenses, consulting, legal and other professional services fees relating to research and development activities, which we do not allocate to specific projects.

The increase in research and development expenses for the three months ended March 31, 2013, as compared to the same period in 2012, is primarily due to start-up and enrollment costs associated with the post-approval studies for STENDRA, including a corresponding increase in headcount to support these projects.

We anticipate that our research and development expenses for the remainder of 2013 will increase as compared to 2012 as we continue the planning phase of a post-approval cardiovascular outcomes study for Qsymia, known as ACQLAIM. The details of ACQLAIM have not yet been agreed with the FDA. This study could cost between $150 and $250 million and take as long as five to six years to complete. There are likely to be additional research and development expenses for other post-approval studies related to STENDRA and Qsymia, and for our investigational drug candidates under development. Our research and development expenses may fluctuate from period to period due to the timing and scope of our development activities and the results of clinical and pre-clinical studies.

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Selling, general and administrative expenses (Unaudited)

	Three Months Ended March 31, 2013	2012	2013 vs. 2012 Increase
	(In thousands, except percentages)		
Selling, general and administrative expenses	$ 44,696	$ 12,481	258%

The increase in selling, general and administrative expenses for the three months ended March 31, 2013 is primarily due to increased spending for Qsymia commercialization activities of $23.0 million, including expenses related to the contract sales organization, marketing programs, market research and analytics, and additional headcount; increased medical affairs-related expenses of $2.2 million primarily related to additional headcount; incremental increases in other corporate expenses totaling $3.8 million; and increased share-based compensation expense (a non-cash expense) of $3.1 million, as compared to the quarter ended March 31, 2012.

We anticipate our selling, general and administrative expenses to be significantly higher for the remainder of 2013 as compared to 2012, primarily due to the additional efforts involved in the commercialization and marketing activities for Qsymia related to the FDA approval of our amendment to the REMS program, allowing for the distribution of Qsymia through certified retail pharmacy locations.

Income (loss) from discontinued operations

Income from discontinued operations of $192,000 in the three months ended March 31, 2013 relates primarily to adjustments to our sales reserves for accrued product returns related to the MUSE product. The net loss from discontinued operations in the three months ended March 31, 2012 was $16,000.

LIQUIDITY AND CAPITAL RESOURCES

Continuing Operations

Cash. Cash, cash equivalents and available-for-sale securities (cash) totaled $150.3 million at March 31, 2013, as compared to $214.6 million at December 31, 2012. The decrease of $64.3 million is primarily due to cash used for operating activities.

Since inception, we have financed operations primarily from the issuance of equity securities. Through March 31, 2013, we have raised $661.0 million from financing activities, received $150 million from the sale of Evamist, and had an accumulated deficit of $539.7 million at March 31, 2013. Additionally, in April 2013, we received a net amount of $48.9 million through the sale of a debt-like instrument to BioPharma.

At March 31, 2013, we had $90.6 million in cash and cash equivalents and $59.7 million in available-for-sale securities. We invest our excess cash balances in money market and marketable securities, primarily U.S. Treasury securities and debt securities of U.S. government agencies, corporate debt securities and asset-backed securities, in accordance with our investment policy. At March 31, 2013, all of our cash equivalents and available-for-sale securities were invested in either U.S. government securities or money market funds that invest only in U.S. Treasury securities. The investment policy has the primary investment objectives of preservation of principal; however, there may be times when certain of the securities in our portfolio will fall below the credit ratings required in the policy. If those securities are downgraded or impaired, we would experience realized or unrealized losses in the value of our portfolio, which would have an adverse effect on our results of operations, liquidity and financial condition.

Investment securities are exposed to various risks, such as interest rate, market and credit. Due to the level of risk associated with certain investment securities and the level of uncertainty related to changes in the value of investment securities, it is possible that changes in these risk factors in the near term could have an adverse material impact on our results of operations or stockholders' equity.

Liabilities. Total liabilities were $35.4 million at March 31, 2013, which is $5.8 million lower than at December 31, 2012.

Operating Activities. Our operating activities used $62.1 million and $13.0 million in cash during the three months ended March 31, 2013 and 2012, respectively. During the three months ended March 31, 2013, the use of cash from our net operating loss from continuing operations of $53.8 million was offset by $6.1 million in non-cash share-based compensation expense due to increased headcount and $5.0 million due to the inventory write-off for Qsymia. Additional cash used in operating activities resulted from changes in assets and liabilities during the quarter including a $5.2 million net increase in prepaid expenses and other assets, which is primarily comprised of medical affairs, sales and marketing activities for Qsymia. In addition, there was a net $7.1 million increase in

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inventories, primarily for Qsymia. Accounts receivable increased approximately $2.2 million as a result of increased shipments of Qsymia to pharmacies in support of growing demand for Qsymia. Accounts payable decreased by $6.9 million during the first quarter of 2013 due to the timing of vendor payments.

During the three months ended March 31, 2012, our net operating loss of $18.8 million was offset by $2.7 million in non-cash share-based compensation expense and a $1.9 million increase in accounts payable, primarily due to the timing of invoices and payments and increased activities related to Qsymia pre-commercialization activity.

We anticipate cash used in operations in 2013 will be higher than cash used in operations in 2012, primarily due to ongoing commercialization activities for Qsymia.

Investing Activities. Our investing activities provided $94.1 million and used $26.5 million in cash during the three months ended March 31, 2013 and 2012, respectively. The fluctuations from period to period are due primarily to the timing of purchases, sales and maturity of investment securities.

Financing Activities. Financing activities were not material during the first quarter of 2013 as compared to cash provided by financing activities of $200.7 million during the first quarter of 2012. In the first three months of 2012, cash provided by financing activities included $8.7 million in proceeds from the exercise of stock options and $192.0 million in net proceeds from an underwritten public offering of our common stock.

On March 25, 2013, we entered into the BioPharma Agreement, which provides for the purchase of a debt-like instrument. Under the BioPharma Agreement, we received $50 million, less $1.1 million in funding and facility payments, at the initial closing, which occurred on April 9, 2013. Subject to the terms and conditions of the BioPharma Agreement and at our sole discretion, we may also elect prior to December 31, 2013 to receive an additional $60 million, less $600,000 in a funding payment, at the secondary closing, which is subject to customary closing conditions and which closing shall occur, if at all, no later than January 15, 2014. We will be responsible for all reasonable and documented out-of-pocket legal costs and fees incurred by BioPharma related to the BioPharma Agreement, subject to a cap of $300,000.

The funding necessary to execute our business strategies is subject to numerous uncertainties, which may adversely affect our liquidity and capital resources. Commercialization of Qsymia and STENDRA may be more costly than we planned. In addition, completion of clinical trials and approval by the FDA of investigational drug candidates may take several years or more, but the length of time generally varies substantially according to the type, complexity, novelty and intended use of an investigational drug candidate. It is also important to note that if an investigational drug candidate is identified, the further development of that candidate can be halted or abandoned at any time due to a number of factors. These factors include, but are not limited to, funding constraints, lack of efficacy or safety or change in market demand.

We anticipate that our existing capital resources combined with anticipated future cash flows will be sufficient to support our operating needs at least through the first quarter of 2014. However, we anticipate that we may require additional funding to continue our commercialization of Qsymia, to conduct post-approval clinical studies for both Qsymia and STENDRA, to conduct non-clinical and clinical research and development work to support regulatory submissions and applications for our current and future investigational drug candidates, to finance the costs involved in filing and prosecuting patent applications and enforcing or defending our patent claims, if any, to fund operating expenses, to establish additional or new manufacturing and marketing capabilities, to manufacture quantities of our drugs and investigational drug candidates and to make payments under our existing license agreements for Qsymia and STENDRA.

While some of our anticipated costs are unknown at the current time, we may need to raise additional capital to continue the funding of our commercialization efforts, product development programs and our research and development plans in future periods beyond the first quarter of 2014. If we require additional capital, we may seek any required additional funding through collaborations, public and private equity or debt financings, capital lease transactions or other available financing sources. Additional financing may not be available on acceptable terms, or at all. If additional funds are raised by issuing equity securities, substantial dilution to existing stockholders may result. If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate one or more of our commercialization or development programs or obtain funds through collaborations with others that are on unfavorable terms or that may require us to relinquish rights to certain of our technologies, product candidates or products that we would otherwise seek to develop on our own.

Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet financing arrangements and have not established any special purpose entities. We have not guaranteed any debt or commitments of other entities or entered into any options on non-financial assets.

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Contractual Obligations

On March 25, 2013, we entered into the BioPharma Agreement, which provides for the purchase of a debt-like instrument. At the initial closing on April 9, 2013, we received $50 million less $1.1 million in funding and facility payments. Subject to the terms and conditions of the BioPharma Agreement and at our sole discretion, we may also elect prior to December 31, 2013 to receive an additional $60 million, less $600,000 in a funding payment, at the secondary closing, which is subject to customary closing conditions and which closing shall occur, if at all, no later than January 15, 2014. We will be responsible for all reasonable and documented out-of-pocket legal costs and fees incurred by BioPharma related to the BioPharma Agreement, subject to a cap of $300,000.

In return, we are obligated to make scheduled quarterly payments to BioPharma, as further described in the BioPharma Agreement and below, until the total amount due under the BioPharma Agreement is paid. Below is a summary of the scheduled quarterly payments:

Year	Scheduled Quarterly Amount	Total Scheduled Annual Amount
2014	$ 3,000,000	$ 12,000,000
2015	$ 5,000,000	20,000,000
2016	$ 5,000,000	20,000,000
2017	$ 5,000,000	20,000,000
First calendar quarter of 2018	$ 1,700,000	1,700,000
Total		**$ 73,700,000**

The scheduled quarterly payments, other than the payment(s) for the first calendar quarter of 2018, are capped at the lower of the scheduled payment amounts or 25% of the net sales of (i) Qsymia (and any derivative or improvement thereof, including Qsiva™ as it relates to the European Union), or the Product, and (ii) any other obesity agent developed or marketed by the Company or its affiliates or licensees. Accordingly, if 25% of the net sales is less than the scheduled quarterly payment, then we can elect to make a payment that is lower than the scheduled payment amount. The final payment, scheduled to be made in the second quarter of 2018, is not subject to this limitation. The final payment will include any unpaid scheduled quarterly payments, plus any accrued and unpaid make-whole premiums. Any quarterly payment less than the scheduled quarterly payment amount will be subject to a make-whole premium equal to the applicable scheduled quarterly payment of the preceding quarter less the actual payment made to BioPharma for the preceding quarter multiplied by 1.03. Regardless, we may pay scheduled quarterly payments out of any available funds notwithstanding Product net sales. We also have the option to prepay all scheduled quarterly payments as specified in the BioPharma Agreement. Assuming all scheduled quarterly payments are made timely and in full, the annual implied effective interest rate is 12.75% compounded quarterly, or 13.37% per annum.

To secure our obligations in connection with the BioPharma Agreement, we granted BioPharma a security interest to certain of our assets, agreed to certain payments upon the occurrence of a change of control transaction and agreed to certain covenants.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

The Securities and Exchange Commission's rule related to market risk disclosure requires that we describe and quantify our potential losses from market risk sensitive instruments attributable to reasonably possible market changes. Market risk sensitive instruments include all financial or commodity instruments and other financial instruments that are sensitive to future changes in interest rates, currency exchange rates, commodity prices or other market factors.

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Market and Interest Rate Risk

Our cash, cash equivalents and available-for-sale securities as of March 31, 2013 consisted primarily of money market funds and U.S. Treasury securities. Our cash is invested in accordance with an investment policy approved by our Board of Directors that specifies the categories (money market funds, U.S. Treasury securities and debt securities of U.S. government agencies, corporate bonds, asset-backed securities, and other securities), allocations, and ratings of securities we may consider for investment. Currently, we have focused on investing in U.S. Treasuries until market conditions improve.

Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because the majority of our investments are in short-term marketable debt securities. The primary objective of our investment activities is to preserve principal. Some of the securities that we invest in may be subject to market risk. This means that a change in prevailing interest rates may cause the value of the investment to fluctuate. For example, if we purchase a security that was issued with a fixed interest rate and the prevailing interest rate later rises, the value of our investment may decline. A hypothetical 100 basis point increase in interest rates would reduce the fair value of our available-for-sale securities at March 31, 2013 by approximately $112,000. In general, money market funds are not subject to market risk because the interest paid on such funds fluctuates with the prevailing interest rate.

ITEM 4. CONTROLS AND PROCEDURES

(a.) Evaluation of disclosure controls and procedures. We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our Exchange Act reports is recorded, processed, summarized and reported within the timelines specified in the rules and forms of the Securities and Exchange Commission, or SEC, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can only provide reasonable assurance of achieving the desired control objectives, and in reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

As required by SEC Rule 13a-15(b), we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, of the effectiveness of the design and operation of VIVUS' disclosure controls and procedures as of the end of the period covered by this Quarterly Report on Form 10-Q. Based on the foregoing, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level.

(b.) Changes in internal controls. There was no change in our internal control over financial reporting that occurred during the period covered by this Quarterly Report on Form 10-Q that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II: OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

Securities Related Class Action Lawsuits

The Company and two of its officers were defendants in a putative class action lawsuit captioned *Kovtun v. Vivus, Inc., et al.*, Case No. 4:10-CV-04957-PJH, in the U.S. District Court, Northern District of California. The action, filed in November 2010, alleged violations of Section 10(b) and 20(a) of the federal Securities Exchange Act of 1934 based on allegedly false or misleading statements made by the defendants in connection with the Company's clinical trials and New Drug Application, or NDA, for Qsymia as a treatment for obesity. Defendants filed a motion to dismiss plaintiff's Amended Class Action Complaint, and that motion was granted with leave to amend. On November 9, 2011, plaintiff filed his Second Amended Class Action Complaint, generally alleging that defendants misled investors regarding the prospects for Qsymia's NDA approval, and Qsymia's efficacy and safety. Defendants again filed a motion to dismiss. After briefing and argument, the District Court on September 27, 2012 granted the motion and dismissed the action with prejudice. The District Court entered final judgment for defendants the same day. On October 26, 2012, plaintiff filed a Notice of Appeal to the U.S. Court of Appeals for the Ninth Circuit. Plaintiff filed his opening appellate brief on February 19, 2013, and defendants filed their answering brief on April 11, 2013. Briefing is expected to continue into May 2013, after which the Court of Appeals may request oral argument.

Additionally, certain of the Company's officers and directors are defendants in a shareholder derivative lawsuit captioned *Turberg v. Logan, et al.*, Case No. CV-10-05271-PJH, pending in the same federal court. In the plaintiff's Verified Amended Shareholder Derivative Complaint filed June 3, 2011, the plaintiff largely restated the allegations of the *Kovtun* action and alleged that the directors breached fiduciary duties to the Company by purportedly permitting the Company to violate the federal securities laws as alleged in the *Kovtun* action. The parties had agreed to stay the litigation pending resolution of the appeal. The same individuals are also named defendants in consolidated shareholder derivative suits pending in the California Superior Court, Santa Clara County under the caption *In re VIVUS, Inc. Derivative Litigation*, Master File No. 11 0 CV188439. The allegations in the state court derivative suits are substantially similar to the other lawsuits. The parties have agreed to stay these consolidated actions on the same terms as the federal derivative litigation.

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The Company and its directors cannot predict the outcome of the various shareholder lawsuits, but they believe the various shareholder lawsuits are without merit and intend to continue vigorously defending them.

ITEM 1A. RISK FACTORS

Set forth below and elsewhere in this Form 10-Q and in other documents we file with the SEC, are risks and uncertainties that could cause actual results to differ materially from the results contemplated by the forward-looking statements contained in this Quarterly Report on Form 10-Q. These are not the only risks and uncertainties facing VIVUS. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations.

Risks Relating to our Business

Our success will depend on our ability to effectively and profitably commercialize Qsymia®.

Our success will depend on our ability to effectively and profitably commercialize Qsymia, formerly known as Qnexa®, which will include our ability to:

- implement and certify thousands of retail pharmacies nationwide in a timely manner;
- expand our commercialization efforts for Qsymia through working with a major pharmaceutical company;
- lower out of pocket costs to patients with discount programs, improve third-party payor coverage and change public policy;
- create market demand for Qsymia through direct-to-consumer advertising, patient and physician education, marketing and sales activities;
- achieve market acceptance and generate product sales;
- comply with the post-marketing requirements established by the U.S. Food and Drug Administration, or FDA, including the Risk Evaluation and Mitigation Strategy, or REMS, and any other requirements established by the FDA in the future;
- conduct the post-marketing studies required by the FDA;
- comply with other healthcare regulatory requirements;
- maintain and defend our patents, if challenged;
- ensure that the APIs for Qsymia and the finished product are manufactured in sufficient quantities and in compliance with requirements of the FDA and similar foreign regulatory agencies and with an acceptable quality and pricing level in order to meet commercial demand; and
- ensure that the entire supply chain for Qsymia, from APIs to finished product, efficiently and consistently delivers Qsymia to our customers.

Prior to the commercialization of Qsymia, we have not had any commercial products since the divestiture of MUSE in November 2010. While our management and key personnel have significant experience developing, launching and commercializing drugs at VIVUS and at other companies, we have only recently begun to work together to commercialize Qsymia and we cannot be certain that we will be successful. If we are unable to successfully commercialize Qsymia, our ability to generate product sales will be severely limited, which will have a material adverse impact on our business, financial condition, and results of operations.

We intend to market and sell STENDRA™ (avanafil) in the U.S. under a collaboration arrangement with a third party. We also intend to market and sell SPEDRA™ (avanafil) outside the U.S., if approved, under collaboration arrangements with third parties. These arrangements might subject us to a number of risks.

We intend to enter into collaborative arrangements or strategic alliances with pharmaceutical partners or others to commercialize STENDRA in the U.S. and, if approved, to commercialize SPEDRA outside the U.S.

We may be unable to enter into agreements with third parties for these arrangements on favorable terms or at all, which could delay or impair our ability to commercialize STENDRA and SPEDRA in the relevant territories. Additionally, dependence on collaborative arrangements or strategic alliances will subject us to a number of risks, including the following:

- we may not be able to control the commercialization of our drug products in the relevant territories, including amount, timing and quality of resources that our collaborators may devote to our drug products;
- our collaborators may experience financial, regulatory or operational difficulties, which may impair their ability to commercialize our drug products;
- our collaborators may be required under the laws of the relevant territory to disclose our confidential information or may fail to protect our confidential information;
- as a requirement of the collaborative arrangement, we may be required to relinquish important rights with respect to our drug products, such as marketing and distribution rights;
- business combinations or significant changes in a collaborator's business strategy may adversely affect a collaborator's willingness or ability to satisfactorily complete its commercialization or other obligations under any collaborative arrangement;
- legal disputes or disagreements may occur with one or more of our collaborators;
- a collaborator could independently move forward with a competing investigational drug candidate developed either independently or in collaboration with others, including with one of our competitors; and
- a collaborator could terminate the collaborative arrangement, which could negatively impact the continued commercialization of our drug products.

Failure to obtain regulatory approval in foreign jurisdictions will prevent us from marketing our products abroad.

We intend to market and sell SPEDRA, if approved, in the European Union, or EU, and in other territories outside the U.S. through collaboration arrangements with third parties. In order to market products in the EU and many other foreign jurisdictions, we must obtain separate regulatory approvals. In March 2012, we filed a Marketing Authorization Application, or MAA, with the European Medicines Agency, or EMA, to market SPEDRA in the EU for the treatment of ED and a final decision from the EC regarding the SPEDRA MAA is expected to take approximately two months. We have had limited interactions with foreign regulatory authorities, and the approval procedures vary among countries and can involve additional testing. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries. For example, Qsymia was approved in the U.S. by the FDA; however, we were denied an MAA for the same product in the EU. Foreign regulatory approvals may not be obtained on a timely basis, or at all, for any of our products and the failure to receive regulatory approvals in a foreign country would prevent us from marketing our products in that country, which could have a material adverse effect on our business, financial condition and results of operations.

We intend to market SPEDRA outside the U.S., if approved, which will subject us to risks related to conducting business internationally.

We, together with our affiliates and partners, intend to manufacture, market, and distribute SPEDRA, if approved, outside the U.S. We expect that we will be subject to additional risks related to conducting business internationally, including:

- different regulatory requirements for drug approvals in foreign countries;
- differing U.S. and foreign drug import and export rules;
- reduced protection for intellectual property rights in some foreign countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- different reimbursement systems;

- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the U.S.;
- production shortages resulting from events affecting raw material supply or manufacturing capabilities abroad;
- potential liability resulting from development work conducted by these distributors; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters.

We could be negatively affected as a result of a threatened proxy contest and other actions of dissident stockholders.

First Manhattan Co. and its affiliates, or First Manhattan, have filed a preliminary proxy statement presenting a proposal to (i) nominate six nominees, or First Manhattan Nominees, for election to the Board at the annual meeting of stockholders, or Annual Meeting, (ii) vote against the Company's proposal to approve, on an advisory basis, the compensation of the Company's named executive officers, (iii) ratify the appointment of OUM & Co., LLP as the Company's independent registered public accounting firm for the fiscal year ending December 31, 2013 and (iv) repeal any bylaw amendments in effect at the time of the Annual Meeting that were not included in our bylaws in effect as of April 18, 2012, as amended on February 20, 2013, and is inconsistent with the election of the First Manhattan Nominees at the Annual Meeting. If First Manhattan carries through with its intention and launches a proxy contest, our business and our stock price could be adversely affected because if individuals are elected to the Board with a different agenda, it may adversely affect our ability to effectively and timely implement our strategic plan. There can be no assurance as to the outcome of this situation, the level of distraction it may cause to our management team, the amount of expenses we may incur relating thereto or the impact on our stock price.

We rely in part on a third-party contract sales organization for certain sales and marketing support services for Qsymia.

We rely on PDI, Inc., or PDI, a third-party contract sales organization, to assist with the hiring of sales representatives and the promotion of Qsymia to physicians. Our internal sales and marketing personnel manage and supervise the activities of this sales force. Nevertheless, we face risks in our partial reliance on the third-party contract sales organization including the following:

- PDI may not apply the expected financial resources or required expertise to successfully promote Qsymia;
- PDI may not invest in the continued development of a sales force and the related infrastructure at levels that ensure that sales of Qsymia reach their full potential;
- PDI, or its sales representatives, may not comply with applicable legal or regulatory requirements, including the requirement to promote drugs only for uses for which they have been approved;
- disputes may arise between us and PDI, including between the contract sales representatives, who are PDI employees, and sales management, who are VIVUS employees, that may adversely affect Qsymia sales or profitability; and
- PDI may enter into agreements with other parties that have products that could compete with Qsymia.

We depend on the success of PDI in performing its services, and we cannot be certain PDI will cooperate with us to perform its obligations under the agreement. Although they are contractually obligated, we cannot control the amount of resources that will be devoted by PDI to the promotion of Qsymia. Any failure of PDI to perform its obligations or to continue to allocate resources to the promotion of Qsymia could adversely affect the commercialization of Qsymia and materially harm our business, financial condition and results of operations.

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Our failure to properly implement the REMS modification and make Qsymia available in certified retail pharmacy locations by the expected target date of the third quarter of 2013 would be detrimental to our business.

On April 16, 2013, we received approval of the previously submitted amendment to the Qsymia REMS that allows for distribution through certified retail pharmacy locations. Our failure to implement the terms of the REMS modification and to certify a sufficient number of pharmacies on a timely basis would have a negative impact on our business. The implementation of the REMS amendment poses several risks including:

- our inability to enter into contracts with wholesalers in a timely fashion, on reasonable terms, or at all, to allow for retail pharmacy dispensing of Qsymia;
- our inability to obtain the proper technology (pharmacy software) to implement the REMS modification;
- the failure by pharmacies to complete the training necessary for certification;
- our failure to properly identify and stock the locations of the pharmacies to be certified based on patient needs and current or future prescribing habits;

- our failure to comply with the assessment and requirements for each of these pharmacies set forth in the amendment; and

- our inability to properly assess the individual pharmacy locations.

Our success in commercializing Qsymia will depend on our ability to effectively advertise to consumers.

We will need to increase awareness of Qsymia to be successful in our commercialization of Qsymia. To increase awareness of Qsymia, we intend to advertise directly to consumers. Direct-to-consumer advertising requires significant financial resources, and we will have to rely on external agencies to provide effective advertisements and run successful campaigns. In addition, we are required to submit all print advertisements to the FDA at the time they are first used. There can be no assurance that our advertisements will be acceptable to the FDA, or that the advertisements will be successful in increasing consumer demand. Even if the advertisements are successful, there can be no assurance that increased consumer demand will result in more physicians prescribing Qsymia.

We have significant inventories on hand and, in the first quarter of 2013, we recorded an inventory charge of $5.8 million, primarily to write off excess inventory related to Qsymia.

We maintain significant inventories and evaluate these inventories on a periodic basis for potential excess and obsolescence. In the first quarter of 2013, we recorded an inventory charge of $5.8 million, primarily to write off inventory in excess of demand. These charges were based on our analysis of current Qsymia inventory on hand and remaining shelf life, in relation to our projected demand for the product. The current FDA-approved commercial product shelf life for Qsymia is 24 months and for STENDRA is 36 months. We have submitted a request to the FDA to extend the shelf life of Qsymia to 36 months, and we have submitted a similar application to extend the shelf life of STENDRA to 48 months.

Our allowance for excess and obsolete inventory is subjective and requires accurate forecasting of the future market demand for our products. We will continue to evaluate our inventories on a periodic basis. The value of our inventories could be impacted if actual sales differ significantly from our estimates of future demand, if the FDA does not approve extensions of the shelf lives for Qsymia and STENDRA, or if any significant unanticipated changes in future product demand or market conditions occur. Any of these events, or a combination thereof, could result in additional inventory write-downs in future periods, which could be material.

Our failure to manage and maintain our distribution network for Qsymia could compromise the commercialization of this product.

We rely on Cardinal Health PTS, LLC, or Cardinal Health, a third-party distribution and supply-chain management company, to warehouse Qsymia and distribute it to the certified home delivery pharmacies that then distribute Qsymia directly to patients. Cardinal Health provides billing, collection and returns services. We also have entered into agreements with select certified pharmacies, including CVS Pharmacy, Express Scripts, Walgreens, Wal-Mart Pharmacy and Kaiser Permanente, to distribute Qsymia to eligible patients through their certified home delivery networks and intend to enter into agreements to establish a certified retail pharmacy distribution network. Patients and physicians have experienced delays in processing prescriptions in the home delivery network. In addition to providing services to support the distribution and use of Qsymia, each of the pharmacies has agreed to comply with the REMS program certified pharmacy requirements and will provide us with the necessary patient and prescribing physician

data. We have contracted with a third-party data warehouse to collect this patient and prescribing physician data from the certified pharmacy home delivery network and report it to us. We rely on this third-party data in order to recognize revenue and comply with the REMS requirements for Qsymia, such as data analysis. This distribution and data collection network requires significant coordination with our sales and marketing, finance, regulatory and medical affairs teams, in light of the REMS requirements applicable to Qsymia.

Cardinal Health is our exclusive supplier of distribution logistics services, and accordingly we depend on Cardinal Health to satisfactorily perform its obligations under our agreement with them. Pursuant to the REMS program applicable to Qsymia, our distribution network is through a small number of certified home delivery pharmacies, and we rely on these pharmacies to implement a number of safety procedures and report certain information to the third-party data warehouse. Failure to maintain our contracts with Cardinal Health, with the select certified home delivery pharmacies, or with the third-party data warehouse, or the inability or failure of any of them to adequately perform under the contracts, could negatively impact the distribution of Qsymia, or adversely affect our ability to comply with the REMS applicable to Qsymia. Failure to comply with a requirement of an approved REMS can result in, among other things, civil penalties, operating restrictions and criminal prosecution. Failure to coordinate financial systems could also negatively impact our ability to accurately report and forecast product revenue. If we are unable to effectively manage the distribution and data collection process, sales of Qsymia could be severely compromised and our business, financial condition and results of operations would be harmed.

If we are unable to enter into agreements with suppliers or our suppliers fail to supply us with the APIs for our products or if we rely on sole source suppliers, we may experience delays in commercializing our products.

We currently do not have supply agreements for extended-release topiramate or phentermine, which are the APIs used in Qsymia. We cannot guarantee that we will be successful in entering into supply agreements on reasonable terms or at all or that we will be able to obtain or maintain the necessary regulatory approvals for these suppliers in a timely manner or at all.

We anticipate that we will continue to rely on single source suppliers for phentermine and extended-release topiramate for the foreseeable future. Any production shortfall on the part of our suppliers that impairs the supply of phentermine or extended-release topiramate could have a material adverse effect on our business, financial condition and results of operations. If we are unable to obtain a sufficient quantity of these compounds, there could be a substantial delay in successfully developing a second source supplier. An inability to continue to source product from any of these suppliers, which could be due to regulatory actions or requirements affecting the supplier, adverse financial or other strategic developments experienced by a supplier, labor disputes or shortages, unexpected demands or quality issues, could adversely affect our ability to satisfy demand for Qsymia, which could adversely affect our product sales and operating results materially, which could significantly harm our business.

The API and the tablets for STENDRA are currently manufactured by Mitsubishi Tanabe Pharma Corporation, or MTPC. MTPC has arrangements for the three main starting materials necessary for the manufacturing of avanafil API. The MTPC manufacturing sites for the API (avanafil) and STENDRA tablets have been inspected by the U.S. authorities. We do not believe the results of those inspections will have an impact on MTPC’s ability to supply

STENDRA, or the approval, or the timing of approval, of SPEDRA in the EU. However, if MTPC is unable to receive approval from foreign regulators and maintain ongoing FDA or foreign regulatory compliance, or manufacture STENDRA's API or tablets in sufficient quantities to meet projected demand, the EU approval, the U.S. commercial launch, and future sales of STENDRA and SPEDRA will be adversely effected, which in turn could have a detrimental impact on our financial results and could impact our ability to enter into a collaboration for the commercialization of STENDRA and SPEDRA, if approved.

In August 2012, we entered into an amendment to our agreement with MTPC that permits us to manufacture the API and tablets for STENDRA ourselves or through third-party suppliers at any time, and we are required under the amendment to transition away from MTPC supply on or before June 2015. In February 2013, we entered into a technology transfer agreement with the manufacturing division of a global pharmaceutical company that can become the contract manufacturer, or CMO, for avanafil. Enabling this CMO to manufacture commercial supply in the future is a critical step in establishing a high quality, reliable supply chain. If this CMO is unable to effectively establish the supply chain, the commercialization of avanafil and any potential commercial agreements will be severely compromised. We currently do not have any manufacturing facilities and intend to continue to rely on third parties for the supply of the starting materials, API and tablets. However, we cannot be certain that we will be successful in entering into such agreements with other suppliers or that we will be able to obtain the necessary regulatory approvals for these suppliers in a timely manner or at all.

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We have in-licensed all or a portion of the rights to Qsymia and STENDRA from third parties. If we default on any of our material obligations under those licenses, we could lose rights to these drugs.

We have in-licensed and otherwise contracted for rights to Qsymia and STENDRA, and we may enter into similar licenses in the future. Under the relevant agreements, we are subject to commercialization, development, supply, sublicensing, royalty, insurance and other obligations. If we fail to comply with any of these requirements, or otherwise breach these license agreements, the licensor may have the right to terminate the license in whole or to terminate the exclusive nature of the license. Loss of any of these licenses or the exclusive rights provided therein could harm our financial condition and operating results.

In particular, we license the rights to avanafil from MTPC, and we have certain obligations to MTPC in connection with that license. For example, we are obligated to use our best commercial efforts to market STENDRA in the U.S. by December 31, 2013. Failure to launch STENDRA in the U.S. before this date may result in us losing our license to STENDRA in the U.S. and could adversely impact the commercial future of STENDRA outside of the U.S. In addition, we license the rights to Qsymia from Dr. Najarian. We believe we are in compliance with the material terms of our license agreements with MPTC and Dr. Najarian. However, there can be no assurance that this compliance will continue or that the licensors will not have a differing interpretation of the material terms of the agreements. If the license agreements were terminated early or if the terms of the licenses were contested for any reason, it would have a material adverse impact on our ability to commercialize products subject to these agreements, our ability to raise funds to finance our operations, our stock price and our overall financial condition. The monetary and disruption costs of any disputes involving our agreements could be significant despite rulings in our favor.

Our ability to gain market acceptance and generate revenues will be subject to a variety of risks, many of which are out of our control.

Qsymia and STENDRA may not gain market acceptance among physicians, patients, healthcare payors or the medical community. We believe that the degree of market acceptance and our ability to generate revenues from such drugs will depend on a number of factors, including:

- our ability to expand our distribution system for Qsymia from a certified home delivery pharmacy network to certified retail pharmacy locations;
- contraindications for Qsymia and STENDRA;
- competition and timing of market introduction of competitive drugs;
- efficacy and safety in the approved setting;
- prevalence and severity of any side effects, including those of the generic components of our drugs;
- emergence of previously unknown side effects, including those of the generic components of our drugs;
- results of any post-approval studies;
- potential or perceived advantages or disadvantages over alternative treatments including generics;
- the relative convenience and ease of administration and dosing schedule;
- the convenience and ease of purchasing the drug, as perceived by potential patients;
- strength of sales, marketing and distribution support;
- price both in absolute terms and relative to alternative treatments;
- the effectiveness of our or any future collaborators' sales and marketing strategies;
- the effect of current and future healthcare laws;
- availability of coverage and reimbursement from government and other third-party payors;

- the level of mandatory discounts required under federal and state healthcare programs and the volume of sales subject to those discounts;
- recommendations for prescribing physicians to complete certain educational programs for prescribing drugs;
- the willingness of patients to pay out of pocket in the absence of government or third-party coverage; and
- product labeling or product insert requirements of the FDA or other regulatory authorities.

Our drugs may fail to achieve market acceptance or generate significant revenue to achieve or sustain profitability. In addition, our efforts to educate the medical community and third-party payors on the safety and benefits of our drugs may require significant resources and may not be successful.

We are required to complete post-approval studies mandated by the FDA for both Qsymia and STENDRA, and such studies are expected to be costly and time consuming. If the results of these studies reveal unacceptable safety risks, Qsymia or STENDRA may be required to be withdrawn from the market.

As part of the approval for STENDRA, the FDA is requiring us to perform two post-approval clinical studies. The first is a randomized, double-blind, placebo-controlled, parallel group multicenter clinical trial on the effect of STENDRA on spermatogenesis in healthy adult males and males with mild erectile dysfunction, or ED. The other study is a double-blind, randomized, placebo-controlled, single-dose clinical trial to assess the effects of STENDRA on multiple parameters of vision, including, but not limited to, visual acuity, intraocular pressure, pupillometry, and color vision discrimination in healthy male subjects. If we are unable to complete these studies or the results of these studies reveal unacceptable safety risks, we could be required to perform additional tests and regulatory approval could even be withdrawn.

As part of the approval of Qsymia, we are required to conduct several post-marketing studies, including a study to assess the long-term treatment effect of Qsymia on the incidence of major adverse cardiovascular events in overweight and obese subjects with confirmed cardiovascular disease, studies to assess the safety and efficacy of Qsymia for weight management in obese pediatric and adolescent subjects, studies to assess drug utilization and pregnancy exposure and a study to assess renal function. The details of the cardiovascular outcomes study, known as ACQLAIM, have not yet been agreed upon with the FDA. This study could cost between $150.0 and $250.0 million and take as long as five to six years to complete. Enrollment in ACQLAIM is expected to begin in the fourth quarter of 2013. There can be no assurance that the FDA will not request or require us to provide additional information or undertake additional prospective studies or retrospective observational studies or that we will be able to agree with the FDA on the details of ACQLAIM.

In addition, at the FDA's request, we initiated a retrospective observational study utilizing existing electronic medical claims healthcare databases to review fetal outcomes, including the incidence of congenital malformations and oral cleft, in the offspring of women who received treatment with topiramate, for any condition or at any dose, or FORTRESS. We announced preliminary results from FORTRESS in December 2011. The results of the study are considered to be preliminary until the results are validated, which we expect to complete in the second half of 2013. If the results of this study reveal unacceptable safety risks for topiramate, we could be required to perform additional studies and regulatory approval could even be withdrawn.

In addition to these studies, the FDA may also require us to commit to perform other lengthy post-approval studies, for which we would have to expend significant additional resources, which could have an adverse effect on our operating results, financial condition and stock price. Failure to comply with the applicable regulatory requirements can result in, among other things, civil penalties, suspensions of regulatory approvals, operating restrictions and criminal prosecution. The restriction, suspension or revocation of regulatory approvals or any other failure to comply with regulatory requirements could have a material adverse effect on our business, financial condition, results of operations and stock price.

We depend upon consultants and outside contractors extensively in important roles within our company.

We outsource many key functions of our business and therefore rely on a substantial number of consultants, and we will need to be able to effectively manage these consultants to ensure that they successfully carry out their contractual obligations and meet expected deadlines. However, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our clinical trials or other development activities may be extended, delayed or terminated, and we may not be able to complete our post-approval clinical trials for Qsymia and STENDRA, obtain regulatory approval for our current and future investigational drug candidates, successfully commercialize our approved drugs or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants or find other competent outside contractors and consultants on commercially reasonable terms, or at all.

Qsymia is a combination of two active ingredient drug products approved individually by the FDA that are commercially available and marketed by other companies, although the specific dose strengths and formulation (extended-release vs. immediate-release) would differ. As a result, Qsymia may be subject to substitution by prescribing physicians with individual drugs contained in the Qsymia formulation, which would adversely affect our business.

Although Qsymia is a once-a-day, proprietary extended-release formulation, each of the approved APIs (phentermine and topiramate extended-release) that is combined to produce Qsymia is commercially available as drug products at prices that together are lower than the price at which we sell Qsymia. In addition, the distribution and sale of these drug products is not limited under a REMS program, as is the case with Qsymia. Further, the individual drugs contained in the Qsymia formulation are available in retail pharmacies and neither has a Pregnancy Category X, which is used to indicate that the risks involved in the use of the drug in pregnant women clearly outweigh potential benefits, as is the case with Qsymia. We cannot be sure that physicians will view Qsymia as sufficiently superior to a treatment regimen of Qsymia's individual APIs to justify the significantly higher cost for Qsymia, and they may prescribe the individual generic drugs already approved and marketed by other companies instead of our combination drug. Although our U.S. and European patents contain composition, product formulation and method-of-use claims that we believe protect Qsymia, these patents may be ineffective or impractical to prevent physicians from prescribing the individual generic constituents marketed by other companies instead of our combination drug. Phentermine and topiramate are currently available in generic form, although the doses used in Qsymia are currently not available and no extended-release formulation of topiramate is currently available. In addition, topiramate is not approved for obesity treatment, and phentermine is only approved for short-term treatment of obesity. However, because the price of Qsymia is significantly higher than the prices of the individual components as marketed by other companies, physicians may have a greater incentive to write prescriptions for the individual components outside of their approved indication, instead of for our combination drug, and this may limit how we price or market Qsymia. Similar concerns could also limit the reimbursement amounts private health insurers or

government agencies in the U.S. are prepared to pay for Qsymia, which could also limit market and patient acceptance of our drug and could negatively impact our revenues.

In many regions and countries where we may plan to market Qsymia, the pricing of reimbursed prescription drugs is controlled by the government or regulatory agencies. The government or regulatory agencies in these countries could determine that the pricing for Qsymia should be based on prices for its APIs when sold separately, rather than allowing us to market Qsymia at a premium as a new drug.

If we become subject to product liability claims, we may be required to pay damages that exceed our insurance coverage.

Qsymia and STENDRA, like all pharmaceutical products, are subject to heightened risk for product liability claims due to inherent potential side effects. For example, because topiramate, a component of Qsymia, may increase the risk of congenital malformation in infants exposed to topiramate during the first trimester of pregnancy and also may increase the risk of suicidal thoughts and behavior, such risks may be associated with Qsymia as well. Other potential risks involving Qsymia may include, but are not limited to, an increase in resting heart rate, acute angle closure glaucoma, cognitive and psychiatric adverse events, metabolic acidosis, an increase in serum creatinine, hypoglycemia in patients with type 2 diabetes, kidney stone formation, decreased sweating and hypokalemia, or lower-than-normal amount of potassium in the blood.

Although we have obtained product liability insurance coverage for Qsymia, we may be unable to maintain this product liability coverage for Qsymia or any other of our approved drugs in amounts or scope sufficient to provide us with adequate coverage against all potential risks. A product liability claim in excess of, or excluded from, our insurance coverage would have to be paid out of cash reserves and could have a material adverse effect upon our business, financial condition and results of operations. Product liability insurance is expensive, difficult to maintain, and current or increased coverage may not be available on acceptable terms, if at all.

In addition, we develop, test, and manufacture through third parties, approved drugs and future investigational drug candidates that are used by humans. We face an inherent risk of product liability exposure related to the testing of our approved drugs and investigational drug candidates in clinical trials. An individual may bring a liability claim against us if one of our approved drugs or future investigational drug candidates causes, or merely appears to have caused, an injury.

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If we cannot successfully defend ourselves against a product liability claim, whether involving Qsymia, STENDRA or a future investigational drug candidate, we may incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- injury to our reputation;
- withdrawal of clinical trial patients;
- costs of defending the claim and/or related litigation;
- cost of any potential adverse verdict;
- substantial monetary awards to patients or other claimants; and
- the inability to commercialize our drugs.

Damages awarded in a product liability action could be substantial and could have a negative impact on our financial condition. Whether or not we were ultimately successful in product liability litigation, such litigation would consume substantial amounts of our financial and managerial resources, and might result in adverse publicity, all of which would impair our business. In addition, product liability claims could result in an FDA investigation of the safety or efficacy of our product, our third-party manufacturing processes and facilities, or our marketing programs. An FDA investigation could also potentially lead to a recall of our products or more serious enforcement actions, limitations on the indications for which they may be used, or suspension or withdrawal of approval.

The markets in which we operate are highly competitive and we may be unable to compete successfully against new entrants or established companies.

Competition in the pharmaceutical and medical products industries is intense and is characterized by costly and extensive research efforts and rapid technological progress. We are aware of several pharmaceutical companies also actively engaged in the development of therapies for the treatment of obesity, diabetes and sexual health and medical device companies for the treatment of sleep apnea. Many of these companies have substantially greater research and development capabilities as well as substantially greater marketing, financial and human resources than we do. Some of the drugs which may compete with Qsymia may not have a REMS requirement and the accompanying complexities such a requirement presents. Our competitors may develop technologies and products that are more effective than those we are currently marketing or researching and developing. Such developments could render Qsymia and STENDRA less competitive or possibly obsolete. We are also competing with respect to marketing capabilities and manufacturing efficiency, areas in which we have limited experience.

Qsymia for the treatment of chronic weight management competes with several approved anti-obesity drugs including, Belviq® (lorcaserin), Arena Pharmaceutical's approved anti-obesity compound to be marketed by Eisai Inc., Eisai Co., Ltd.'s U.S. subsidiary; Xenical (orlistat), marketed by Roche; alli®, the over-the-counter version of orlistat, marketed by GlaxoSmithKline; and Suprenza (phentermine hydrochloride), marketed by Akrimax Pharmaceuticals, LCL. In addition, Orexigen Therapeutics, Inc., or Orexigen, has an investigational drug in late stage testing, Contrave®, which, according to Orexigen, could be approved and on the market in 2014. Contrave would be marketed by Takeda Pharmaceutical Company Limited.

There are also several drugs in development for obesity including an investigational drug candidate, liraglutide, in Phase 3 clinical trials being developed by Novo Nordisk A/S. Victoza® (liraglutide) is approved by the FDA for the treatment of type 2 diabetes and also is being developed for the treatment of obesity. In addition, there are several other investigational drug candidates in Phase 2 clinical trials. There are also a number of generic pharmaceutical drugs that are prescribed for obesity, predominantly phentermine. Phentermine is sold at much lower prices than we charge for Qsymia and is

available in retail pharmacies. The availability of branded prescription drugs, generic drugs and over-the-counter drugs could limit the demand for, and the price we are able to charge for, Qsymia.

We also may face competition from the off-label use of the generic components in our drugs. In particular, it is possible that patients will seek to acquire phentermine and topiramate, the generic components of Qsymia. Neither of these generic components has a REMS program and both are available at retail pharmacies. Although the dose strength of these generic components has not been approved by the FDA for use in the treatment of obesity, the off-label use of the generic components in the U.S. or the importation of the generic components from foreign markets could adversely affect the commercial potential for our drugs and adversely affect our overall business, financial conditions and results of operations.

There are also surgical approaches to treat severe obesity that are becoming increasingly accepted. Two of the most well established surgical procedures are gastric bypass surgery and adjustable gastric banding, or lap bands. In February 2011, the FDA approved the use of a lap band in patients with a BMI of 30 (reduced from 35) with comorbidities. The lowering of the BMI requirement will make more obese patients eligible for lap band surgery. In addition, other potential approaches that utilize various implantable devices or surgical tools are in development. Some of these approaches are in late stage development and may be approved for marketing.

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We anticipate that STENDRA (avanafil) for the treatment of erectile dysfunction will compete with PDE5 inhibitors in the form of oral medications including Viagra® (sildenafil citrate), marketed by Pfizer, Inc.; Cialis® (tadalafil), marketed by Eli Lilly and Company; Levitra® (vardenafil), co-marketed by GlaxoSmithKline plc and Schering-Plough Corporation in the U.S.; and STAXYN™ (vardenafil in an oral disintegrating tablet, or ODT), co-marketed by GlaxoSmithKline plc and Merck & Co., Inc.

As patents for the three major PDE5 inhibitors, sildenafil citrate, tadalafil and vardenafil, expire beginning in 2017, we anticipate that generic PDE5 inhibitors will enter the market. Generic PDE5 inhibitors would likely be sold at lower prices and may reduce the demand for STENDRA especially at the prices we would be required to charge for STENDRA to cover our manufacturing and other costs. In addition, PDE5 inhibitors are in various stages of development by other companies. Warner-Chilcott plc has licensed the U.S. rights to udenafil, a PDE5 inhibitor from Dong-A Pharmaceutical. Warner-Chilcott continues Phase 3 development of this compound. Other treatments for ED exist, such as needle injection therapies, vacuum constriction devices and penile implants, and the manufacturers of these products will most likely continue to develop or improve these therapies.

Qsymia and STENDRA may also face challenges and competition from newly developed generic products. Under the U.S. Drug Price Competition and Patent Term Restoration Act of 1984, known as the Hatch-Waxman Act, newly approved drugs and indications may benefit from a statutory period of non-patent marketing exclusivity. The Hatch-Waxman Act stimulates competition by providing incentives to generic pharmaceutical manufacturers to introduce non-infringing forms of patented pharmaceutical products and to challenge patents on branded pharmaceutical products. If we are unsuccessful at challenging an Abbreviated New Drug Application, or ANDA, filed pursuant to the Hatch-Waxman Act, a generic version of Qsymia or STENDRA may be launched, which would harm our business.

New developments, including the development of other drug technologies and methods of preventing the incidence of disease, occur in the pharmaceutical and medical technology industries at a rapid pace. These developments may render our drugs and future investigational drug candidates obsolete or noncompetitive. Compared to us, many of our potential competitors have substantially greater:

- research and development resources, including personnel and technology;
- regulatory experience;
- investigational drug candidate development and clinical trial experience;
- experience and expertise in exploitation of intellectual property rights; and
- access to strategic partners and capital resources.

As a result of these factors, our competitors may obtain regulatory approval of their products more rapidly than we or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our investigational drug candidates. Our competitors may also develop drugs or surgical approaches that are more effective, more useful and less costly than ours and may also be more successful in manufacturing and marketing their products. In addition, our competitors may be more effective in commercializing their products. We currently outsource our manufacturing and therefore rely on third parties for that competitive expertise. There can be no assurance that we will be able to develop or contract for these capabilities on acceptable economic terms, or at all.

We may participate in new partnerships and other strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management.

From time to time we consider strategic transactions, such as out-licensing or in-licensing of compounds or technologies, acquisitions of companies and asset purchases. Additional potential transactions we may consider include a variety of different business arrangements, including strategic partnerships, joint ventures, spin-offs, restructurings, divestitures, business combinations and investments. In addition, another entity may pursue us as an acquisition target. Any such transactions may require us to incur non-recurring or other charges, may increase our near and long-term expenditures and may pose significant integration challenges, require additional expertise or disrupt our management or business, any of which could harm our operations and financial results.

As part of an effort to enter into significant transactions, we conduct business, legal and financial due diligence with the goal of identifying and evaluating material risks involved in the transaction. Despite our efforts, we ultimately may be unsuccessful in ascertaining or evaluating all such risks and, as a result, might not realize the expected benefits of the transaction. If we fail to realize the expected benefits from any transaction we may consummate, whether as a result of unidentified risks, integration difficulties, regulatory setbacks or other events, our business, results of operations and financial condition could be adversely affected.

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Our failure to successfully acquire, develop and market additional investigational drug candidates or approved drugs would impair our ability to grow.

As part of our growth strategy, we may acquire, in-license, develop and/or market additional products and investigational drug candidates. We have not in-licensed any new product candidates in several years. Because our internal research capabilities are limited, we may be dependent upon pharmaceutical and biotechnology companies, academic scientists and other researchers to sell or license products or technology to us. The success of this strategy depends partly upon our ability to identify, select and acquire promising pharmaceutical investigational drug candidates and products.

The process of proposing, negotiating and implementing a license or acquisition of an investigational drug candidate or approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing and sales resources, may compete with us for the license or acquisition of investigational drug candidates and approved products. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses and technologies and integrate them into our current infrastructure. Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. We may not be able to acquire the rights to additional investigational drug candidates on terms that we find acceptable, or at all.

In addition, future acquisitions may entail numerous operational and financial risks, including:

- exposure to unknown liabilities;
- disruption of our business and diversion of our management's time and attention to develop acquired products or technologies;
- incurrence of substantial debt or dilutive issuances of securities to pay for acquisitions;
- higher than expected acquisition, integration and maintenance costs;
- increased amortization expenses;
- difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to retain key employees of any acquired businesses.

Further, any investigational drug candidate that we acquire may require additional development efforts prior to commercial sale, including extensive clinical testing and obtaining approval by the FDA and applicable foreign regulatory authorities. All investigational drug candidates are prone to certain failures that are relatively common in the field of drug development, including the possibility that an investigational drug candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot be certain that any drugs that we develop or approved products that we may acquire will be commercialized profitably or achieve market acceptance.

If we fail to retain our key personnel and hire, train and retain qualified employees, we may not be able to compete effectively, which could result in reduced revenues or delays in the development of our investigational drug candidates or commercialization of our approved drugs.

Our success is highly dependent upon the skills of a limited number of key management personnel. To reach our business objectives, we will need to retain and hire qualified personnel in the areas of manufacturing, commercial operations, research and development, regulatory and legal affairs, business development, clinical trial design, execution and analysis, and pre-clinical testing. There can be no assurance that we will be able to hire or retain such personnel, as we must compete with other companies, academic institutions, government entities and other agencies. The loss of any of our key personnel or the failure to attract or retain necessary new employees could have an adverse effect on our research programs, investigational drug candidate development, approved drug commercialization efforts and business operations.

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We rely on third parties and collaborative partners to manufacture sufficient quantities of compounds within product specifications as required by regulatory agencies for use in our pre-clinical and clinical trials and commercial operations and an interruption to this service may harm our business.

We do not have the ability to manufacture the materials we use in our pre-clinical and clinical trials and commercial operations. Rather, we rely on various third parties to manufacture these materials and there may be long lead times to obtain materials. There can be no assurance that we will be able to identify, qualify and obtain prior regulatory approval for additional sources of clinical materials. If interruptions in this supply occur for any reason, including a decision by the third parties to discontinue manufacturing, technical difficulties, labor disputes, natural or other disasters, or a failure of the third parties to follow regulations, we may not be able to obtain regulatory approvals for our investigational drug candidates and may not be able to successfully commercialize these investigational drug candidates or our approved drugs.

Our third-party manufacturers and collaborative partners, may encounter delays and problems in manufacturing our investigational drug candidates or approved drugs for a variety of reasons, including accidents during operation, failure of equipment, delays in receiving materials, natural or other disasters, political or governmental changes, or other factors inherent in operating complex manufacturing facilities. Supply chain management is difficult. Commercially available starting materials, reagents, excipients, and other materials may become scarce, more expensive to procure, or not meet quality standards, and we may not be able to obtain favorable terms in agreements with subcontractors. Our third-party manufacturers, may not be able to operate manufacturing facilities in a cost-effective manner or in a time frame that is consistent with our expected future manufacturing needs. If our third-party manufacturers, cease or interrupt production or if our third-party manufacturers and other service providers fail to supply materials, products or services to us

for any reason, such interruption could delay progress on our programs, or interrupt the commercial supply, with the potential for additional costs and lost revenues. If this were to occur, we may also need to seek alternative means to fulfill our manufacturing needs.

For example, Catalent Pharma Solutions, LLC, or Catalent, supplied the product for the Phase 3 program for Qsymia and is our sole source of clinical and commercial supplies for Qsymia. Catalent has been successful in validating the commercial manufacturing process for Qsymia at an initial scale, which has been able to support the launch of Qsymia in the U.S. market. While Catalent has significant experience in commercial scale manufacturing, there is no assurance that Catalent will be successful in increasing the scale of the initial Qsymia manufacturing process, should the market demand for Qsymia expand beyond the level supportable by the current validated manufacturing process. Such a failure by Catalent to further scale up the commercial manufacturing process for Qsymia could have a material adverse impact on our ability to realize commercial success with Qsymia in the U.S. market, and have a material adverse impact on our plan, market price of our common stock and financial condition.

In the case of STENDRA, we currently rely on MTPC to supply the API (avanafil) and the tablets for STENDRA. MTPC is responsible for all aspects of manufacture, including obtaining the starting materials for the production of API. If MTPC is unable to manufacture the API for STENDRA or tablets in sufficient quantities to meet projected demand future sales of STENDRA could be adversely effected, which in turn could have a detrimental impact on our financial results and could impact our ability to enter into a collaboration for the commercialization of STENDRA.

In August 2012, we entered into an amendment to our agreement with MTPC that permits us to manufacture the API and tablets for avanafil ourselves or through third parties. According to the amendment, the transition of manufacturing from MTPC must occur on or before June 2015. The transfer of technology to, and qualification of, a new supplier is expensive, time consuming and logistically complicated. The technology transfer needed for this transition is highly dependent on the cooperation of MTPC and its current suppliers. If MTPC, or its current suppliers, is unable to effectively transfer the technology or supply on commercially reasonable terms, the approvability, partnerability and commercial success of STENDRA could be adversely impacted. In February 2013, we entered into a technology transfer agreement with the manufacturing division of a global pharmaceutical company that can become the contract manufacturer, or CMO, for avanafil. Enabling this CMO to manufacture commercial supply in the future is a critical step in establishing a high quality, reliable supply chain. If this CMO is unable to effectively establish the supply chain, the commercialization of avanafil and any potential commercial agreements will be severely compromised. Any future manufacturing sites would need to be inspected by the U.S. and EU authorities, and any failure of such manufacturing sites to receive approval from FDA or foreign authorities, obtain and maintain ongoing FDA or foreign regulatory compliance, or manufacture avanafil API or STENDRA tablets in expected quantities, could adversely affect future sales of STENDRA, which in turn could have a detrimental impact on our financial results and could impact our ability to enter into a collaboration for the commercialization of STENDRA.

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We rely on third parties to maintain appropriate levels of confidentiality of the data compiled during clinical, pre-clinical and retrospective observational studies and trials.

We seek to maintain the confidential nature of our confidential information through contractual provisions in our agreements with third parties, including our agreements with clinical research organizations, or CROs, that manage our clinical studies for our investigational drug candidates. These CROs may fail to comply with their obligations of confidentiality or may be required as a matter of law to disclose our confidential information. As the success of our clinical studies depends in large part on our confidential information remaining confidential prior to, during and after a clinical study, any disclosure could have a material adverse effect on the outcome of a clinical study, our business, financial condition and results of operations.

If we fail to comply with applicable healthcare regulations, we could face substantial penalties and our business, operations and financial condition could be adversely affected.

Even though we do not bill directly to Medicare, Medicaid or other third-party payors, certain federal and state healthcare laws and regulations pertaining to fraud and abuse are and will be applicable to our business. The regulations that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Law, which prohibits, among other things, knowingly or willingly offering, paying, soliciting or receiving remuneration, directly or indirectly, to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any health care items or service reimbursable under federal healthcare programs such as Medicare and Medicaid. Further, the Affordable Care Act, among other things, amends the intent requirement of the federal anti-kickback statute. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. In addition, the Affordable Care Act provides that the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the false claims statutes. This statute has been interpreted to apply to arrangements between pharmaceutical companies on one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common manufacturer business arrangements and activities from prosecution, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations of our products may be subject to scrutiny if they do not qualify for an exemption or safe harbor. We seek to comply with the exemptions and safe harbors whenever possible, but our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability;

- the federal False Claims Laws, which prohibits, among other things, individuals or entities from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, or causing to be made, a false statement to get a false claim paid. Many pharmaceutical and other healthcare companies have been investigated and have reached substantial financial settlements with the federal government under the False Claims Act for a variety of alleged improper marketing activities, including providing free product to customers with the expectation that the customers would bill federal programs for the product; providing consulting fees, grants, free travel, and other benefits to physicians to induce them to prescribe the company’s products; and inflating prices reported to private price publication services, which are used to set drug payment rates under government healthcare programs. In addition, in recent years the government has pursued False Claims Act cases against a number of pharmaceutical companies for causing false claims to be submitted as a result of the marketing of their products for unapproved, and thus non-reimbursable, uses. Pharmaceutical and other healthcare companies also are subject to other federal false claim laws, including federal criminal healthcare fraud and false statement statutes that extend to non-government health benefit programs;

- numerous federal and state laws, including state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, govern the collection, use and disclosure of personal information. Other countries also have, or are developing, laws

governing the collection, use and transmission of personal information. In addition, most healthcare providers who prescribe our product and from whom we obtain patient health information are subject to privacy and security requirements under the Health Insurance Portability and Accountability Act of 1996, or HIPAA. We are not a HIPAA covered entity and we do not operate as a business associate to any covered entities. Therefore, these privacy and security requirements do not apply to us. However, we could be subject to criminal penalties if we knowingly obtain individually identifiable health information from a covered entity in a manner that is not authorized or permitted by HIPAA or for aiding and abetting the violation of HIPAA. We are unable to predict whether our actions could be subject to prosecution in the event of an impermissible disclosure of health information to us. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues with the potential to affect our business, including

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recently enacted laws in a majority of states requiring security breach notification. These laws could create liability for us or increase our cost of doing business;

- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws that may apply to items or services reimbursed under Medicaid and other state programs or, in several states, apply regardless of the payor. Some state laws also require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products and to report gifts and payments to individual physicians in the states. Other states prohibit providing meals to prescribers or other marketing related activities. Still other states require the posting of information relating to clinical studies and their outcomes. In addition, California, Nevada, and Massachusetts require pharmaceutical companies to implement compliance programs or marketing codes of conduct. Additional states are considering or recently have considered similar proposals. Foreign governments often have similar regulations which we also will be subject to in those countries where we market and sell products; and

- the federal Physician Payment Sunshine Act will require extensive tracking of physician and teaching hospital payments, maintenance of a payments database, and public reporting of the payment data. Centers for Medicare and Medicaid Services, or CMS, recently issued a final rule implementing the Physician Payment Sunshine Act provisions and clarified the scope of the reporting obligations, as well as that manufacturers must begin tracking on August 1, 2013 and must report payment data to CMS by March 31, 2014.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from government healthcare programs, like Medicare and Medicaid, and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

Marketing activities for our approved drugs are subject to continued governmental regulation.

The FDA has the authority to impose significant restrictions, including REMS requirements, on approved products through regulations on advertising, promotional and distribution activities. After approval, if products are marketed in contradiction with FDA laws and regulations, the FDA may issue warning letters that require specific remedial measures to be taken, as well as an immediate cessation of the impermissible conduct resulting in adverse publicity. The FDA may also require that all future promotional materials receive prior agency review and approval before use. We intend to begin print direct-to-consumer advertising for Qsymia in the fourth quarter of 2013. In the second quarter of 2013, we plan to submit the print advertisements for review by the FDA. There can be no assurance that the FDA will find our print advertisements acceptable as submitted. Certain states have also adopted regulations and reporting requirements surrounding the promotion of pharmaceuticals. Qsymia and STENDRA are subject to these regulations. Failure to comply with state requirements may affect our ability to promote or sell pharmaceuticals drugs in certain states. This in turn could have a material adverse impact on our financial results and financial condition and could subject us to significant liability, including civil and administrative remedies as well as criminal sanctions.

We are subject to ongoing regulatory obligations and restrictions, which may result in significant expense and limit our ability to commercialize our drugs.

We are required to comply with extensive regulations for drug manufacturing, labeling, packaging, adverse event reporting, storage, distribution, advertising, promotion and record keeping in connection with the marketing of Qsymia and STENDRA. Regulatory approvals may also be subject to significant limitations on the indicated uses or marketing of the investigational drug candidates or to whom and how we may distribute our products. Even after FDA approval is obtained, the FDA may still impose significant restrictions on a drug's indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies. For example, the labeling approved for Qsymia includes restrictions on use, including recommendations for pregnancy testing, level of obesity and duration of treatment. We are subject to ongoing regulatory obligations and restrictions which may result in significant expense and limit our ability to commercialize Qsymia. The FDA has also required the distribution of a Medication Guide to patients outlining the increased risk of teratogenicity with fetal exposure and the possibility of suicidal thinking or behavior. In addition, the FDA has required a REMS that may act to limit access to the drug, reduce our revenues and/or increase our costs. The FDA may modify the Qsymia REMS in the future to be more or less restrictive.

Even if we receive FDA and other regulatory approvals, if we or others identify adverse side effects after any of our products are on the market, or if manufacturing problems occur, regulatory approval may be withdrawn and reformulation of our products, additional clinical trials, changes in labeling and additional marketing applications may be required, any of which could harm our business and cause our stock price to decline.

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We and our contract manufacturers are subject to significant regulation with respect to manufacturing of our products.

All of those involved in the preparation of a therapeutic drug for clinical trials or commercial sale, including our existing supply contract manufacturers, and clinical trial investigators, are subject to extensive regulation. Components of a finished drug product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with current Good Manufacturing Practices, or cGMP. These regulations govern quality control of the manufacturing processes and documentation policies and procedures, and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Our facilities and quality systems and the facilities and quality systems of our third-party contractors must be inspected routinely for compliance. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulation occurs independent of such an inspection or audit, we or the FDA may require remedial measures that may be costly and/or time consuming for us or a third party to implement and that may include the issuance of a warning letter, temporary or permanent suspension of a clinical trial or commercial sales, recalls, market withdrawals, seizures, or the temporary or permanent closure of a facility. Any such remedial measures would be imposed upon us or third parties with whom we contract until satisfactory cGMP compliance is achieved. The FDA could also impose civil penalties. We must also comply with similar regulatory requirements of foreign regulatory agencies.

We obtain the necessary raw materials and components for the manufacture of Qsymia and STENDRA as well as certain services, such as analytical testing packaging and labeling, from third parties. In particular, we rely on Catalent Pharma Solutions, LLC to supply Qsymia capsules and Packaging Coordinators, Inc., or PCI, for Qsymia packaging services. We and these suppliers and service providers are required to follow cGMP requirements and are subject to routine and unannounced inspections by the FDA and by state and foreign regulatory agencies for compliance with cGMP requirements and other applicable regulations. Upon inspection of these facilities, the FDA or foreign regulatory agencies may find the manufacturing process or facilities are not in compliance with cGMP requirements and other regulations. Because manufacturing processes are highly complex and are subject to a lengthy regulatory approval process, alternative qualified supply may not be available on a timely basis or at all. Difficulties, problems or delays in our suppliers and service providers' manufacturing and supply of raw materials, components and services could delay our clinical trials, increase our costs, damage our reputation and cause us to lose revenue or market share if we are unable to timely meet market demands.

In addition, we have an agreement with MTPC to supply the API and the tablets for STENDRA. The MTPC manufacturing sites have been inspected by the U.S. authorities. We do not believe the results of those inspections will have an impact on MTPC's ability to supply STENDRA, or the approval, or the timing of approval, of SPEDRA in the EU. However, if MTPC is unable to receive approval from foreign authorities, and maintain ongoing FDA or foreign regulatory compliance, or manufacture avanafil API or STENDRA tablets in sufficient quantities to meet projected demand, the EU approval, the U.S. commercial launch, and future sales of STENDRA will be adversely effected, which in turn could have a detrimental impact on our financial results and could impact our ability to enter into a collaboration for the commercialization of STENDRA. In August 2012, we entered into an amendment to our agreement with MTPC that permits us to manufacture the API and STENDRA tablets for avanafil ourselves or through third parties. According to the amendment, the transition of manufacturing from MTPC must occur on or before June 2015. The technology transfer needed for this transition is highly dependent on the cooperation of MTPC and its current suppliers. If MTPC, or its current suppliers, is unable to effectively transfer the technology or supply on commercially reasonable terms, the approvability, partnerability and commercial success of STENDRA could be adversely impacted. In February 2013, we entered into a technology transfer agreement with the manufacturing division of a global pharmaceutical company that can become the contract manufacturer, or CMO, for avanafil. The identification of this CMO is a critical step in establishing a high quality, reliable supply chain. If this CMO is unable to effectively establish the supply chain, the commercialization of avanafil and any potential commercial agreements will be severely compromised. Any future manufacturing sites would need to be inspected by the U.S. and EU authorities, and any failure of such manufacturing sites to receive approval from FDA or foreign authorities, obtain and maintain ongoing FDA or foreign regulatory compliance, or manufacture avanafil API or tablets in expected quantities, could adversely affect future sales of STENDRA, which in turn could have a detrimental impact on our financial results and could impact our ability to enter into a collaboration for the commercialization of STENDRA.

Any adverse changes in reimbursement procedures by government and other third-party payors may limit our ability to market and sell our approved drugs, or any future drugs, if approved or limit our product revenues and delay profitability.

In the U.S. and abroad, sales of pharmaceutical drugs are dependent, in part, on the availability of reimbursement to the consumer from third-party payors, such as government and private insurance plans. Third-party payors are increasingly challenging the prices charged for medical products and services. Some third-party payor benefit packages restrict reimbursement, charge co-pays to patients, or do not provide coverage for specific drugs or drug classes.

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In addition, certain healthcare providers are moving towards a managed care system in which such providers contract to provide comprehensive healthcare services, including prescription drugs, for a fixed cost per person. We are unable to predict the reimbursement policies employed by third-party healthcare payors.

The healthcare industry in the U.S. and abroad is undergoing fundamental changes that are the result of political, economic and regulatory influences. The levels of revenue and profitability of pharmaceutical companies may be affected by the continuing efforts of governmental and third-party payors to contain or reduce healthcare costs through various means. Reforms that have been and may be considered include mandated basic healthcare benefits, controls on healthcare spending through limitations on the increase in private health insurance premiums and the types of drugs eligible for reimbursement and Medicare and Medicaid spending, the creation of large insurance purchasing groups and fundamental changes to the healthcare delivery system. These proposals include measures that would limit or prohibit payments for some medical treatments or subject the pricing of drugs to government control and regulations changing the rebates we are required to provide. These changes could impact our ability to maximize revenues in the federal marketplace.

The Affordable Care Act substantially changed the way healthcare is financed by both governmental and private insurers, and could have a material adverse effect on our future business, cash flows, financial condition and results of operations, including by operation of the following provisions:

- Effective March 23, 2010, drug rebates are due on the utilization of Medicaid managed care organizations. This expanded eligibility affects rebate liability for that utilization.

- Effective January 1, 2011, pharmaceutical companies must provide a 50% discount on branded prescription drugs dispensed to beneficiaries within the Medicare Part D coverage gap or "donut hole," which is a funding gap that currently exists in the Medicare Part D prescription drug program. We currently do not anticipate coverage under Medicare Part D, but this could change in the future.

- Effective January 1, 2011, the U.S. Federal government must allocate an annual branded prescription drug fee among pharmaceutical manufacturers of branded prescription drugs based on the dollar value of their branded prescription drug sales to certain federal health care programs identified in the law. The Affordable Care Act determines an individual manufacturer's market share as the ratio of its aggregate sales of branded prescription drugs during the preceding calendar year as a percentage of the aggregate branded prescription drug sales for all covered manufacturers. Each individual pharmaceutical manufacturer will pay a prorated share of the branded prescription drug fee of $2.8 billion in 2013 (and set to increase in ensuing years) based on the dollar value of its branded prescription drug sales to certain federal programs identified in the law.

- Changes made by the Affordable Care Act are expected to result in the coverage of 32 million uninsured individuals through an expansion of the Medicaid program, and private sector coverage either through their employer or the new state-based Health Insurance Exchanges effective in 2014. In 2012, the Supreme Court of the United States heard challenges to the constitutionality of the individual mandate and the viability of certain provisions of the Affordable Care Act. The Supreme Court's decision upheld most of the Affordable Care Act and determined that requiring individuals to maintain "minimum essential" health insurance coverage or pay a penalty to the Internal Revenue Service was within Congress's constitutional taxing authority. However, the Supreme Court struck down a provision in the Affordable Act that penalized states that choose not to expand their Medicaid programs through an increase in the Medicaid eligibility income limit from a state's current eligibility levels to 133% of the federal poverty limit. As a result of the Supreme Court's ruling, it is unclear whether states will expand their Medicaid programs by raising the income limit to 133% of the federal poverty level and whether there will be more uninsured patients in 2014 than anticipated when Congress passed the Affordable Care Act. For each state that does not choose to expand its Medicaid program, there will be fewer insured patients overall, which could impact our sales, business and financial condition. We expect any Medicaid expansion to impact the number of adults in Medicaid more than children because many states have already set their eligibility criteria for children at or above the level designated in the Affordable Care Act. An increase in the proportion of patients who receive our drugs and who are covered by Medicaid could adversely affect our net sales.

Presently, uncertainty exists as many of the specific determinations necessary to implement the Affordable Care Act have yet to be decided and communicated to industry participants. At this time, we cannot predict the full impact of the Affordable Care Act, or the timing and impact of any future rules or regulations promulgated to implement the Affordable Care Act.

There can be no assurance that future healthcare legislation or other changes in the administration or interpretation of government healthcare or third-party reimbursement programs will not have a material adverse effect on us. Healthcare reform is also under consideration in other countries where we intend to market Qsymia.

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We expect to experience pricing and reimbursement pressures in connection with the sale of Qsymia, STENDRA and our investigational drug candidates, if approved, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative proposals. In addition, we may confront limitations in insurance coverage for Qsymia, STENDRA and our investigational drug candidates. For example, the Medicare program generally does not provide coverage for drugs used to treat erectile dysfunction or drugs used to treat obesity. Similarly, other insurers may determine that such products are not covered under their programs. If we fail to successfully secure and maintain reimbursement coverage for our investigational drug candidates or are significantly delayed in doing so, we will have difficulty achieving market acceptance of our investigational drug candidates and our business will be harmed. Congress has enacted healthcare reform and may enact further reform, which could adversely affect the pharmaceutical industry as a whole, and therefore could have a material adverse effect on our business.

Both of the active pharmaceutical ingredients in Qsymia, phentermine and topiramate, are available as generics and do not have a REMS requirement. The exact doses of the active ingredients in Qsymia are different than those currently available for the generic components. State pharmacy laws prohibit pharmacists from substituting drugs with differing doses and formulations. The safety and efficacy of Qsymia is dependent on the titration, dosing and formulation, which we believe could not be easily duplicated, if at all, with the use of generic substitutes. However, there can be no assurance that we will be able to provide for optimal reimbursement of Qsymia as a treatment for obesity or any other indication, if approved, from third-party payors or the U.S. government. Furthermore, there can be no assurance that healthcare providers would not actively seek to provide patients with generic versions of the active ingredients in Qsymia in order to treat obesity at a potential lower cost and outside of the REMS requirements.

Setbacks and consolidation in the pharmaceutical and biotechnology industries, and our or our collaborators' inability to obtain third-party coverage and adequate reimbursement, could make partnering more difficult and diminish our revenues.

Setbacks in the pharmaceutical and biotechnology industries, such as those caused by safety concerns relating to high-profile drugs like Avandia, Vioxx and Celebrex, or investigational drug candidates, as well as competition from generic drugs, litigation, and industry consolidation, may have an adverse effect on us. For example, pharmaceutical companies may be less willing to enter into new collaborations or continue existing collaborations if they are integrating a new operation as a result of a merger or acquisition or if their therapeutic areas of focus change following a merger. Moreover, our and our collaborators' ability to commercialize any of our approved drugs or future investigational drug candidates will depend in part on government regulation and the availability of coverage and adequate reimbursement from third-party payors, including private health insurers and government payors, such as the Medicaid and Medicare programs, increases in government-run, single-payor health insurance plans and compulsory licenses of drugs. Government and third-party payors are increasingly attempting to contain healthcare costs by limiting coverage and reimbursement levels for new drugs. Given the continuing discussion regarding the cost of healthcare, managed care, universal healthcare coverage and other healthcare issues, we cannot predict with certainty what additional healthcare initiatives, if any, will be implemented or the effect any future legislation or regulation will have on our business. These efforts may limit our commercial opportunities by reducing the amount a potential collaborator is willing to pay to license our programs or investigational drug candidates in the future due to a reduction in the potential revenues from drug sales. Adoption of legislation and regulations could limit pricing approvals for, and reimbursement of, drugs. A government or third-party payor decision not to approve pricing for, or provide adequate coverage and reimbursements of, our drugs could limit market acceptance of these drugs.

Our business and operations would suffer in the event of system failures.

Despite the implementation of security measures, our internal computer systems and those of our contract sales organization, or CSO, CROs, safety monitoring company and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, accidents, terrorism, war and telecommunication and electrical failures. While we have not experienced any such system failure, accident or security breach to date, if

such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our investigational drug candidate development programs and drug manufacturing operations. For example, the loss of clinical trial data from completed or ongoing clinical trials for our investigational drug candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach was to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our investigational drug candidates, or commercialization of our approved drugs, could be delayed. If we are unable to restore our information systems in the event of a systems failure, our communications, daily operations and the ability to develop our investigational drug candidates and approved drug commercialization efforts would be severely affected.

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Natural disasters or resource shortages could disrupt our investigational drug candidate development and approved drug commercialization efforts and adversely affect results.

Our ongoing or planned clinical trials and approved drug commercialization efforts could be delayed or disrupted indefinitely upon the occurrence of a natural disaster. For example, Hurricane Sandy in October 2012 has hindered our Qsymia sales efforts, the nature and extent of which is not yet known. In 2005, our clinical trials in the New Orleans area were interrupted by Hurricane Katrina. In addition, our offices are located in the San Francisco Bay Area near known earthquake fault zones and are therefore vulnerable to damage from earthquakes. In October 1989, a major earthquake in our area caused significant property damage and a number of fatalities. Our supplier of STENDRA is located in Japan near known earthquake fault zones and is vulnerable to damage from earthquakes and tsunamis. We are also vulnerable to damage from other disasters, such as power loss, fire, floods and similar events. If a significant disaster occurs, our ability to continue our operations could be seriously impaired and we may not have adequate insurance to cover any resulting losses. Any significant unrecoverable losses could seriously impair our operations and financial conditions.

Risks Relating to our Intellectual Property

Obtaining intellectual property rights is a complex process, and we may be unable to adequately protect our proprietary technologies.

We hold various patents and patent applications in the U.S. and abroad targeting obesity and morbidities related to obesity, including sleep apnea and diabetes, and sexual health, among other indications. The procedures for obtaining a patent in the U.S. and in most foreign countries are complex. These procedures require an analysis of the scientific technology related to the invention and many sophisticated legal issues. Consequently, the process for having our pending patent applications issue as patents will be difficult, complex and time consuming. We do not know when, or if, we will obtain additional patents for our technologies, or if the scope of the patents obtained will be sufficient to protect our investigational drug candidates or products, or be considered sufficient by parties reviewing our patent positions pursuant to a potential licensing or financing transaction.

In addition, even if our patent applications issue as patents, we cannot make assurances as to how much protection, if any, will be provided by these patents. Our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from practicing our technologies or from developing competing products. Others may independently develop similar or alternative technologies or design around our patented technologies or products. These companies would then be able to develop, manufacture and sell products that compete directly with our products. In that case, our revenues and operating results could decline.

Other entities may also challenge the validity or enforceability of our patents and patent applications in litigation or administrative proceedings. The sponsor of a generic application seeking to rely on one of our approved drug products as the reference listed drug must make one of several certifications regarding each listed patent. A “Paragraph III” certification is the sponsor’s statement that it will wait for the patent to expire before obtaining approval for its product. A “Paragraph IV” certification is a challenge to the patent; it is an assertion that the patent does not block approval of the later product, either because the patent is invalid or unenforceable or because the patent, even if valid, is not infringed by the new product. Once the FDA accepts for filing a generic application containing a Paragraph IV certification, the applicant must within 20 days provide notice to the reference listed drug, or RLD, NDA holder and patent owner that the application with patent challenge has been submitted, and provide the factual and legal basis for the applicant’s assertion that the patent is invalid or not infringed. If the NDA holder or patent owner file suit against the generic applicant for patent infringement within 45 days of receiving the Paragraph IV notice, the FDA is prohibited from approving the generic application for a period of 30 months from the date of receipt of the notice. If the RLD has new chemical entity exclusivity and the notice is given and suit filed during the fifth year of exclusivity, the 30-month stay does not begin until five years after the RLD approval. The FDA may approve the proposed product before the expiration of the 30-month stay if a court finds the patent invalid or not infringed or if the court shortens the period because the parties have failed to cooperate in expediting the litigation. If a competitor or a generic pharmaceutical provider successfully challenges our patents, the protection provided by these patents could be reduced or eliminated and our ability to commercialize any approved drugs would be at risk. In addition, if a competitor or generic manufacturer were to receive approval to sell a generic or follow-on version of one of our products, our approved product would become subject to increased competition and our revenues for that product would be adversely affected.

On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These changes include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The U.S. Patent Office has recently developed regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act have only recently become effective. Accordingly, it is too early to tell what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

We also may rely on trade secrets and other unpatented confidential information to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We seek to protect our trade secrets and other confidential information by entering into confidentiality agreements with employees, collaborators, vendors

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(including CROs and our CSO), consultants and, at times, with potential investors. Nevertheless, employees, collaborators, vendors, consultants or potential investors may still disclose or misuse our trade secrets and other confidential information, and we may not be able to meaningfully protect our trade secrets. In addition, others may independently develop substantially equivalent information or techniques or otherwise gain access to our trade secrets. Disclosure or misuse of our confidential information would harm our competitive position and could cause our revenues and operating results to decline.

If we believe that others have infringed or misappropriated our proprietary rights, we may need to institute legal action to protect our intellectual property rights. Such legal action may be expensive, and we may not be able to afford the costs of enforcing or defending our intellectual property rights against others.

We may be sued for infringing the intellectual property rights of others, which could be costly and result in delays or termination of our future research, development, manufacturing and sales activities.

Our commercial success also depends, in part, upon our ability to develop future investigational drug candidates, market and sell approved drugs and conduct our other research, development and commercialization activities without infringing or misappropriating the patents and other proprietary rights of others. There are many patents and patent applications owned by others that could be relevant to our business. For example, there are numerous U.S. and foreign issued patents and pending patent applications owned by others that are related to the therapeutic areas in which we have approved drugs or future investigational drug candidates as well as the therapeutic targets to which these drugs and candidates are directed. There are also numerous issued patents and patent applications covering chemical compounds or synthetic processes that may be necessary or useful to use in our research, development, manufacturing or commercialization activities. Because patent applications can take many years to issue, there may be currently pending applications, unknown to us, which may later result in issued patents that our approved drugs, future investigational drug candidates or technologies may infringe. There also may be existing patents, of which we are not aware, that our approved drugs, investigational drug candidates or technologies may infringe. Further, it is not always clear to industry participants, including us, which patents cover various types of products or methods. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. We cannot assure you that others holding any of these patents or patent applications will not assert infringement claims against us for damages or seek to enjoin our activities. If we are sued for patent infringement, we would need to demonstrate that our products or methods do not infringe the patent claims of the relevant patent and/or that the patent claims are invalid or unenforceable, and we may not be able to do this.

There can be no assurance that approved drugs or future investigational drug candidates do not or will not infringe on the patents or proprietary rights of others. In addition, third parties may already own or may obtain patents in the future and claim that use of our technologies infringes these patents.

If a person or entity files a legal action or administrative action against us, or our collaborators, claiming that our drug discovery, development, manufacturing or commercialization activities infringes a patent owned by the person or entity, we could incur substantial costs and diversion of the time and attention of management and technical personnel in defending ourselves against any such claims. Furthermore, parties making claims against us may be able to obtain injunctive or other equitable relief that could effectively block our ability to further develop, commercialize and sell any current or future approved drugs, and such claims could result in the award of substantial damages against us. In the event of a successful claim of infringement against us, we may be required to pay damages and obtain one or more licenses from third parties. We may not be able to obtain these licenses at a reasonable cost, if at all. In that case, we could encounter delays in product introductions while we attempt to develop alternative investigational drug candidates or be required to cease commercializing any affected current or future approved drugs and our operating results would be harmed.

Furthermore, because of the substantial amount of pre-trial document and witness discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, during the course of this kind of litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the trading price of our common stock.

We may face additional competition outside of the U.S. as a result of a lack of patent coverage in some territories and differences in patent prosecution and enforcement laws in foreign counties.

Filing, prosecuting, defending and enforcing patents on all of our drug discovery technologies and all of our approved drugs and potential investigational drug candidates throughout the world would be prohibitively expensive. While we have filed patent applications in many countries outside the U.S., and have obtained some patent coverage for approved drugs in certain foreign countries, we do not currently have widespread patent protection for these drugs outside the U.S. and have no protection in many foreign jurisdictions. Competitors may use our technologies to develop their own drugs in jurisdictions where we have not obtained patent protection. These drugs may compete with our approved drugs or future investigational drug candidates and may not be covered by any of our patent claims or other intellectual property rights.

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Even if international patent applications ultimately issue or receive approval, it is likely that the scope of protection provided by such patents will be different from, and possibly less than, the scope provided by our corresponding U.S. patents. The success of our international market opportunity is dependent upon the enforcement of patent rights in various other countries. A number of countries in which we have filed or intend to file patent applications have a history of weak enforcement and/or compulsory licensing of intellectual property rights. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the aggressive enforcement of patents and other intellectual property protection, particularly those relating to biotechnology and/or pharmaceuticals, which makes it difficult for us to stop the infringement of our patents. Even if we have patents issued in these jurisdictions, there can be no assurance that our patent rights will be sufficient to prevent generic competition or unauthorized use.

Attempting to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

Our failure to successfully acquire, develop and market additional investigational drug candidates or approved drugs would impair our ability to grow.

As part of our growth strategy, we may acquire, in-license, develop and/or market additional products and investigational drug candidates. Because our internal research capabilities are limited, we may be dependent upon pharmaceutical and biotechnology companies, academic scientists and other researchers to sell or license products or technology to us. The success of this strategy depends partly upon our ability to identify, select and acquire promising pharmaceutical investigational drug candidates and products.

The process of proposing, negotiating and implementing a license or acquisition of an investigational drug candidate or approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing and sales resources, may compete with us for the license or acquisition of investigational drug candidates and approved products. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses and technologies and integrate them into our current infrastructure. Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. We may not be able to acquire the rights to additional investigational drug candidates on terms that we find acceptable, or at all.

In addition, future acquisitions may entail numerous operational and financial risks, including:

- exposure to unknown liabilities;
- disruption of our business and diversion of our management's time and attention to develop acquired products or technologies;
- incurrence of substantial debt or dilutive issuances of securities to pay for acquisitions;
- higher than expected acquisition, integration and maintenance costs;
- increased amortization expenses;
- difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to retain key employees of any acquired businesses.

Further, any investigational drug candidate that we acquire may require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All investigational drug candidates are prone to risks of failure typical of pharmaceutical investigational drug candidate development, including the possibility that an investigational drug candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot provide assurance that any drugs that we develop or approved products that we may acquire will be commercialized profitably or achieve market acceptance.

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Risks Relating to our Financial Position and Need for Financing

We may require additional capital for our future operating plans, and we may not be able to secure the requisite additional funding on acceptable terms, or at all, which would force us to delay, reduce or eliminate commercialization efforts.

We expect that our existing capital resources combined with future anticipated cash flows will be sufficient to support our operating activities at least through the first quarter of 2014. Should product sales be significantly less than internal expectations, we would need to raise additional capital to support operating activities through 2014 and beyond. However, we anticipate that we will be required to obtain additional financing to fund our commercialization efforts, additional clinical studies for approved products and the development of our research and development pipeline in future periods. Our future capital requirements will depend upon numerous factors, including:

- the cost required to maintain the certified home delivery pharmacy network and REMS program for Qsymia, including a substantial cost to expand into certified retail pharmacy locations;
- our ability to successfully commercialize Qsymia in the U.S. on a timely basis;
- our ability to successfully commercialize through marketing partnerships for STENDRA in the U.S. and SPEDRA, if approved, in our territories outside the U.S.;
- the cost, timing and outcome of the post-approval clinical studies the FDA has required us to perform as part of the approval for STENDRA and Qsymia;
- the progress and costs of our research and development programs;
- the scope, timing, costs and results of pre-clinical, clinical and retrospective observational studies and trials;
- the cost of access to electronic records and databases that allow for retrospective observational studies;
- patient recruitment and enrollment in future clinical trials;
- the costs involved in seeking regulatory approvals for future drug candidates;
- the costs involved in filing and pursuing patent applications, defending and enforcing patent claims;
- the establishment of collaborations, sublicenses and strategic alliances and the related costs, including milestone payments;
- the costs involved in establishing a commercial operation and in launching a product without a partner;
- the cost of manufacturing and commercialization activities and arrangements;

- the level of resources devoted to our future sales and marketing capabilities;
- the cost, timing and outcome of litigation, if any;
- the impact of healthcare reform, if any, imposed by the federal government;
- the activities of competitors; and
- maintaining compliance to our agreement with BioPharma and maintaining our ability to receive an additional $60 million at a secondary closing.

Future capital requirements will also depend on the extent to which we acquire or invest in additional complementary businesses, products and technologies. We currently have no commitments or agreements relating to any of these types of transactions.

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To obtain additional capital when needed, we will evaluate alternative financing sources, including, but not limited to, the issuance of equity or debt securities, corporate alliances, joint ventures and licensing agreements. However, there can be no assurance that funding will be available on favorable terms, if at all. We are continually evaluating our existing portfolio and we may choose to divest, sell or spin-off one or more of our drugs and/or investigational drug candidates at any time. We cannot assure you that our drugs will generate revenues sufficient to enable us to earn a profit. If we are unable to obtain additional capital, management may be required to explore alternatives to reduce cash used by operating activities, including the termination of research and development efforts that may appear to be promising to us, the sale of certain assets and the reduction in overall operating activities. If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate one or more of our development programs or our commercialization efforts.

Raising additional funds by issuing securities will cause dilution to existing stockholders and raising funds through lending and licensing arrangements may restrict our operations or require us to relinquish proprietary rights.

To the extent that we raise additional capital by issuing equity securities, our existing stockholders' ownership will be diluted. We have financed our operations, and we expect to continue to finance our operations, primarily by issuing and selling our common stock. For example, in March 2012, we sold 9,000,000 shares of our common stock resulting in net proceeds to us of approximately $192.0 million. Moreover, any issuances by us of equity securities may be at or below the prevailing market price of our common stock and in any event may have a dilutive impact on your ownership interest, which could cause the market price of our common stock to decline. To raise additional capital, we may choose to issue additional securities at any time and at any price.

We may also raise additional capital through the incurrence of debt, and the holders of any debt we may issue would have rights superior to our stockholders' rights in the event we are not successful and are forced to seek the protection of bankruptcy laws. In addition, debt financing typically contains covenants that restrict operating activities. For example, on March 25, 2013, we entered into the Purchase and Sale Agreement with BioPharma, which provides for the purchase of a debt-like instrument. Under the BioPharma Agreement, we received $50 million, less $1.1 million in funding and facility payments, on April 9, 2013. To secure our obligations in connection with the BioPharma Agreement, we granted BioPharma a security interest to certain of our assets. During the term of the BioPharma Agreement, we are required to use commercially reasonable efforts to undertake certain obligations and activities to develop, market, promote and commercialize Qsymia and maximize net sales of Qsymia. Additionally, during the term of the BioPharma Agreement we may not (i) incur indebtedness greater than a specified amount, (ii) pay a dividend or other cash distribution on our capital stock, unless we have cash and cash equivalents in excess of a specified amount, (iii) amend or restate our certificate of incorporation or bylaws unless such amendments or restatements do not affect BioPharma's interests under the BioPharma Agreement, (iv) encumber the collateral, or (v) abandon certain patent rights, in each case without the consent of BioPharma. Any future debt financing we enter into may involve similar or more onerous covenants that restrict our operations.

If we raise additional capital through collaboration, licensing or other similar arrangements, it may be necessary to relinquish potentially valuable rights to our drugs or future investigational drug candidates, potential products or proprietary technologies, or grant licenses on terms that are not favorable to us. If adequate funds are not available, our ability to achieve profitability or to respond to competitive pressures would be significantly limited and we may be required to delay, significantly curtail or eliminate the commercialization of one or more of our approved drugs or the development of one or more of our future investigational drug candidates.

The investment of our cash balance and our available-for-sale securities are subject to risks which may cause losses and affect the liquidity of these investments.

At March 31, 2013, we had $90.6 million in cash and cash equivalents and $59.7 million in available-for-sale securities. While at March 31, 2013, our excess cash balances were invested in money market and U.S. Treasury securities, our investment policy as approved by our Board of Directors, also provides for investments in debt securities of U.S. government agencies, corporate debt securities and asset-backed securities. Our investment policy has the primary investment objectives of preservation of principal. However, there may be times when certain of the securities in our portfolio will fall below the credit ratings required in the policy. Although the U.S. Congress was able to resolve the debt ceiling issue in time to avoid default, the major credit rating agencies have expressed their ongoing concern about the high levels of debt that the U.S. government has taken on. Standard & Poor's announced that it had revised its outlook on the long-term credit rating of the U.S. to negative, which could affect the trading market for U.S. government securities. These factors could impact the liquidity or valuation of our available-for-sale securities, all of which were invested in U.S. treasury securities as of March 31, 2013. If those securities are downgraded or impaired we would experience losses in the value of our portfolio which would have an adverse effect on our results of operations, liquidity and financial condition. An investment in money market mutual funds is not insured or guaranteed by the Federal Deposit Insurance Corporation or any other government agency. Although money market mutual funds seek to preserve the value of the investment at $1 per share, it is possible to lose money by investing in money market mutual funds.

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Our involvement in securities related class action litigation could divert our resources and management's attention and harm our business.

The stock markets have from time to time experienced significant price and volume fluctuations that have affected the market prices for the common stock of pharmaceutical companies. These broad market fluctuations may cause the market price of our common stock to decline. In the past, securities related class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and biopharmaceutical companies often experience significant stock price volatility in connection with their investigational drug candidate development programs, the review of marketing applications by regulatory authorities and the commercial launch of newly approved drugs. We are a defendant in federal and consolidated state shareholder derivative lawsuits. These securities related class action lawsuits generally allege that we and our officers misled the investing public regarding the safety and efficacy of Qsymia and the prospects for the FDA's approval of the Qsymia NDA as a treatment for obesity. Securities related class action litigation often is expensive and diverts management's attention and our financial resources, which could adversely affect our business. For example, following the Court's granting of our prior motion to dismiss with leave to amend, on September 27, 2012, the U.S. District Court for the Northern District of California granted, with prejudice, our motion to dismiss the putative class action lawsuit captioned *Kovtun v. Vivus, Inc., et al.*, Case No. 4:10-CV-04957-PJH. Despite the granting of the prior two motions to dismiss, on October 26, 2012, plaintiff filed a Notice of Appeal to the U.S. Court of Appeals for the Ninth Circuit. Plaintiff filed his opening appellate brief on February 19, 2013, and defendants filed their answering brief on April 11, 2013. Briefing is expected to continue into May 2013, after which the Court of Appeals may request oral argument.

We have an accumulated deficit of $539.7 million as of March 31, 2013, and we may continue to incur substantial operating losses for the future.

We have generated a cumulative net loss of $539.7 million for the period from our inception through March 31, 2013, and we anticipate losses in future years due to continued investment in our research and development programs. There can be no assurance that we will be able to achieve or maintain profitability or that we will be successful in the future.

Our ability to utilize our net operating loss carryforwards and other tax attributes to offset future taxable income may be limited.

As of December 31, 2012, we had approximately $449.0 million and $118.1 million of net operating loss, or NOL, carryforwards with which to offset our future taxable income for federal and state income tax reporting purposes, respectively. We used $121.2 million federal and $32.2 million state NOLs to offset our year ended December 31, 2007 federal and state taxable income, which included the $150.0 million in gain recognized from our sale of Evamist. Utilization of our net operating loss and tax credit carryforwards, or Tax Attributes, may be subject to substantial annual limitations provided by the Internal Revenue Code and similar state provisions to the extent certain ownership changes are deemed to occur. Such an annual limitation could result in the expiration of the Tax Attributes before utilization. The Tax Attributes reflected above have not been reduced by any limitations. To the extent it is determined upon completion of the analysis that such limitations do apply, we will adjust the Tax Attributes accordingly. We face the risk that our ability to use our Tax Attributes will be substantially restricted if we undergo an "ownership change" as defined in Section 382 of the U.S. Internal Revenue Code, or Section 382. An ownership change under Section 382 would occur if "5-percent shareholders," within the meaning of Section 382, collectively increased their ownership in the Company by more than fifty percentage points over a rolling three-year period. There can be no assurance that a Section 382 ownership change has not occurred or will not occur in the future.

We may have exposure to additional tax liabilities that could negatively impact our income tax provision, net income, and cash flow.

We are subject to income taxes and other taxes in both the U.S. and the foreign jurisdictions in which we currently operate or have historically operated. The determination of our worldwide provision for income taxes and current and deferred tax assets and liabilities requires judgment and estimation. In the ordinary course of our business, there are many transactions and calculations where the ultimate tax determination is uncertain. We are subject to regular review and audit by U.S. tax authorities as well as subject to the prospective and retrospective effects of changing tax regulations and legislation. Although we believe our tax estimates are reasonable, the ultimate tax outcome may materially differ from the tax amounts recorded in our consolidated financial statements and may materially affect our income tax provision, net income, or cash flows in the period or periods for which such determination and settlement is made.

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Risks Relating to an Investment in our Common Stock

Our stock price has been and may continue to be volatile.

The market price of our common stock has been volatile and is likely to continue to be so. The market price of our common stock may fluctuate due to factors including, but not limited to:

- our ability to meet the expectations of investors related to the commercialization of Qsymia and STENDRA;
- the costs, timing and outcome of post-approval clinical studies which the FDA has required us to perform as part of the approval for STENDRA and Qsymia;
- the cost required to maintain the certified home delivery pharmacy network and REMS program for Qsymia, including a substantial cost to expand into certified retail pharmacy locations;
- results within the clinical trial programs for Qsymia and STENDRA or other results or decisions affecting the development of our investigational drug candidates;
- announcements of technological innovations or new products by us or our competitors;
- approval of or announcements of other anti-obesity compounds in development;
- publication of generic drug combination weight loss data by outside individuals or companies;
- actual or anticipated fluctuations in our financial results;

- our ability to obtain needed financing;
- sales by insiders or major stockholders;
- economic conditions in the U.S. and abroad;
- the volatility and liquidity of the financial markets;
- comments by or changes in assessments of us or financial estimates by security analysts;
- negative reports by the media or industry analysts on various aspects of our products, our performance and our future operations;
- adverse regulatory actions or decisions;
- any loss of key management;
- deviations in our operating results from the estimates of securities analysts or other analyst comments;
- discussions about us or our stock price by the financial and scientific press and in online investor communities;
- investment activities employed by short sellers of our common stock;
- developments or disputes concerning patents or other proprietary rights;
- reports of prescription data by us or from independent third parties for our products;
- licensing, product, patent or securities litigation; and
- public concern as to the safety and efficacy of our drugs or future investigational drug candidates developed by us.

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These factors and fluctuations, as well as political and other market conditions, may adversely affect the market price of our common stock. Securities related class action litigation is often brought against a company and senior officers following periods of volatility in the market price of its securities. We have been a defendant in shareholder lawsuits—a securities class action against the Company and several senior officers has been dismissed with prejudice but plaintiff has filed an appeal—and we could be the target of similar litigation in the future, particularly if we release news about the Company and its performance that proves to be disappointing to investors. Securities related litigation, whether with or without merit, could result in substantial costs and divert management's attention and financial resources, which could harm our business and financial condition, as well as the market price of our common stock.

Additionally, volatility or a lack of positive performance in our stock price may adversely affect our ability to retain or recruit key employees, all of whom have been or will be granted stock options as an important part of their compensation packages.

Our operating results are unpredictable and may fluctuate. If our operating results are below the expectations of securities analysts or investors, the trading price of our stock could decline.

Our operating results will likely fluctuate from fiscal quarter to fiscal quarter, and from year to year, and are difficult to predict. Although we have commenced sales of Qsymia, we may never increase these sales or become profitable. In addition, we have not entered into a marketing, sales or promotional arrangement with a pharmaceutical partner to commercialize STENDRA. Our operating expenses are largely independent of sales in any particular period. We believe that our quarterly and annual results of operations may be negatively affected by a variety of factors. These factors include, but are not limited to, the level of patient demand for Qsymia and STENDRA, the ability of our distribution partners to process and ship product on a timely basis, the success of our third-party's manufacturing efforts to meet customer demand, fluctuations in foreign exchange rates, investments in sales and marketing efforts to support the sales of Qsymia and STENDRA, investments in the research and development efforts, and expenditures we may incur to acquire additional products.

Future sales of our common stock may depress our stock price.

Sales of our stock by our executive officers and directors, or the perception that such sales may occur, could adversely affect the market price of our stock. We have also registered all common stock that we may issue under our employee benefits plans. As a result, these shares can be freely sold in the public market upon issuance, subject to restrictions under the securities laws. Some of our executive officers have adopted trading plans under SEC Rule 10b5-1 to dispose of a portion of their stock. Any of our executive officers or directors may adopt such trading plans in the future. If any of these events cause a large number of our shares to be sold in the public market, the sales could reduce the trading price of our common stock and impede our ability to raise future capital.

Our charter documents and Delaware law could make an acquisition of our company difficult, even if an acquisition may benefit our stockholders.

Our Board of Directors has adopted a Preferred Shares Rights Plan. The Preferred Shares Rights Plan has the effect of causing substantial dilution to a person or group that attempts to acquire us on terms not approved by our Board of Directors. The existence of the Preferred Shares Rights Plan could limit the price that certain investors might be willing to pay in the future for shares of our common stock and could discourage, delay or prevent a merger or acquisition that a stockholder may consider favorable.

Some provisions of our Amended and Restated Certificate of Incorporation and Bylaws could delay or prevent a change in control of our Company. Some of these provisions:

- authorize the issuance of preferred stock by the Board of Directors without prior stockholder approval, commonly referred to as “blank check” preferred stock, with rights senior to those of common stock;
- prohibit stockholder actions by written consent;
- specify procedures for director nominations by stockholders and submission of other proposals for consideration at stockholder meetings; and
- eliminate cumulative voting in the election of directors.

In addition, we are governed by the provisions of Section 203 of Delaware General Corporation Law. These provisions may prohibit large stockholders, in particular those owning 15% or more of our outstanding voting stock, from merging or combining with us. These and other provisions in our charter documents could reduce the price that investors might be willing to pay for shares of our common stock in the future and result in the market price being lower than it would be without these provisions.

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ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

None.

ITEM 3. DEFAULTS UPON SENIOR SECURITIES

None.

ITEM 4. REMOVED AND RESERVED

ITEM 5. OTHER INFORMATION

None.

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ITEM 6. EXHIBITS

The following documents are filed as Exhibits to this report:

EXHIBIT NUMBER	DESCRIPTION
3.1(1)	Amended and Restated Certificate of Incorporation of the Registrant.
3.2	Amended and Restated Bylaws of the Registrant.
3.3	Amendment No. 1 to the Amended and Restated Bylaws of the Registrant
3.4	Amendment No. 2 to the Amended and Restated Bylaws of the Registrant
3.5(2)	Amended and Restated Certificate of Designation of Rights, Preferences and Privileges of Series A Participating Preferred Stock of the Registrant.
4.1(3)	Specimen Common Stock Certificate of the Registrant.
4.2(4)	Preferred Stock Rights Agreement dated as of March 27, 2007 between the Registrant and Computershare Investor Services, LLC.
10.1††	Purchase and Sale Agreement effective as of March 25, 2013 between the Registrant and BioPharma Secured Investments III Holdings Cayman LP.
10.2††	Master Services Agreement dated as of September 12, 2007 between the Registrant and Medpace Inc.
10.3(5)*	Fourth Amendment dated January 25, 2013 to the Employment Agreement dated December 20, 2007 between the Registrant and Leland F. Wilson.
10.4(6)†	Third Amendment effective as of February 21, 2013 to the Agreement dated as of December 28, 2000 between the Registrant and Mitsubishi Tanabe Pharma Corporation (formerly Tanabe Seiyaku Co., Ltd).
31.1	Certification of Chief Executive Officer, dated May 8, 2013, pursuant to Rules 13a-14 and 15d-14 promulgated under the Securities Exchange Act of 1934, as amended.
31.2	Certification of Chief Financial Officer, dated May 8, 2013, pursuant to Rules 13a-14 and 15d-14 promulgated under the Securities Exchange Act of 1934, as amended.
32	Certification of Chief Executive Officer and Chief Financial Officer pursuant to Section 18 U.S.C. 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101	The following materials from the Registrant’s Quarterly Report on Form 10-Q for the quarter ended March 31, 2013, formatted in

Extensible Business Reporting Language (XBRL), include: (i) the Condensed Consolidated Balance Sheets, (ii) the Condensed Consolidated Statements of Operations, (iii) the Condensed Consolidated Statements of Cash Flows, and (iv) related notes (furnished herewith).

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† Confidential treatment granted.

†† Confidential portions of this exhibit have been redacted and filed separately with the Commission pursuant to a confidential treatment request in accordance with Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

* Indicates management contract or compensatory plan or arrangement.

(1) Incorporated by reference to Exhibit 3.2 filed with the Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 1996 filed with the Commission on March 28, 1997.

(2) Incorporated by reference to Exhibit 3.3 filed with the Registrant's Registration Statement on Form 8-A filed with the Commission on March 28, 2007.

(3) Incorporated by reference to the same numbered exhibit filed with the Registrant's Annual Report on Form 10-K/A for the fiscal year ended December 31, 1996 filed with the Commission on April 16, 1997.

(4) Incorporated by reference to Exhibit 4.1 filed with the Registrant's Registration Statement on Form 8-A filed with the Commission on March 28, 2007.

(5) Incorporated by reference to Exhibit 10.1 filed with the Registrant's Current Report on Form 8-K filed with the Commission on January 30, 2013.

(6) Incorporated by reference to Exhibit 10.1 filed with the Registrant's Current Report on Form 8-K filed with the Commission on February 25, 2013.

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SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Date: May 8, 2013

VIVUS, Inc.

/s/ TIMOTHY E. MORRIS
Timothy E. Morris
Sr. Vice President Finance and Global Corporate Development, Chief Financial Officer

/s/ LELAND F. WILSON
Leland F. Wilson
Chief Executive Officer

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VIVUS, INC.

INDEX TO EXHIBITS

EXHIBIT NUMBER	DESCRIPTION
3.1(1)	Amended and Restated Certificate of Incorporation of the Registrant.
3.2	Amended and Restated Bylaws of the Registrant.
3.3	Amendment No. 1 to the Amended and Restated Bylaws of the Registrant
3.4	Amendment No. 2 to the Amended and Restated Bylaws of the Registrant
3.5(2)	Amended and Restated Certificate of Designation of Rights, Preferences and Privileges of Series A Participating Preferred Stock of the Registrant.
4.1(3)	Specimen Common Stock Certificate of the Registrant.
4.2(4)	Preferred Stock Rights Agreement dated as of March 27, 2007 between the Registrant and Computershare Investor Services, LLC.
10.1††	Purchase and Sale Agreement effective as of March 25, 2013 between the Registrant and BioPharma Secured Investments III Holdings Cayman LP.

10.2††	Master Services Agreement dated as of September 12, 2007 between the Registrant and Medpace Inc.
10.3(5)*	Fourth Amendment dated January 25, 2013 to the Employment Agreement dated December 20, 2007 between the Registrant and Leland F. Wilson.
10.4(6)†	Third Amendment effective as of February 21, 2013 to the Agreement dated as of December 28, 2000 between the Registrant and Mitsubishi Tanabe Pharma Corporation (formerly Tanabe Seiyaku Co., Ltd).
31.1	Certification of Chief Executive Officer, dated May 8, 2013, pursuant to Rules 13a-14 and 15d-14 promulgated under the Securities Exchange Act of 1934, as amended.
31.2	Certification of Chief Financial Officer, dated May 8, 2013, pursuant to Rules 13a-14 and 15d-14 promulgated under the Securities Exchange Act of 1934, as amended.
32	Certification of Chief Executive Officer and Chief Financial Officer pursuant to Section 18 U.S.C. 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101	The following materials from the Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2013, formatted in Extensible Business Reporting Language (XBRL), include: (i) the Condensed Consolidated Balance Sheets, (ii) the Condensed Consolidated Statements of Operations, (iii) the Condensed Consolidated Statements of Cash Flows, and (iv) related notes (furnished herewith).

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† Confidential treatment granted.

†† Confidential portions of this exhibit have been redacted and filed separately with the Commission pursuant to a confidential treatment request in accordance with Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

* Indicates management contract or compensatory plan or arrangement.

(1) Incorporated by reference to Exhibit 3.2 filed with the Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 1996 filed with the Commission on March 28, 1997.

(2) Incorporated by reference to Exhibit 3.3 filed with the Registrant's Registration Statement on Form 8-A filed with the Commission on March 28, 2007.

(3) Incorporated by reference to the same numbered exhibit filed with the Registrant's Annual Report on Form 10-K/A for the fiscal year ended December 31, 1996 filed with the Commission on April 16, 1997.

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(6) Incorporated by reference to Exhibit 10.1 filed with the Registrant's Current Report on Form 8-K filed with the Commission on February 25, 2013.

Exhibit 3.2

AMENDED AND RESTATED BYLAWS OF

VIVUS, INC.

(initially adopted on May 16, 1996)

(as amended and restated on April 20, 2012)

AMENDED AND RESTATED BYLAWS OF

VIVUS, Inc.

(a Delaware corporation)

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ARTICLE I

CORPORATE OFFICES

1.1 REGISTERED OFFICE

The registered office of the corporation shall be fixed in the certificate of incorporation of the corporation.

1.2 OTHER OFFICES

The board of directors may at any time establish branch or subordinate offices at any place or places where the corporation is qualified to do business.

ARTICLE II

MEETINGS OF STOCKHOLDERS

2.1 PLACE OF MEETINGS

Meetings of stockholders shall be held at any place within or outside the State of Delaware designated by the board of directors. In the absence of any such designation, stockholders' meetings shall be held at the principal executive office of the corporation.

2.2 ANNUAL MEETING

The annual meeting of stockholders shall be held each year on a date and at a time designated by the board of directors. In the absence of such designation, the annual meeting of stockholders shall be held on the third Tuesday of May in each year at 10:00 a.m. However, if such day falls on a legal holiday, then the meeting shall be held at the same time and place on the next succeeding full business day. At the meeting, directors shall be elected, and any other proper business may be transacted.

2.3 SPECIAL MEETING

A special meeting of the stockholders may be called at any time by the board of directors, the chairman of the board, or the chief executive officer or president (in the absence of a chief executive officer) but such special meetings may not be called by any other person or persons.

No business may be transacted at such special meeting other than the business specified in the notice to stockholders sent by the corporation in connection with such special meeting. Nothing contained in this paragraph of this Section 2.3 shall be construed as limiting, fixing, or affecting the time when a meeting of stockholders called by action of the board of directors may be held.

2.4 ADVANCE NOTICE PROCEDURES

(i) At an annual meeting of the stockholders, only such business shall be conducted as shall have been properly brought before the meeting. To be properly brought before an annual meeting, business must be: (A) specified in the notice of meeting (or any supplement thereto) given by or at the direction of the board of directors, (B) otherwise properly brought before the meeting by or at the direction of the board of directors, or (C) otherwise properly brought before the meeting by a stockholder. For business to be properly brought before an annual meeting by a stockholder, the stockholder must have given timely notice thereof in writing to the secretary of the corporation. To be timely, a stockholder's notice must be delivered to or mailed and received at the principal executive offices of the corporation (A) not later than the close of business on the ninetieth (90th) day nor earlier than the close of business on the one hundred twentieth (120th) day prior to the first anniversary of the preceding year's annual meeting, or (B) not less than the later of the close of business on the forty-fifth (45th) day nor earlier than the close of business on the seventy-fifth (75th) day prior to the first anniversary of the date on which the corporation first sent or gave its proxy statement to stockholders for the preceding year's annual meeting, whichever period described in clause (A) or (B) of this sentence first occurs; provided, however, that in the event that no annual meeting was held in the previous year or the date of the annual meeting is more than thirty (30) days before or more than sixty (60) days after the anniversary date of the previous year's annual meeting, notice by the stockholder to be timely must be so received not earlier than the close of business on the one hundred twentieth (120th) day prior to the annual meeting and not later than the close of business on the later of (x) the ninetieth (90th) day prior to the annual meeting and (y) the tenth (10) day following the date on which public announcement of the date of such meeting is first made. For purposes of this Section 2.2, a "public announcement" will mean disclosure in a press release reported by the Dow Jones News Service, Associated Press or a comparable national news service or in a document publicly filed by the corporation with the Securities and Exchange Commission, or in a notice pursuant to the applicable rules of an exchange on which the securities of the corporation are listed. In no event will the public announcement of an adjournment of a stockholders meeting commence a new time period for the giving of a stockholder's notice as described above. A stockholder's notice to the secretary shall set forth as to each matter the stockholder proposes to bring before the annual meeting: (a) a brief description of the business desired to be brought before the annual meeting and the reasons for conducting such business at the annual meeting, (b) the name and address, as they appear on the corporation's books, of the stockholder proposing such business, (c) the class and number of shares of the corporation that are beneficially owned by the stockholder, (d) any material interest of the stockholder in such business, and (e) any other information that is required to be provided by the stockholder pursuant to Regulation 14A under the Securities Exchange Act of 1934, as amended (the " **1934 Act** "), in the stockholder's capacity as a proponent to a stockholder proposal. Notwithstanding the foregoing, in order to include information with respect to a stockholder proposal in the proxy statement and form of proxy for a stockholder's meeting, stockholders must provide notice as required by the regulations promulgated under the 1934 Act. Notwithstanding anything in these bylaws to the contrary, no business shall be conducted at any annual meeting except in accordance with the procedures set forth in this paragraph (i). The chairperson of the annual meeting shall, if the facts warrant, determine and declare at the meeting that business was not properly brought before the meeting and in accordance with the provisions of this paragraph (i), and, if the chairperson should so

determine, he or she shall so declare at the meeting that any such business not properly brought before the meeting shall not be transacted.

(ii) Only persons who are nominated in accordance with the procedures set forth in this paragraph (ii) shall be eligible for election as directors. Nominations of persons for election to the board of directors of the corporation may be made at a meeting of stockholders by or at the direction of the board of directors or by any stockholder of the corporation entitled to vote in the election of directors at the meeting who complies with the notice procedures set forth in this paragraph (ii). Such nominations, other than those made by or at the direction of the board of directors, shall be made pursuant to timely notice in writing to the secretary of the corporation in accordance with the provisions of paragraph (i) of this Section 2.4. Such stockholder's notice shall set forth (a) as to each person, if any, whom the stockholder proposes to nominate for election or re-election as a director: (A) the name, age, business address and residence address of such person, (B) the principal occupation or employment of such person, (C) the class and number of shares of the corporation that are beneficially owned by such person, (D) a description of all arrangements or understandings between the stockholder and each nominee and any other person or persons (naming such person or persons) pursuant to which the nominations are to be made by the stockholder, and (E) any other information relating to such person that is required to be disclosed in solicitations of proxies for elections of directors, or is otherwise required, in each case pursuant to Regulation 14A under the 1934 Act (including without limitation such person's written consent to being named in the proxy statement, if any, as a nominee and to serving as a director if elected); and (b) as to such stockholder giving notice, the information required to be provided pursuant to paragraph (i) of this Section 2.4. At the request of the board of directors, any person nominated by a stockholder for election as a director shall furnish to the secretary of the corporation that information required to be set forth in the stockholder's notice of nomination which pertains to the nominee. No person shall be eligible for election as a director of the corporation unless nominated in accordance with the procedures set forth in this paragraph (ii). The chairperson of the meeting shall, if the facts warrant, determine and declare at the meeting that a nomination was not made in accordance with the procedures prescribed by these bylaws, and if the chairperson should so determine, he or she shall so declare at the meeting, and the defective nomination shall be disregarded.

These provisions shall not prevent the consideration and approval or disapproval at an annual meeting of reports of officers, directors and committees of the board of directors, but in connection therewith no new business shall be acted upon at any such meeting unless stated, filed and received as herein provided. Notwithstanding anything in these bylaws to the contrary, no business brought before a meeting by a stockholder shall be conducted at an annual meeting except in accordance with procedures set forth in this Section 2.4.

2.5 NOTICE OF STOCKHOLDERS' MEETINGS

Whenever stockholders are required or permitted to take any action at a meeting, a written notice of the meeting shall be given which shall state the place, if any, date and hour of the meeting, the means of remote communication, if any, by which stockholders and proxy holders may be deemed to be present in person and vote at such meeting, and, in the case of a special meeting, the purpose or purposes for which the meeting is called.

Except as otherwise provided in the DGCL, the certificate of incorporation or these bylaws, the written notice of any meeting of stockholders shall be given not less than 10 nor more than 60 days before the date of the meeting to each stockholder entitled to vote at such meeting.

2.6 MANNER OF GIVING NOTICE; AFFIDAVIT OF NOTICE

Written notice of any meeting of stockholders shall be given either personally or by first-class mail or by telegraphic or other written communication. Notices not personally delivered shall be sent charges prepaid and shall be addressed to the stockholder at the address of that stockholder appearing on the books of the corporation or given by the stockholder to the corporation for the purpose of notice. Notice shall be deemed to have been given at the time when delivered personally or deposited in the mail or sent by telegram or other means of written communication.

An affidavit of the mailing or other means of giving any notice of any stockholders' meeting, executed by the secretary, assistant secretary or any transfer agent of the corporation giving the notice, shall be prima facie evidence of the giving of such notice.

2.7 QUORUM

The holders of a majority in voting power of the stock issued and outstanding and entitled to vote thereat, present in person or represented by proxy, shall constitute a quorum at all meetings of the stockholders for the transaction of business except as otherwise provided by statute or by the certificate of incorporation. If, however, such quorum is not present or represented at any meeting of the stockholders, then either (i) the chairman of the meeting or (ii) the stockholders entitled to vote thereat, present in person or represented by proxy, shall have power to adjourn the meeting in accordance with Section 2.7 of these bylaws.

When a quorum is present at any meeting, the vote of the holders of a majority of the stock having voting power present in person or represented by proxy shall decide any question brought before such meeting, unless the question is one upon which, by express provision of the laws of the State of Delaware or of the certificate of incorporation or these bylaws, a different vote is required, in which case such express provision shall govern and control the decision of the question.

If a quorum be initially present, the stockholders may continue to transact business until adjournment, notwithstanding the withdrawal of enough stockholders to leave less than a quorum, if any action taken is approved by a majority of the stockholders initially constituting the quorum.

2.8 ADJOURNED MEETING; NOTICE

When a meeting is adjourned to another time and place, unless these bylaws otherwise require, notice need not be given of the adjourned meeting if the time and place thereof are announced at the meeting at which the adjournment is taken. At the adjourned meeting the corporation may

transact any business that might have been transacted at the original meeting. If the adjournment is for more than thirty (30) days, or if after the adjournment a new record date is fixed for the adjourned meeting, a notice of the adjourned meeting shall be given to each stockholder of record entitled to vote at the meeting.

2.9 VOTING

The stockholders entitled to vote at any meeting of stockholders shall be determined in accordance with the provisions of Section 2.11 of these bylaws, subject to the provisions of Sections 217 and 218 of the General Corporation Law of Delaware (relating to voting rights of fiduciaries, pledgors and joint owners, and to voting trusts and other voting agreements).

Except as may be otherwise provided in the articles of incorporation or these bylaws, each stockholder shall be entitled to one vote for each share of capital stock held by such stockholder and stockholders shall not be entitled to cumulate their votes in the election of directors of with respect to any matter submitted to a vote of the stockholders.

Notwithstanding the foregoing, if the stockholders of the corporation are entitled, pursuant to Sections 2115 and 301.5 of the California Corporations Code, to cumulate their votes in the election of directors, each such stockholder shall be entitled to cumulate votes (i.e., cast for any candidate a number of votes greater than the number of votes that such stockholder normally is entitled to cast) only if the candidates' names have been properly placed in nomination (in accordance with these bylaws) prior to commencement of the voting, and the stockholder requesting cumulative voting has given notice prior to commencement of the voting of the stockholder's intention to cumulate votes. If cumulative voting is properly requested, each holder of stock, or of any class or classes or of a series or series thereof, who elects to cumulate votes shall be entitled to as many votes as equals the number of votes that (absent this provision as to cumulative voting) he or she would be entitled to cast for the election of directors with respect to his or her shares of stock multiplied by the number of directors to be elected by him, and he or she may cast all of such votes for a single director or may distribute them among the number to be voted for, or for any two or more of them, as he or she may see fit.

2.10 WAIVER OF NOTICE

Whenever notice is required to be given under any provision of the General Corporation Law of Delaware or of the certificate of incorporation or these bylaws, a written waiver thereof, signed by the person entitled to notice, whether before or after the time stated therein, shall be deemed equivalent to notice. Attendance of a person at a meeting shall constitute a waiver of notice of such meeting, except when the person attends a meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Neither the business to be transacted at, nor the purpose of, any regular or special meeting of the stockholders need be specified in any written waiver of notice unless so required by the certificate of incorporation or these bylaws.

2.11 RECORD DATE FOR STOCKHOLDER NOTICE; VOTING

For purposes of determining the stockholders entitled to notice of any meeting or to vote thereat, the board of directors may fix, in advance, a record date, which shall not precede the date upon which the resolution fixing the record date is adopted by the board of directors and which shall not be more than sixty (60) days nor less than ten (10) days before the date of any such meeting, and in such event only stockholders of record on the date so fixed are entitled to notice and to vote, notwithstanding any transfer of any shares on the books of the corporation after the record date.

If the board of directors does not so fix a record date, the record date for determining stockholders entitled to notice of or to vote at a meeting of stockholders shall be at the close of business on the business day next preceding the day on which notice is given, or, if notice is waived, at the close of business on the business day next preceding the day on which the meeting is held.

A determination of stockholders of record entitled to notice of or to vote at a meeting of stockholders shall apply to any adjournment of the meeting unless the board of directors fixes a new record date for the adjourned meeting, but the board of directors shall fix a new record date if the meeting is adjourned for more than thirty (30) days from the date set for the original meeting.

The record date for any other purpose shall be as provided in Section 8.1 of these bylaws.

2.12 PROXIES

Every person entitled to vote for directors, or on any other matter, shall have the right to do so either in person or by one or more agents authorized by a written proxy signed by the person and filed with the secretary of the corporation, but no such proxy shall be voted or acted upon after three (3) years from its date unless the proxy provides for a longer period. A proxy shall be deemed signed if the stockholder's name is placed on the proxy (whether by manual signature, typewriting, telegraphic transmission, telefacsimile or otherwise) by the stockholder or the stockholder's attorney-in-fact. The revocability of a proxy that states on its face that it is irrevocable shall be governed by the provisions of Section 212(e) of the General Corporation Law of Delaware.

2.13 ORGANIZATION

The president, or in the absence of the president, the chairman of the board, or, in the absence of the president and the chairman of the board, one of the corporation's vice presidents, shall call the meeting of the stockholders to order, and shall act as chairman of the meeting. In the absence of the president, the chairman of the board, and all of the vice presidents, the stockholders shall appoint a chairman for such meeting. The chairman of any meeting of stockholders shall determine the order of business and the procedures at the meeting, including such matters as the regulation of the manner of voting and the conduct of business. The secretary of the corporation shall act as secretary of all meetings of the stockholders, but in the absence of the secretary at any meeting of the stockholders, the chairman of the meeting may appoint any person to act as secretary of the meeting.

2.14 LIST OF STOCKHOLDERS ENTITLED TO VOTE

The officer who has charge of the stock ledger of the corporation shall prepare and make, at least ten (10) days before every meeting of stockholders, a complete list of the stockholders entitled to vote at the meeting, arranged in alphabetical order, and showing the address of each stockholder and the number of shares registered in the name of each stockholder. Such list shall be open to the examination of any stockholder, for any purpose germane to the meeting, during ordinary business hours, for a period of at least ten (10) days prior to the meeting, either at a place within the city where the meeting is to be held, which place shall be specified in the notice of the meeting, or, if not so specified, at the place where the meeting is to be held. The list shall also be produced and kept at the time and place of the meeting during the whole time thereof, and may be inspected by any stockholder who is present.

ARTICLE III

DIRECTORS

3.1 POWERS

Subject to the provisions of the General Corporation Law of Delaware and any limitations in the certificate of incorporation and these bylaws relating to action required to be approved by the stockholders or by the outstanding shares, the business and affairs of the corporation shall be managed and all corporate powers shall be exercised by or under the direction of the board of directors.

3.2 NUMBER OF DIRECTORS

The board of directors shall be not less than five (5) nor more than seven (7) members. The exact number of directors shall be six (6) until changed, within the limits specified above, by a bylaw amending this Section 3.2, duly adopted by the board of directors or by the stockholders. The indefinite number of directors may be changed, or a definite number may be fixed without provision for an indefinite number, by an amendment to this bylaw, duly adopted by the board of directors or by the stockholders, or by a duly adopted amendment to the certificate of incorporation.

No reduction of the authorized number of directors shall have the effect of removing any director before that director's term of office expires.

3.3 ELECTION AND TERM OF OFFICE OF DIRECTORS

Except as provided in Section 3.4 of these bylaws, directors shall be elected at each annual meeting of stockholders to hold office until the next annual meeting. Each director, including a director elected or appointed to fill a vacancy, shall hold office until the expiration of the term for which elected and until a successor has been elected and qualified.

3.4 RESIGNATION AND VACANCIES

Any director may resign effective on giving written notice to the chairman of the board, the president, the secretary or the board of directors, unless the notice specifies a later time for that resignation to become effective. If the resignation of a director is effective at a future time, the board of directors may elect a successor to take office when the resignation becomes effective.

Vacancies in the board of directors may be filled by a majority of the remaining directors, even if less than a quorum, or by a sole remaining director; however, a vacancy created by the removal of a director by the vote of the stockholders or by court order may be filled only by the affirmative vote of a majority of the shares represented and voting at a duly held meeting at which a quorum is present (which shares voting affirmatively also constitute a majority of the required quorum). Each director so elected shall hold office until the next annual meeting of the stockholders and until a successor has been elected and qualified.

Unless otherwise provided in the certificate of incorporation or these bylaws:

(i) Vacancies and newly created directorships resulting from any increase in the authorized number of directors elected by all of the stockholders having the right to vote as a single class may be filled by a majority of the directors then in office, although less than a quorum, or by a sole remaining director.

(ii) Whenever the holders of any class or classes of stock or series thereof are entitled to elect one or more directors by the provisions of the certificate of incorporation, vacancies and newly created directorships of such class or classes or series may be filled by a majority of the directors elected by such class or classes or series thereof then in office, or by a sole remaining director so elected.

If at any time, by reason of death or resignation or other cause, the corporation should have no directors in office, then any officer or any stockholder or an executor, administrator, trustee or guardian of a stockholder, or other fiduciary entrusted with like responsibility for the person or estate of a stockholder, may call a special meeting of stockholders in accordance with the provisions of the certificate of incorporation or these bylaws, or may apply to the Court of Chancery for a decree summarily ordering an election as provided in Section 211 of the General Corporation Law of Delaware.

If, at the time of filling any vacancy or any newly created directorship, the directors then in office constitute less than a majority of the whole board (as constituted immediately prior to any such increase), then the Court of Chancery may, upon application of any stockholder or stockholders holding at least ten (10) percent of the total number of the shares at the time outstanding having the right to vote for such directors, summarily order an election to be held to fill any such vacancies or newly created directorships, or to replace the directors chosen by the directors then in office as aforesaid, which election shall be governed by the provisions of Section 211 of the General Corporation Law of Delaware as far as applicable.

3.5 PLACE OF MEETINGS; MEETINGS BY TELEPHONE

Regular meetings of the board of directors may be held at any place within or outside the State of Delaware that has been designated from time to time by resolution of the board. In the absence of such a designation, regular meetings shall be held at the principal executive office of the corporation. Special meetings of the board may be held at any place within or outside the State of Delaware that has been designated in the notice of the meeting or, if not stated in the notice or if there is no notice, at the principal executive office of the corporation.

Any meeting, regular or special, may be held by conference telephone or similar communication equipment, so long as all directors participating in the meeting can hear one another; and all such directors shall be deemed to be present in person at the meeting.

3.6 REGULAR MEETINGS

Regular meetings of the board of directors may be held without notice if the times of such meetings are fixed by the board of directors. If any regular meeting day shall fall on a legal holiday, then the meeting shall be held next succeeding full business day.

3.7 SPECIAL MEETINGS; NOTICE

Special meetings of the board of directors for any purpose or purposes may be called at any time by the chairman of the board, the president, any vice president, the secretary or any two directors.

Notice of the time and place of special meetings shall be delivered personally or by telephone to each director or sent by first-class mail or telegram, charges prepaid, addressed to each director at that director's address as it is shown on the records of the corporation. If the notice is mailed, it shall be deposited in the United States mail at least four (4) days before the time of the holding of the meeting. If the notice is delivered personally or by telephone or telegram, it shall be delivered personally or by telephone or to the telegraph company at least forty-eight (48) hours before the time of the holding of the meeting. Any oral notice given personally or by telephone may be communicated either to the director or to a person at the office of the director who the person giving the notice has reason to believe will promptly communicate it to the director. The notice need not specify the purpose or the place of the meeting, if the meeting is to be held at the principal executive office of the corporation.

3.8 QUORUM

A majority of the authorized number of directors shall constitute a quorum for the transaction of business, except to adjourn as provided in Section 3.10 of these bylaws. Every act or decision done or made by a majority of the directors present at a duly held meeting at which a quorum is present shall be regarded as the act of the board of directors, subject to the provisions of the certificate of incorporation and other applicable law.

A meeting at which a quorum is initially present may continue to transact business notwithstanding the withdrawal of directors, if any action taken is approved by at least a majority of the required quorum for that meeting.

3.9 WAIVER OF NOTICE

Notice of a meeting need not be given to any director (i) who signs a waiver of notice or a consent to holding the meeting or an approval of the minutes thereof, whether before or after the meeting, or (ii) who attends the meeting without protesting, prior thereto or at its commencement, the lack of notice to such directors. All such waivers, consents, and approvals shall be filed with the corporate records or made part of the minutes of the meeting. A waiver of notice need not specify the purpose of any regular or special meeting of the board of directors.

3.10 ADJOURNMENT

A majority of the directors present, whether or not constituting a quorum, may adjourn any meeting to another time and place.

3.11 NOTICE OF ADJOURNMENT

Notice of the time and place of holding an adjourned meeting need not be given unless the meeting is adjourned for more than twenty-four (24) hours. If the meeting is adjourned for more than twenty-four (24) hours, then notice of the time and place of the adjourned meeting shall be given before the adjourned meeting takes place, in the manner specified in Section 3.7 of these bylaws, to the directors who were not present at the time of the adjournment.

3.12 BOARD ACTION BY WRITTEN CONSENT WITHOUT A MEETING

Any action required or permitted to be taken by the board of directors may be taken without a meeting, provided that all members of the board individually or collectively consent in writing to that action. Such action by written consent shall have the same force and effect as a unanimous vote of the board of directors. Such written consent and any counterparts thereof shall be filed with the minutes of the proceedings of the board.

3.13 FEES AND COMPENSATION OF DIRECTORS

Directors and members of committees may receive such compensation, if any, for their services and such reimbursement of expenses as may be fixed or determined by resolution of the board of directors. This Section 3.13 shall not be construed to preclude any director from serving the corporation in any other capacity as an officer, agent, employee or otherwise and receiving compensation for those services.

3.14 APPROVAL OF LOANS TO OFFICERS

The corporation may lend money to, or guarantee any obligation of, or otherwise assist any officer or other employee of the corporation or any of its subsidiaries, including any officer or

employee who is a director of the corporation or any of its subsidiaries, whenever, in the judgment of the directors, such loan, guaranty or assistance may reasonably be expected to benefit the corporation. The loan, guaranty or other assistance may be with or without interest and may be unsecured, or secured in such manner as the board of directors shall approve, including, without limitation, a pledge of shares of stock of the corporation. Nothing contained in this section shall be deemed to deny, limit or restrict the powers of guaranty or warranty of the corporation at common law or under any statute.

ARTICLE IV

COMMITTEES

4.1 COMMITTEES OF DIRECTORS

The board of directors may, by resolution adopted by a majority of the authorized number of directors, designate one (1) or more committees, each consisting of two or more directors, to serve at the pleasure of the board. The board may designate one (1) or more directors as alternate members of any committee, who may replace any absent member at any meeting of the committee. The appointment of members or alternate members of a committee requires the vote of a majority of the authorized number of directors. Any committee, to the extent provided in the resolution of the board, shall have and may exercise all the powers and authority of the board, but no such committee shall have the power of authority to:

(a) amend the certificate of incorporation (except that a committee may, to the extent authorized in the resolution or resolutions providing for the issuance of shares of stock adopted by the board of directors as provided in Section 151(a) of the General Corporation Law of Delaware, fix the designations and any of the preferences or rights of such shares relating to dividends, redemption, dissolution, any distribution of assets of the corporation or the conversion into, or the exchange of such shares for, shares of any other class or classes or any other series of the same or any other class or classes of stock of the corporation);

(b) adopt an agreement of merger or consolidation under Sections 251 or 252 of the General Corporation Law of Delaware;

(c) recommend to the stockholders the sale, lease or exchange of all or substantially all of the corporation’s property and assets;

(d) recommend to the stockholders a dissolution of the corporation or a revocation of a dissolution; or

(e) amend the bylaws of the corporation; and, unless the board resolution establishing the committee, the bylaws or the certificate of incorporation expressly so provide, no such committee shall have the power or authority to declare a dividend, to authorize the issuance of stock, or to adopt a certificate of ownership and merger pursuant to Section 253 of the General Corporation Law of Delaware.

4.2 MEETINGS AND ACTION OF COMMITTEES

Meetings and actions of committees shall be governed by, and held and taken in accordance with, the provisions of Article III of these bylaws, Section 3.5 (place of meetings), Section 3.6 (regular meetings), Section 3.7 (special meetings and notice), Section 3.8 (quorum), Section 3.9 (waiver of notice), Section 3.10 (adjournment), Section 3.11 (notice of adjournment), and Section 3.12 (action without meeting), with such changes in the context of those bylaws as are necessary to substitute the committee and its members for the board of directors and its members; provided, however, that the time of regular meetings of committees may be determined either by resolution of the board of directors or by resolution of the committee, that special meetings of committees may also be called by resolution of the board of directors, and that notice of special meetings of committees shall also be given to all alternate members, who shall have the right to attend all meetings of the committee. The board of directors may adopt rules for the government of any committee not inconsistent with the provisions of these bylaws.

4.3 COMMITTEE MINUTES.

Each committee shall keep regular minutes of its meetings and report the same to the board of directors when required.

ARTICLE V

OFFICERS

5.1 OFFICERS

The officers of the corporation shall be a president, a secretary, and a chief financial officer. The corporation may also have, at the discretion of the board of directors, a chairman of the board, one or more vice presidents, one or more assistant secretaries, one or more assistant treasurers, and such other officers as may be appointed in accordance with the provisions of Section 5.3 of these bylaws. Any number of offices may be held by the same person.

5.2 ELECTION OF OFFICERS

The officers of the corporation, except such officers as may be appointed in accordance with the provisions of Section 5.3 or Section 5.5 of these bylaws, shall be chosen by the board, subject to the rights, if any, of an officer under any contract of employment.

5.3 SUBORDINATE OFFICERS

The board of directors may appoint, or may empower the president to appoint, such other officers as the business of the corporation may require, each of whom shall hold office for such period, have such authority, and perform such duties as are provided in these bylaws or as the board of directors may from time to time determine.

5.4 REMOVAL AND RESIGNATION OF OFFICERS

Subject to the rights, if any, of an officer under any contract of employment, any officer may be removed, either with or without cause, by the board of directors at any regular or special meeting of the board or, except in case of an officer chosen by the board of directors, by any officer upon whom such power of removal may be conferred by the board of directors.

Any officer may resign at any time by giving written notice to the corporation. Any resignation shall take effect at the date of the receipt of that notice or at any later time specified in that notice; and, unless otherwise specified in that notice, the acceptance of the resignation shall not be necessary to make it effective. Any resignation is without prejudice to the rights, if any, of the corporation under any contract to which the officer is a party.

5.5 VACANCIES IN OFFICES

A vacancy in any office because of death, resignation, removal, disqualification or any other cause shall be filled in the manner prescribed in these bylaws for regular appointments to that office.

5.6 CHAIRMAN OF THE BOARD

The chairman of the board, if such an officer be elected, shall, if present, preside at meetings of the board of directors and exercise and perform such other powers and duties as may from time to time be assigned to him by the board of directors or as may be prescribed by these bylaws. If there is no president, then the chairman of the board shall also be the chief executive officer of the corporation and shall have the powers and duties prescribed in Section 5.7 of these bylaws.

5.7 PRESIDENT

Subject to such supervisory powers, if any, as may be given by the board of directors to the chairman of the board, if there be such an officer, the president shall be the chief executive officer of the corporation and shall, subject to the control of the board of directors, have general supervision, direction, and control of the business and the officers of the corporation. He shall preside at all meetings of the stockholders and, in the absence or nonexistence of a chairman of the board, at all meetings of the board of directors. He shall have the general powers and duties of management usually vested in the office of president of a corporation, and shall have such other powers and duties as may be prescribed by the board of directors or these bylaws.

5.8 VICE PRESIDENTS

In the absence or disability of the president, the vice presidents, if any, in order of their rank as fixed by the board of directors or, if not ranked, a vice president designated by the board of directors, shall perform all the duties of the president and when so acting shall have all the powers of, and be subject to all the restrictions upon, the president. The vice presidents shall have such other powers and perform such other duties as from time to time may be prescribed for

them respectively by the board of directors, these bylaws, the president or the chairman of the board.

5.9 SECRETARY

The secretary shall keep or cause to be kept, at the principal executive office of the corporation or such other place as the board of directors may direct, a book of minutes of all meetings and actions of directors, committees of directors and stockholders. The minutes shall show the time and place of each meeting, whether regular or special (and, if special, how authorized and the notice given), the names of those present at directors' meetings or committee meetings, the number of shares present or represented at stockholders' meetings, and the proceedings thereof.

The secretary shall keep, or cause to be kept, at the principal executive office of the corporation or at the office of the corporation's transfer agent or registrar, as determined by resolution of the board of directors, a share register, or a duplicate share register, showing the names of all stockholders and their addresses, the number and classes of shares held by each, the number and date of certificates evidencing such shares, and the number and date of cancellation of every certificate surrendered for cancellation.

The secretary shall give, or cause to be given, notice of all meetings of the stockholders and of the board of directors required to be given by law or by these bylaws. He shall keep the seal of the corporation, if one be adopted, in safe custody and shall have such other powers and perform such other duties as may be prescribed by the board of directors or by these bylaws.

5.10 CHIEF FINANCIAL OFFICER

The chief financial officer shall keep and maintain, or cause to be kept and maintained, adequate and correct books and records of accounts of the properties and business transactions of the corporation, including accounts of its assets, liabilities, receipts, disbursements, gains, losses, capital, retained earnings, and shares. The books of account shall at all reasonable times be open to inspection by any director.

The chief financial officer shall deposit all money and other valuables in the name and to the credit of the corporation with such depositaries as may be designated by the board of directors. He shall disburse the funds of the corporation as may be ordered by the board of directors, shall render to the president and directors, whenever they request it, an account of all of his transactions as chief financial officer and of the financial condition of the corporation, and shall have such other powers and perform such other duties as may be prescribed by the board of directors or these bylaws.

ARTICLE VI

INDEMNIFICATION OF DIRECTORS, OFFICERS, EMPLOYEES, AND OTHER AGENTS

6.1 INDEMNIFICATION OF DIRECTORS AND OFFICERS

The corporation shall, to the maximum extent and in the manner permitted by the General Corporation Law of Delaware as the same now exists or may hereafter be amended, indemnify any person against expenses (including attorneys' fees), judgments, fines, and amounts paid in settlement actually and reasonably incurred in connection with any threatened, pending or completed action, suit, or proceeding in which such person was or is a party or is threatened to be made a party by reason of the fact that such person is or was a director or officer of the corporation. For purposes of this Section 6.1, a "director" or "officer" of the corporation shall mean any person (i) who is or was a director or officer of the corporation, (ii) who is or was serving at the request of the corporation as a director or officer of another corporation, partnership, joint venture, trust or other enterprise, or (iii) who was a director or officer of a corporation which was a predecessor corporation of the corporation or of another enterprise at the request of such predecessor corporation.

The corporation shall be required to indemnify a director or officer in connection with an action, suit, or proceeding (or part thereof) initiated by such director or officer only if the initiation of such action, suit, or proceeding (or part thereof) by the director or officer was authorized by the Board of Directors of the corporation.

The corporation shall pay the expenses (including attorney's fees) incurred by a director or officer of the corporation entitled to indemnification hereunder in defending any action, suit or proceeding referred to in this Section 6.1 in advance of its final disposition; provided, however, that payment of expenses incurred by a director or officer of the corporation in advance of the final disposition of such action, suit or proceeding shall be made only upon receipt of an undertaking by the director or officer to repay all amounts advanced if it should ultimately be determined that the director of officer is not entitled to be indemnified under this Section 6.1 or otherwise.

The rights conferred on any person by this Article shall not be exclusive of any other rights which such person may have or hereafter acquire under any statute, provision of the corporation's Certificate of Incorporation, these bylaws, agreement, vote of the stockholders or disinterested directors or otherwise.

Any repeal or modification of the foregoing provisions of this Article shall not adversely affect any right or protection hereunder of any person in respect of any act or omission occurring prior to the time of such repeal or modification.

6.2 INDEMNIFICATION OF OTHERS

The corporation shall have the power, to the maximum extent and in the manner permitted by the General Corporation Law of Delaware as the same now exists or may hereafter be amended, to indemnify any person (other than directors and officers) against expenses (including attorneys' fees), judgments, fines,

and amounts paid in settlement actually and reasonably incurred in connection with any threatened, pending or completed action, suit, or proceeding, in which such person was or is a party or is threatened to be made a party by reason of the fact that such person

is or was an employee or agent of the corporation. For purposes of this Section 6.2, an "employee" or "agent" of the corporation (other than a director or officer) shall mean any person (i) who is or was an employee or agent of the corporation, (ii) who is or was serving at the request of the corporation as an employee or agent of another corporation, partnership, joint venture, trust or other enterprise, or (iii) who was an employee or agent of a corporation which was a predecessor corporation of the corporation or of another enterprise at the request of such predecessor corporation.

6.3 INSURANCE

The corporation may purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against any liability asserted against him or her and incurred by him or her in any such capacity, or arising out of his or her status as such, whether or not the corporation would have the power to indemnify him or her against such liability under the provisions of the General Corporation Law of Delaware.

ARTICLE VII

RECORDS AND REPORTS

7.1 MAINTENANCE AND INSPECTION OF RECORDS

The corporation shall, either at its principal executive office or at such place or places as designated by the board of directors, keep a record of its stockholders listing their names and addresses and the number and class of shares held by each stockholder, a copy of these bylaws as amended to date, accounting books and other records of its business and properties.

Any stockholder of record, in person or by attorney or other agent, shall, upon written demand under oath stating the purpose thereof, have the right during the usual hours for business to inspect for any proper purpose the corporation's stock ledger, a list of its stockholders, and its other books and records and to make copies or extracts therefrom. A proper purpose shall mean a purpose reasonably related to such person's interest as a stockholder. In every instance where an attorney or other agent is the person who seeks the right to inspection, the demand under oath shall be accompanied by a power of attorney or such other writing that authorizes the attorney or other agent to so act on behalf of the stockholder. The demand under oath shall be directed to the corporation at its registered office in Delaware or at its principal place of business.

7.2 INSPECTION BY DIRECTORS

Any director shall have the right to examine (and to make copies of) the corporation's stock ledger, a list of its stockholders and its other books and records for a purpose reasonably related to his or her position as a director.

7.3 ANNUAL STATEMENT TO STOCKHOLDERS

The board of directors shall present at each annual meeting, and at any special meeting of the stockholders when called for by vote of the stockholders, a full and clear statement of the business and condition of the corporation.

7.4 REPRESENTATION OF SHARES OF OTHER CORPORATIONS

The chairman of the board, if any, the president, any vice president, the chief financial officer, the secretary or any assistant secretary of this corporation, or any other person authorized by the board of directors or the president or a vice president, is authorized to vote, represent and exercise on behalf of this corporation all rights incident to any and all shares of the stock of any other corporation or corporations standing in the name of this corporation. The authority herein granted may be exercised either by such person directly or by any other person authorized to do so by proxy or power of attorney duly executed by such person having the authority.

7.5 CERTIFICATION AND INSPECTION OF BYLAWS

The original or a copy of these bylaws, as amended or otherwise altered to date, certified by the secretary, shall be kept at the corporation's principal executive office and shall be open to inspection by the stockholders of the corporation, at all reasonable times during office hours.

ARTICLE VIII

GENERAL MATTERS

8.1 RECORD DATE FOR PURPOSES OTHER THAN NOTICE AND VOTING

For purposes of determining the stockholders entitled to receive payment of any dividend or other distribution or allotment of any rights or the stockholders entitled to exercise any rights in respect of any other lawful action (other than action by stockholders by written consent without a meeting), the board of directors may fix, in advance, a record date, which shall not be more than sixty (60) days before any such action. In that case, only stockholders of record at the close of business on the date so fixed are entitled to receive the dividend, distribution or allotment of rights, or to exercise such rights, as the case may be, notwithstanding any transfer of any shares on the books of the corporation after the record date so fixed, except as otherwise provided in the General Corporation Law of Delaware.

If the board of directors does not so fix a record date, then the record date for determining stockholders for any such purpose shall be at the close of business on the day on which the board adopts the applicable resolution.

8.2 CHECKS; DRAFTS; EVIDENCES OF INDEBTEDNESS

From time to time, the board of directors shall determine by resolution which person or persons may sign or endorse all checks, drafts, other orders for payment of money, notes or other evidences of indebtedness that are issued in the name of or payable to the corporation, and only the persons so authorized shall sign or endorse those instruments.

8.3 CORPORATE CONTRACTS AND INSTRUMENTS: HOW EXECUTED

The board of directors, except as otherwise provided in these bylaws, may authorize any officer or officers, or agent or agents, to enter into any contract or execute any instrument in the name of and on behalf of the corporation; such authority may be general or confined to specific instances. Unless so authorized or ratified by the board of directors or within the agency power of an officer, no officer, agent or employee shall have any power or authority to bind the corporation by any contract or engagement or to pledge its credit or to render it liable for any purpose or for any amount.

8.4 STOCK CERTIFICATES; TRANSFER; PARTLY PAID SHARES

The shares of the corporation shall be represented by certificates, provided that the board of directors of the corporation may provide by resolution or resolutions that some or all of any or all classes or series of its stock shall be uncertificated shares. Any such resolution shall not apply to shares represented by a certificate until such certificate is surrendered to the corporation. Notwithstanding the adoption of such a resolution by the board of directors, every holder of stock represented by certificates and, upon request, every holder of uncertificated shares, shall be entitled to have a certificate signed by, or in the name of the corporation by, the chairman or vice-chairman of the board of directors, or the president or vice-president, and by the treasurer or an assistant treasurer, or the secretary or an assistant secretary of such corporation representing the number of shares registered in certificate form. Any or all of the signatures on the certificate may be a facsimile. In case any officer, transfer agent or registrar who has signed or whose facsimile signature has been placed upon a certificate has ceased to be such officer, transfer agent or registrar before such certificate is issued, it may be issued by the corporation with the same effect as if he or she were such officer, transfer agent or registrar at the date of issue.

Certificates for shares shall be of such form and device as the board of directors may designate and shall state the name of the record holder of the shares represented thereby; its number; date of issuance; the number of shares for which it is issued; a summary statement or reference to the powers, designations, preferences or other special rights of such stock and the qualifications, limitations or restrictions of such preferences and/or rights, if any; a statement or summary of liens, if any; a conspicuous notice of restrictions upon transfer or registration of transfer, if any; a statement as to any applicable voting trust agreement; if the shares be assessable, or, if assessments are collectible by personal action, a plain statement of such facts.

Upon surrender to the secretary or transfer agent of the corporation of a certificate for shares duly endorsed or accompanied by proper evidence of succession, assignment or authority to

transfer, it shall be the duty of the corporation to issue a new certificate to the person entitled thereto, cancel the old certificate and record the transaction upon its books.

The corporation may issue the whole or any part of its shares as partly paid and subject to call for the remainder of the consideration to be paid therefor. Upon the face or back of each stock certificate issued to represent any such partly paid shares, or upon the books and records of the corporation in the case of uncertificated partly paid shares, the total amount of the consideration to be paid therefor and the amount paid thereon shall be stated. Upon the declaration of any dividend on fully paid shares, the corporation shall declare a dividend upon partly paid shares of the same class, but only upon the basis of the percentage of the consideration actually paid thereon.

8.5 SPECIAL DESIGNATION ON CERTIFICATES

If the corporation is authorized to issue more than one class of stock or more than one series of any class, then the powers, the designations, the preferences and the relative, participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights shall be set forth in full or summarized on the face or back of the certificate that the corporation shall issue to represent such class or series of stock; provided, however, that, except as otherwise provided in Section 202 of the General Corporation Law of Delaware, in lieu of the foregoing requirements there may be set forth on the face or back of the certificate that the corporation shall issue to represent such class or series of stock a statement that the corporation will furnish without charge to each stockholder who so requests the powers, the designations, the preferences and the relative, participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights.

8.6 LOST CERTIFICATES

Except as provided in this Section 8.6, no new certificates for shares shall be issued to replace a previously issued certificate unless the latter is surrendered to the corporation and cancelled at the same time. The board of directors may, in case any share certificate or certificate for any other security is lost, stolen or destroyed, authorize the issuance of replacement certificates on such terms and conditions as the board may require; the board may require indemnification of the corporation secured by a bond or other adequate security sufficient to protect the corporation against any claim that may be made against it, including any expense or liability, on account of the alleged loss, theft or destruction of the certificate or the issuance of the replacement certificate.

8.7 TRANSFER AGENTS AND REGISTRARS

The board of directors may appoint one or more transfer agents or transfer clerks, and one or more registrars, each of which shall be an incorporated bank or trust company — either domestic or foreign, who shall be appointed at such times and places as the requirements of the corporation may necessitate and the board of directors may designate.

8.8 CONSTRUCTION; DEFINITIONS

Unless the context requires otherwise, the general provisions, rules of construction, and definitions in the General Corporation Law of Delaware shall govern the construction of these bylaws. Without limiting the generality of this provision, the singular number includes the plural, the plural number includes the singular, and the term “person” includes both a corporation and a natural person.

ARTICLE IX

AMENDMENTS

The original or other bylaws of the corporation may be adopted, amended or repealed by the stockholders entitled to vote or by the board of directors of the corporation. The fact that such power has been so conferred upon the directors shall not divest the stockholders of the power, nor limit their power to adopt, amend or repeal bylaws.

Whenever an amendment or new bylaw is adopted, it shall be copied in the book of bylaws with the original bylaws, in the appropriate place. If any bylaw is repealed, the fact of repeal with the date of the meeting at which the repeal was enacted or the filing of the operative written consent(s) shall be stated in said book.

Exhibit 3.3

AMENDMENT NO. 1
TO THE AMENDED AND RESTATED BYLAWS OF
VIVUS, INC.

February 20, 2013

The Amended and Restated Bylaws of VIVUS, Inc., a Delaware corporation (the "**Company**"), initially adopted by the Board of Directors of the Company on May 16, 1996 and as amended and restated on April 18, 2012 (the "**Bylaws**"), are hereby amended by this Amendment No. 1 (this "**Amendment**") pursuant to Article IX thereof as set forth below.

1. **Amendment**. Article II, Section 2.7 of the Bylaws is hereby amended by deleting such Article II, Section 2.7 in its entirety and replacing such Section with the following new Article II, Section 2.7:

   "The holders of a majority in voting power of the stock issued and outstanding and entitled to vote thereat, present in person or represented by proxy, shall constitute a quorum at all meetings of the stockholders for the transaction of business except as otherwise provided by applicable law, the certificate of incorporation or these bylaws. If, however, such quorum is not present or represented at any meeting of the stockholders, then either (i) the chairman of the meeting or (ii) the holders of a majority of the voting power of the shares entitled to vote, who are present in person or represented by proxy, shall have power to adjourn the meeting. If a quorum be initially present, the stockholders may continue to transact business until adjournment, notwithstanding the withdrawal of enough stockholders to leave less than a quorum.

   Except as otherwise provided by the certificate of incorporation, directors shall be elected by a plurality of the votes cast by stockholders present in person or represented by proxy at the meeting and entitled to vote on the election of directors. Except as otherwise provided by applicable law, the certificate of incorporation or these bylaws, every matter other than the election of directors shall be decided by the affirmative vote of a majority of the votes cast by stockholders present in person or represented by proxy at the meeting and entitled to vote on such matter."

2. **Miscellaneous**. Except as modified by this Amendment, which shall be effective as of the date first written above, the Bylaws shall remain in full force and effect.

[*Signature Page Follows*]

IN WITNESS WHEREOF, to record adoption of this Amendment by the Board of Directors of the Company as of the date first written above, the Company has caused its authorized officer to execute this Amendment as of the date first written above.

By: /s/ Leland F. Wilson
Name: Leland F. Wilson
Title: Chief Executive Officer

Exhibit 3.4

AMENDMENT NO. 2
TO THE AMENDED AND RESTATED BYLAWS OF
VIVUS, INC.

April 26, 2013

The Amended and Restated Bylaws of VIVUS, Inc., a Delaware corporation (the "**Company**"), initially adopted by the Board of Directors of the Company on May 16, 1996, as amended and restated on April 18, 2012 and as amended by Amendment No. 1 on February 20, 2013 (the "**Bylaws**"), are hereby amended by this Amendment No. 2 (this "**Amendment**") pursuant to Article IX thereof as set forth below.

1. **Amendment**. Article III, Section 3.2 of the Bylaws is hereby amended by deleting such Article III, Section 3.2 in its entirety and replacing such Section with the following new Article III, Section 3.2:

   "The board of directors shall be set at seven (7) members until changed by an amendment to this bylaw, duly adopted by the board of directors or by the stockholders, or by a duly adopted amendment to the certificate of incorporation. No reduction of the authorized number of directors shall have the effect of removing any director before that director's term of office expires."

2. **Miscellaneous**. Except as modified by this Amendment, which shall be effective as of the date first written above, the Bylaws shall remain in full force and effect.

IN WITNESS WHEREOF, to record adoption of this Amendment by the Board of Directors of the Company as of the date first written above, the Company has caused its authorized officer to execute this Amendment as of the date first written above.

By: /s/ Leland F. Wilson
Name: Leland F. Wilson
Title: Chief Executive Officer

*** *Certain confidential information contained in this document, marked with three asterisks, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.*

PURCHASE AND SALE AGREEMENT

BY AND BETWEEN

VIVUS, INC.

AND

BIOPHARMA SECURED INVESTMENTS III HOLDINGS CAYMAN LP

EFFECTIVE AS OF

MARCH 25, 2013

PURCHASE AND SALE AGREEMENT

THIS PURCHASE AND SALE AGREEMENT (this ***"Agreement"***) is made and entered into as of March 25, 2013 (the ***"Effective Date"***), by and between **VIVUS, INC.**, a Delaware corporation, and its permitted successors and assigns (***"Seller"***), and **BIOPHARMA SECURED INVESTMENTS III HOLDINGS CAYMAN LP**, a Cayman Islands exempted limited partnership, and its permitted successors and assigns (***"Purchaser"***). Purchaser and Seller are sometimes referred to individually as a ***"Party"*** and collectively as the ***"Parties."*** Capitalized terms used but not otherwise defined will have the respective meanings given to such terms in **Annex A** attached hereto.

BACKGROUND

WHEREAS, Seller desires additional funding to develop and commercialize the Product in the Territory and Purchaser desires, on the terms and conditions set forth herein, to provide Seller with such additional funding; and

WHEREAS, upon and subject to the terms and conditions contained herein, Seller desires to sell, convey, transfer and assign to Purchaser, and Purchaser desires to purchase and accept from Seller, all of Seller's right, title and interest in, to and under the Purchased Receivables.

NOW, THEREFORE, in consideration of the premises and mutual covenants herein contained, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties hereby agree as follows:

ARTICLE 1

PURCHASE AND SALE OF PURCHASED RECEIVABLES

1.1 PURCHASE AND SALE OF PURCHASED RECEIVABLES. On the terms and subject to the conditions set forth in this Agreement, Seller will sell, convey, transfer and assign to Purchaser, and Purchaser agrees to purchase and accept from Seller, on the Tranche A Closing Date, all of Seller's right, title and interest in, to and under the Purchased Receivables, free and clear of any and all Encumbrances (other than Permitted Encumbrances). It is understood and agreed that Purchaser shall not, by purchase of the Purchased Receivables, acquire any assets or rights of Seller relating to the Product other than those specified in the immediately preceding sentence or as otherwise specified under this Agreement.

1.2 PURCHASE PRICE; USE OF PROCEEDS.

(a) The aggregate purchase price for the Purchased Receivables is $110,000,000.00 (the ***"Purchase Price"***), payable in accordance with the terms and conditions set forth in Section 1.4. The Purchase Price will be paid as follows:

*** *Certain confidential information contained in this document, marked with three asterisks, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.*

(i) $50,000,000.00 (the "***Tranche A Amount***") will be paid on the Tranche A Closing Date (the "***Tranche A Transaction***"), less the Up-Front Payments, by wire transfer in immediately available U.S. dollar funds to an account to be designated in writing by Seller prior to the Tranche A Closing; and

(ii) subject to Section 1.4(b), $60,000,000.00 (the "***Tranche B Amount***") will be paid on the Tranche B Closing Date (the "***Tranche B Transaction***"), less the Tranche B Funding Payment, by wire transfer in immediately available U.S. dollar funds to an account to be designated in writing by Seller prior to the Tranche B Closing.

(b) Seller will use the proceeds of the Purchase Price for Funded Activities. Purchaser will have no obligation or responsibility to pay any portion of the Purchase Price to any providers of Funded Activities or anyone else, besides Seller as set forth in Section 1.2(a).

1.3 MANNER OF EFFECTIVE SALE. The sale, conveyance, transfer, assignment and delivery of the Purchased Receivables by Seller to Purchaser will be effected by Purchaser and Seller executing the Bill of Sale.

1.4 CLOSINGS AND CLOSING DATES.

(a) The Tranche A Transaction will take place at the offices of Akin Gump Strauss Hauer & Feld LLP, 1 Bryant Park, New York, NY 10036, commencing at 9:00 a.m. (local time) on the tenth Business Day following the Effective Date (the ***"Tranche A Closing"***), or at such other place, time and date as the Parties may mutually agree. The date of the Tranche A Closing is referred to as the ***"Tranche A Closing Date."***

(b) Subject to the terms and conditions set forth herein, Seller shall have the option to consummate the Tranche B Transaction by providing written notice to Purchaser prior to December 31, 2013 (the "***Tranche B Election***"); provided that if Seller does not so provide a written notice to Purchaser prior to December 31, 2013, then Seller shall be deemed to have declined the Tranche B Election. If Seller properly makes the Tranche B Election, then the Tranche B Transaction will take place at the offices of Akin Gump Strauss Hauer & Feld LLP, 1 Bryant Park, New York, NY 10036, commencing at 9:00 a.m. (local time) on the *** following the date on which Purchaser receives the Tranche B Election (the ***"Tranche B Closing"***), or at such other place, time and date as the Parties may mutually agree. The date of the Tranche B Closing is referred to as the ***"Tranche B Closing Date."*** The Tranche B Closing Date shall occur no earlier than April 30, 2013 and no later than January 15, 2014.

1.5 CONDITIONS TO PURCHASER'S OBLIGATIONS FOR TRANCHE A TRANSACTION.

(a) Seller shall have delivered to Purchaser the Bill of Sale, duly executed by Seller.

(b) Seller shall have delivered to Purchaser the Patent Security Agreement, duly executed by Seller.

*** *Certain confidential information contained in this document, marked with three asterisks, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.*

(c) An executive officer of Seller shall have delivered to Purchaser a certificate, dated as of the Tranche A Closing Date and duly executed:

(i) (A) attaching copies, certified by such officer as true and complete, of resolutions of the board of directors of Seller authorizing and approving the execution, delivery and performance by Seller of the Transaction Documents and the transactions contemplated herein and therein; and (B) setting forth the incumbency of the officer or officers of Seller who have executed and delivered the Transaction Documents, including therein a signature specimen of each officer or officers; (C) attaching copies, certified by such officer as true and complete, of each of the certificate of incorporation and by-laws of Seller as in effect on the Tranche A Closing Date; and (D) attaching a copy, certified by such officer as true and complete, of a short form good standing certificate of the appropriate Governmental Authority of Seller's jurisdiction of incorporation, stating that Seller is in good standing under the laws of such jurisdiction; and

(ii) (A) as to the accuracy in all material respects of Seller's representations and warranties in this Agreement as of the Effective Date (other than those made as of a specified date earlier than the Effective Date); (B) as to the accuracy in all material respects of each of Seller's representations and warranties in this Agreement as of a specified date earlier than the Effective Date; and (C) as to Seller's compliance with and performance of in all material respects each of its covenants and obligations to be performed or complied with at or before the Effective Date.

(d) Seller shall sign or deliver to Purchaser such other certificates, documents and financing statements as Purchaser may reasonably request, including a financing statement, in each case reasonably satisfactory to Purchaser to perfect under the applicable UCC (or any comparable law) of all applicable jurisdictions in the United States and maintain the perfection of Purchaser's ownership interest in the Purchased Receivables, the back-up security interest granted pursuant to Section 4.7 and the security interest granted pursuant to Section 4.8, in each case in the United States.

(e) Purchaser shall have received the corporate opinion of Hogan Lovells LLP, special counsel to Seller, in mutually agreeable form.

1.6 CONDITIONS TO SELLER'S OBLIGATIONS FOR TRANCHE A TRANSACTION.

(a) Purchaser shall have delivered to Seller the Bill of Sale, duly executed by Purchaser.

(b) Purchaser shall have delivered to Seller the Patent Security Agreement, duly executed by Purchaser.

(c) The general partner of Pharmakon Advisors, LP, the investment manager of Purchaser ("***Pharmakon***"), shall have delivered to Seller a certificate, dated as of the Tranche A Closing Date and duly executed:

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(i) setting forth the incumbency of the authorized person or persons of Pharmakon who have executed and delivered the Transaction Documents, including therein a signature specimen of each authorized person or persons;

(ii) (A) as to the accuracy in all material respects of each of Purchaser's representations and warranties in this Agreement as of the Effective Date (other than those made as of a specified date earlier than the Effective Date); (B) as to the accuracy in all material respects of each of Purchaser's representations and warranties in this Agreement as of a specified date earlier than the Effective Date; and (C) as to Purchaser's compliance with and performance of in all material respects each of its covenants and obligations to be performed or complied with at or before the Effective Date.

(d) Seller shall have received from Purchaser validly executed IRS Forms W-8IMY, W-8BEN and W-9, as applicable, and such additional IRS Form or Forms as are, in Seller's good faith judgment, reasonably required in order to satisfy the requirements of Sections 871(h)(2)(B)(ii), 881(c)(2)(B)(ii) and 1471 through 1474 of the Code and the Treasury Regulations thereunder.

(e) If the Tranche A Closing does not occur on the tenth Business Day following the Effective Date, Purchaser shall provide to Seller a schedule containing an updated table of Tranche A Scheduled Quarterly Amounts based upon the Tranche A Closing Date, which schedule shall supersede the table in Section 2.1(a)(i) and shall be incorporated into and become a part of this Agreement.

1.7 CONDITIONS TO PURCHASER'S OBLIGATIONS FOR TRANCHE B TRANSACTION.

(a) An executive officer of Seller shall have delivered to Purchaser a certificate (the ***"Bring-Down Certificate"***), dated as of the Tranche B Closing Date and duly executed (A) as to the accuracy in all material respects of Seller's representations and warranties in this Agreement as of the Tranche B Closing Date (other than those made as of a specified date earlier than then Tranche B Closing Date); (B) as to the accuracy in all material respects of each of Seller's representations and warranties in this Agreement as of a specified date earlier than the Tranche B Closing Date; and (C) as to Seller's compliance with and performance of in all material respects each of its covenants and obligations to be performed or complied with at or before the Tranche B Closing Date.

(b) The Bring-Down Certificate shall be accompanied by an Updated Disclosure Schedule if Seller has determined, in its sole discretion, that such Updated Disclosure Schedule is necessary in order to satisfy the conditions set forth in Section 1.7(a)(B), which Updated Disclosure Schedule shall be satisfactory to Purchaser in its sole discretion, provided that Purchaser may not withhold approval to the Updated Disclosure Schedule solely on the basis of changes that are immaterial in nature or as to matters of form.

(c) All Tranche A Scheduled Quarterly Amounts then payable shall have been paid in full.

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(d) From the Effective Date, there shall not have occurred any Material Adverse Effect, nor shall any event or events have occurred that, individually or in the aggregate, with or without the lapse of time, could reasonably be expected to result in a Material Adverse Effect; provided that if a Material Adverse Effect has occurred following the Effective Date and this condition to the Tranche B Transaction is knowingly waived in writing by Purchaser with respect to such specific Material Adverse Effect, then Purchaser shall also waive any other rights it may have under this Agreement with respect to such Material Adverse Effect.

(e) Seller shall have delivered a written certification to Purchaser that it has no Knowledge of a Material Adverse Effect as of the Tranche B Closing Date.

1.8 CONDITIONS TO SELLER'S OBLIGATIONS FOR TRANCHE B TRANSACTION.

(a) Pharmakon shall have delivered to Seller a certificate, dated as of the Tranche B Closing Date and duly executed (A) as to the accuracy in all material respects of each of Purchaser's representations and warranties in this Agreement as of the Tranche B Closing Date (other than those made as of a specified date earlier than the Tranche B Closing Date); (B) as to the accuracy in all material respects of each of Purchaser's representations and warranties in this Agreement as of a specified date earlier than the Tranche B Closing Date; and (C) as to Purchaser's compliance with and performance of in all material respects each of its covenants and obligations to be performed or complied with at or before the Tranche B Closing Date.

(b) Purchaser shall provide to Seller such new or updated forms, as described in Section 1.6(d), as are, in Seller's good faith judgment, reasonably required pursuant to the requirements of the Code and Treasury Regulations described in Section 1.6(d).

(c) Purchaser shall provide to Seller the amount of the Tranche B Final Amount, calculated in accordance with Section 2.1(a)(ii) based upon the Tranche B Closing Date, and all references to the Tranche B Final Amount in this Agreement shall be deemed to refer to such amount.

(d) Purchaser shall have delivered a written certification to Seller that it has no Knowledge of a Material Adverse Effect as of the Tranche B Closing Date.

1.9 RETAINED RIGHTS; NO ASSUMED OBLIGATIONS; SELLER AUTHORITY. Notwithstanding any provision in this Agreement to the contrary:

(a) Purchaser is acquiring only the Purchased Receivables and does not, by purchase of the Purchased Receivables hereunder, acquire any other assets of Seller or its Affiliates other than the Purchased Receivables, and Seller shall retain all its right, title and interest in and to all Excluded Assets;

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(b) Purchaser does not, by purchase of the Purchased Receivables hereunder, assume any Liability of Seller or any of its Affiliates. All such Liabilities will be retained by and remain Liabilities of Seller or its Affiliates; and

(c) Except as otherwise expressly provided herein, Seller has sole discretion, authority and responsibility for the research, development, commercialization and exploitation of the Product, including regulatory compliance, intellectual property protection, manufacturing, marketing, clinical development, distribution, sales, product liability and reimbursement with respect thereto.

ARTICLE 2

PAYMENTS; RECORDS AND AUDITS

2.1 PAYMENTS DUE TO PURCHASER.

(a) (i) *Tranche A Scheduled Quarterly Amounts*. Subject to the Quarterly Cap in Section 2.1(b) and to the limitations in Section 2.1(d) and Section 2.1(f), Seller will, or will cause its Affiliates to, during the Payment Period, as applicable, pay Purchaser the scheduled quarterly amount set forth in the corresponding table below (each, a ***"Tranche A Scheduled Quarterly Amount"***):

each Calendar Quarter occurring	Scheduled Quarterly Amount
in 2014	$3,000,000 *plus* the Make-Whole Premium, if any
in 2015	$5,000,000 *plus* the Make-Whole Premium, if any
in 2016	$5,000,000 *plus* the Make-Whole Premium, if any
in 2017	$5,000,000 *plus* the Make-Whole Premium, if any
in the first Calendar Quarter of 2018	$1,700,000 *plus* the Make-Whole Premium, if any

(ii) *Tranche B Scheduled Quarterly Amounts*. In the event that the Tranche B Closing occurs and subject to the Quarterly Cap in Section 2.1(b) and to the limitations in Section 2.1(d) and Section 2.1(f), Seller will, or will cause its Affiliates to, during the Payment Period, as applicable, pay Purchaser the scheduled quarterly amount set forth in the corresponding table below (each, a ***"Tranche B Scheduled Quarterly Amount"***):

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each Calendar Quarter occurring	Scheduled Quarterly Amount
in 2014	$4,000,000 *plus* the Make-Whole Premium, if any
in 2015	$5,300,000 *plus* the Make-Whole Premium, if any
in 2016	$5,300,000 *plus* the Make-Whole Premium, if any
in 2017	$5,300,000 *plus* the Make-Whole Premium, if any
in the first Calendar Quarter of 2018	the Tranche B Final Amount (as set forth below) *plus* the Make-Whole Premium, if any

The ***"Tranche B Final Amount"*** shall be calculated as follows:

If the Tranche B Closing Date occurs on any of the following dates (each a "Fixed Tranche B Date"):	Then, the Tranche B Final Amount shall be:
April 30, 2013	$ 8,800,000
May 31, 2013	$ 7,600,000
July 1, 2013	$ 6,400,000
July 31, 2013	$ 5,300,000
August 30, 2013	$ 4,200,000
September 30, 2013	$ 3,000,000
October 31, 2013	$ 1,900,000
November 29, 2013	$ 800,000
December 23, 2013	$ 0

If the Tranche B Closing Date occurs on any day other than a Fixed Tranche B Date, then the Tranche B Final Amount shall be prorated based on the number of days between the

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previous and next Fixed Tranche B Date. For the avoidance of doubt, the Tranche B Final Amount shall never be greater than $8,800,000 or less than $0.

(iii) The Scheduled Quarterly Amount will be calculated and payable by Seller or its Affiliates on a Calendar Quarter basis during the Payment Period, and Seller will, or will cause its Affiliates to, pay the Scheduled Quarterly Amount to Purchaser within *** after the end of such Calendar Quarter (each, a "***Payment Date***").

(b) Each Calendar Quarter during the Payment Period (other than the Scheduled Quarterly Amount payable for the first Calendar Quarter of 2018 which, for the avoidance of doubt, will not be subject to a Quarterly Cap), the Scheduled Quarterly Amount payable by Seller and its Affiliates pursuant to Section 2.1(a) will be subject to a cap of twenty-five percent (25%) of Net Sales for any such Calendar Quarter (each, a ***"Quarterly Cap"***). In the event a Scheduled Quarterly Amount shall be subject to a Quarterly Cap for any particular Calendar Quarter (other than the Scheduled Quarterly Amount payable for the first Calendar Quarter of 2018 which, for the avoidance of doubt, will not be subject to a Quarterly Cap), Seller shall first make payment of the Tranche A Scheduled Quarterly Amount and then, to the extent the Quarterly Cap has not been attained with such payment, Seller shall make payment of the Tranche B Scheduled Quarterly Amount up to the Quarterly Cap.

(c) Notwithstanding Section 2.1(b) above, the Parties acknowledge and agree that Seller shall be permitted to make payments of Scheduled Quarterly Amounts irrespective of attainment of any Quarterly Cap (or any portion thereof) using funds from any source, and not necessarily out of revenues derived from Net Sales in the Territory for the applicable period.

(d) Seller shall have the option to prepay all Scheduled Quarterly Amounts due hereunder at any time during the Payment Period for an amount equal to the Outstanding Payment Amount (the "***Payoff Date***"). Seller shall provide written notice to Purchaser of the exercise of this option not less than *** prior to the Payoff Date. Upon payment of the Outstanding Payment Amount on the Payoff Date, neither Seller nor any of its Affiliates will have any obligation to pay to Purchaser any additional Scheduled Quarterly Amount pursuant to this Section 2.1 and this Agreement and the other Transaction Documents shall terminate.

(e) All payments of Scheduled Quarterly Amount under this Section 2.1 and any other payment made by Seller or its Affiliates to Purchaser under this Agreement will be made in U.S. dollars by wire transfer of immediately available funds, free and clear of all Encumbrances and without offset or reduction by Seller or its Affiliates of any kind, to such account as Purchaser will notify Seller in writing.

(f) Neither Seller nor any of its Affiliates will have any obligation to pay to Purchaser any Scheduled Quarterly Amount pursuant to this Section 2.1 and Purchaser will not have an obligation to fund the Tranche B Amount once Seller satisfied in full its obligations under Section 4.8(m), Section 4.12 or Section 4.13. If Purchaser has funded the Tranche B Amount and a Retail Pharmacy Failure has occurred, neither Seller nor any of its Affiliates will

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have any obligation to pay to Purchaser any Tranche B Scheduled Quarterly Amount once Seller has satisfied its obligations in full under Section 4.14.

2.2 DELIVERABLES DUE TO PURCHASER.

(a) Each Calendar Quarter during the Payment Period, Seller will send a written report to Purchaser on each Payment Date showing (i) the Net Sales for the Calendar Quarter in question (and for that Calendar Year to date), showing in reasonably specific detail how calculated, (ii) a breakdown of such Net Sales by Product and territory, and (iii) any Quarterly Cap applicable to such Scheduled Quarterly Amount (each such report containing the items set forth in this Section 2.2(a)(i) — (iii), a ***"Quarterly Report"***). Seller shall prepare and maintain and shall cause its Affiliates and any Permitted Partner to prepare and maintain reasonably complete and accurate records of the information to be disclosed in each Quarterly Report specified in Section 2.2(a)(i) and (ii).

(b) Within *** after the end of each of the first three Calendar Quarters of a Calendar Year during the Payment Period, Seller will provide Purchaser with copies of the unaudited balance sheets of Seller and its consolidated subsidiaries for the corresponding Calendar Quarter, the related unaudited consolidated statements of income and cash flows for such Calendar Quarter and the notes to such financial statements (the "***Unaudited Financial Statements***") certified by an executive officer of Seller as true and complete in all material respects; provided, however, that Seller's obligation under this Section 2.2(b) shall be satisfied with respect to any Calendar Quarter for which Seller has filed with the Securities and Exchange Commission the Unaudited Financial Statements on Form 10-Q pursuant to the Securities and Exchange Act of 1934, as amended. Each set of the Unaudited Financial Statements shall be the Confidential Information of the Seller.

(c) Within *** after the end of each Calendar Year during the Payment Period, the Seller will provide Purchaser with copies of the audited balance sheets of Seller and its consolidated subsidiaries for such Calendar Year, the related audited consolidated statements of income and cash flows for such Calendar Year and the notes to such financial statements (the ***"Audited Financial Statements"***) certified by an executive officer of Seller as true and complete in all material respects; provided, however, that Seller's obligation under this Section 2.2(c) shall be satisfied with respect to any Calendar Year for which Seller has filed with the Securities and Exchange Commission the Audited Financial Statements on Form 10-K pursuant to the Securities and Exchange Act of 1934, as amended. Each set of the Audited Financial Statements shall be the Confidential Information of Seller.

2.3 RECORDS; AUDIT RIGHTS.

(a) Seller will, and will cause its Affiliates to, consistent with their respective internal financial control and reporting practices and procedures, keep and maintain, for a period of *** from the end of an applicable ***, accounts and records of all data reasonably required to verify payments of Scheduled Quarterly Amounts and Quarterly Reports, to verify and calculate the amounts to be paid to Purchaser under this Agreement.

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(b) During the Term and for *** thereafter, during normal business hours and upon at least *** prior written notice to Seller, but no more frequently than ***, and no more than *** during the Payment Period, Purchaser has the right to audit, through a nationally recognized "Big 4" accounting firm (which firm shall be independent of Seller and Purchaser and their respective Affiliates) mutually acceptable to the Parties (the "***Accounting Firm***"), those accounts and records of Seller and Seller's Affiliates as may be reasonably necessary to verify the accuracy of the Quarterly Reports and the amounts received by Purchaser (provided, however, that, prior to conducting any such audit, the Accounting Firm will have entered into a confidentiality agreement in form and substance reasonably satisfactory to Seller). The Accounting Firm will keep confidential all information obtained during such audit and will issue a written report to Purchaser and to Seller with only: (i) the actual amount of Net Sales made during the *** in question, (ii) the resulting over- or under-payment of Scheduled Quarterly Amounts to Purchaser that occurred during the *** in question; and (iii) the details of any discrepancies between the Scheduled Quarterly Amounts that were paid and the Scheduled Quarterly Amounts that should have been paid. The determination of the actual amount of Scheduled Quarterly Amounts to be paid to Purchaser under this Agreement with respect to any *** will be binding and conclusive on the Parties upon the expiration of *** following the end of such ***, unless an audit of such *** has been initiated before the expiration of such *** period and is on-going, in which case, such determination will be binding and conclusive on the Parties upon completion of such audit. Without limiting the generality of the preceding sentence, absent a substantive error, the report from the Accounting Firm will be final and non-appealable. In the event that either Party identifies a substantive error in the report from the Accounting Firm, the Parties agree to cooperate in good faith with each other and the Accounting Firm to resolve the error and the related report within *** of such Party notifying the Accounting Firm of the substantive error. If the Parties and the Accounting Firm cannot resolve the error to the mutual satisfaction of the Parties within such *** period, then the original determination of the Accounting Firm shall be final and non-appealable.

(c) Purchaser is solely responsible for all the expenses of the Accounting Firm, unless the Accounting Firm's report shows any underpayment by Seller exceeding *** of the payment it owed Purchaser for any of the *** then-being reviewed. If the Accounting Firm's report shows that Seller underpaid by more than ***, Seller is responsible for the reasonable expenses incurred by Purchaser for the Accounting Firm's services. Any payment owed by one Party to another as a result of the audit shall be made within *** of the date that the audit report is deemed to be final and non-appealable, free and clear of any and all Encumbrances. In addition, any payment under this Section 2.3 shall bear interest in accordance with Section 2.5.

2.4 TAXES.

(a) During the Term, Purchaser (i) will provide Seller written notice as soon as reasonably practicable, but in no event later than ***, upon (I) the inaccuracy, obsoletion or invalidity of any form or information provided by Purchaser to Seller pursuant to this Section 2.4, or (II) any assignment of this Agreement or any portion thereof (including the Purchased

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Receivables) pursuant to Section 7.3, (ii) will provide Seller with validly executed IRS Forms in accordance with the provisions of Section 1.6(d) and Section 1.8(b) of this Agreement and will provide Seller (x) updated versions of such Form or Forms (or any successor forms) as required by Applicable Law, and (y) in the event that this Agreement or any portion thereof (including the Purchased Receivables) is assigned pursuant to Section 7.3, the assignee will provide Seller with IRS Forms W-8IMY, W-8BEN and W-9, as applicable, and such additional IRS Form or Forms as are, in Seller's good faith judgment, reasonably required in order to satisfy the requirements of Sections 871(h)(2)(B)(ii), 881(c)(2)(B)(ii) and 1471 through 1474 of the Code and the Treasury Regulations thereunder, subject to the obligation to provide updated versions of such forms (or any successor form) under Section 2.4(a)(ii)(x), and (iii) will provide any other forms or information as Seller may reasonably request in connection with Seller's determination as to the applicability of any withholding Taxes to payments hereunder.

(b) Unless there is (i) a Change in Law, (ii) delivery of a notice pursuant to Section 2.4(a)(i)(I) and failure to cure the inaccuracy, obsoletion or invalidity described in such notice within ***, (iii) a failure to deliver any form or information required by Section 2.4(a)(ii) or (iii), (iv) a failure of any payment (or portion of such payment) pursuant to this Agreement to qualify as portfolio interest within the meaning of Section 871(h) or Section 881(c) of the Code because the person or persons who are treated for U.S. tax purposes as having received such payment or portion are described in Section 871(h)(3) or 881(c)(3) of the Code, or (v) a failure by Purchaser to provide to Seller such information and documents as may be required pursuant to the provisions of Section 1471 through 1474 of the Code and the Treasury Regulations thereunder, Seller shall make all payments to Purchaser under this Agreement free and clear of any withholding or other United States Tax; provided that Seller shall have no responsibility for any Tax imposed on or with respect to a payment because such payment is treated as effectively connected with the conduct of a trade or business in the United States by Purchaser or an Affiliate of Purchaser or is otherwise subject to net income taxation by the United States.

(c) In the event of the occurrence of any of the events described in clauses (i) through (v) of Section 2.4(b), Seller shall be entitled to deduct and withhold from any payments payable or otherwise deliverable pursuant to this Agreement such amounts as may be required to be deducted or withheld therefrom under any provision of federal, state, local or foreign Tax law. To the extent such amounts are so deducted or withheld, such amounts shall be treated for all purposes under this Agreement as having been paid to Purchaser.

(d) Notwithstanding anything in this Agreement to the contrary, the Parties intend the transactions contemplated under this Agreement to be characterized as and treated as debt for all U.S. tax purposes and each Party shall prepare and file all tax returns and reports in a manner consistent with that characterization.

2.5 INTEREST. In the event a payment under this Agreement is not made when due hereunder, the amount of such outstanding payment will accrue interest (from the date such payment is due through and including the date on which full payment is made) at an annual rate equal to the lesser of (a) 12% per annum plus the Prime Rate on the date when the payment was

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due and calculated daily on the basis of a 365-day or 366-day year, as applicable or (b) the maximum rate permitted under Applicable Law; provided, however, that under no circumstances will the maximum interest rate payable under this Section 2.5 exceed 12.75% per annum. Payment of accrued interest will accompany payment of the outstanding payment. ***"Prime Rate"*** means the prime rate as reported in The Wall Street Journal, Eastern U.S. Edition, on the date such payment is due.

2.6 NO OTHER COMPENSATION. Purchaser and Seller hereby agree that the terms of this Agreement fully define all consideration, compensation and benefits, monetary or otherwise, to be paid, granted or delivered by Purchaser to Seller and by Seller to Purchaser in connection with the transactions contemplated herein. Neither Seller nor Purchaser have previously paid or entered into any other commitment to pay, whether orally or in writing, any Seller or Purchaser employee, directly or indirectly, any consideration, compensation or benefits, monetary or otherwise, in connection with the transactions contemplated herein.

ARTICLE 3

REPRESENTATIONS AND WARRANTIES

3.1 REPRESENTATIONS AND WARRANTIES OF SELLER. Seller represents and warrants to Purchaser as of the Effective Date, except as disclosed in the schedules attached hereto, and, in the event the Tranche B Election is made, as of the Tranche B Closing Date, except as disclosed in the Updated Disclosure Schedule, as follows:

(a) Organization. Seller is a corporation duly incorporated and validly existing under the laws of the State of Delaware. Seller is duly qualified to do business as a foreign corporation and is in good standing in every jurisdiction in which the failure to do so would reasonably be expected to result, individually or in the aggregate, in a Material Adverse Effect.

(b) Ownership Rights. To the extent the Purchased Receivables constitute an asset and not an obligation of Seller, Seller is the sole owner of all legal and equitable title to the Purchased Receivables, entitled to exercise its rights in connection therewith, free and clear of all Encumbrances, other than Permitted Encumbrances, such that, upon consummation of this Agreement, Purchaser will become entitled to receive, free and clear of all Encumbrances, other than Permitted Encumbrances, the Purchased Receivables. Seller has not pledged, sold, transferred, conveyed, assigned or delivered any interest in the Purchased Receivables to any other Person, or agreed to do so, other than the Permitted Encumbrances, and to the extent the Purchased Receivables constitute an asset and not an obligation of Seller, Seller has the full right, power and authority to sell, transfer, convey, assign and deliver the Purchased Receivables to Purchaser, free and clear of all Encumbrances, other than the Permitted Encumbrances. Upon the sale, transfer, conveyance, assignment and delivery of the Purchased Receivables to Purchaser pursuant to this Agreement, Purchaser will be the sole owner of all legal and equitable title to the Purchased Receivables, free and clear of any Encumbrances,

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other than the Permitted Encumbrances. Upon the filing of a duly prepared UCC financing statement against the Seller in the proper filing office of the Seller's jurisdiction of organization and to the extent the Purchased Receivables constitute an asset and not an obligation of Seller, there will have been duly filed all financing statements or other similar instruments or documents necessary under the applicable UCC of all applicable jurisdictions in the United States to perfect and maintain the perfection of Purchaser's ownership interest in the Purchased Receivables and of the security interest in the Purchased Receivables granted by Seller to Purchaser pursuant to Section 4.8, in each case, under the UCC.

(c) Authorization. Seller has all requisite power, right and authority, and all material licenses, authorizations, consents and approvals of all Governmental Authorities, in each case, to enter into, execute and deliver this Agreement, the other Transaction Documents to which it is a party and the other documents to be delivered by Seller pursuant to Section 1.5, to sell, assign, transfer, convey and deliver the Purchased Receivables to Purchaser and to perform all of the covenants, agreements, and obligations to be performed by Seller under the Transaction Documents. Seller has (i) all requisite power, right and authority, and (ii) all licenses, authorizations, consents and approvals of all Governmental Authorities, in each case, required to carry on its business as it is presently carried on by Seller, except, in the case of clause (ii) above, where the failure to have such licenses, authorizations, consents or approvals would not reasonably be expected to result in a Material Adverse Effect. The Transaction Documents to which Seller is a party have been duly executed and delivered by an authorized officer of Seller and each constitutes Seller's valid and binding obligation, enforceable against Seller in accordance with its respective terms, subject to bankruptcy, insolvency, reorganization or similar laws affecting the rights of creditors generally and to equitable principles (whether considered in a Proceeding in equity or at law).

(d) No Conflicts. Neither the execution and delivery of this Agreement or the other Transaction Documents by Seller nor the performance or consummation of this Agreement or the other Transaction Documents to which Seller is a party or the transactions contemplated hereby or thereby by Seller will: (i) contravene or conflict with, result in a Breach or violation of, constitute a default or accelerate the performance under (with due notice or lapse of time or both), in any respect, the terms of (A) to Seller's Knowledge, any Applicable Law, (B) any provisions of the certificate of incorporation or bylaws of Seller, or (C) any material contract or agreement to which Seller is a party or by which Seller is bound or committed; or (ii) result in the creation or imposition of any Encumbrance (except as provided in this Agreement and any Permitted Encumbrance) on the Purchased Receivables or the Additional Collateral.

(e) No Consent. The execution and delivery by Seller of this Agreement and the other Transaction Documents, and the performance by Seller of its obligations and the consummation by Seller of any of the transactions contemplated hereby and thereby, do not require any consent, approval, license, order, authorization or declaration from, notice to, action or registration by or filing with any Governmental Authority or any other Person, except for (i) the filing of proper financing statements under the UCC, (ii) the filing of the Patent Security

Agreement with the PTO and (iii) filings required by federal securities laws or stock exchange rules.

(f) Solvency. Immediately after consummation of the transactions contemplated by the Transaction Documents, (i) the fair value of Seller's assets will be greater than the sum of its debts and other obligations, including contingent liabilities, (ii) the present fair saleable value of Seller's assets will be greater than the amount that would be required to pay its probable liabilities on its existing debts and other obligations, including contingent liabilities, as they become absolute and matured, (iii) Seller will not have unreasonably small capital with which to engage in its business, as currently conducted, and (iv) Seller does not have present plans or intentions to incur debts or other obligations or liabilities beyond its ability to pay such debts or other obligations or liabilities as they become absolute and matured in the ordinary course of business. The amount of contingent liabilities at any time shall be computed as the amount that, in the light of all the facts and circumstances existing at such time, represents the amount that can reasonably be expected to become an actual or matured liability.

(g) No Litigation. Except as set forth on Schedule 3.1(g), there is no Proceeding against Seller, or to the Knowledge of Seller, investigation, pending or, to the Knowledge of Seller, threatened against Seller, at law or in equity (including that challenges the validity, ownership or enforceability of any of the Qsymia Patent Rights or Qsymia Trademarks), which, in each case, (i) if adversely determined, would reasonably be expected to have, individually or in the aggregate, a Material Adverse Effect, or (ii) challenges, or may have the effect of preventing, delaying, making illegal or otherwise interfering with, any of the transactions contemplated by any of the Transaction Documents.

(h) Compliance with Laws. Seller is not in violation of, or has violated, or has been given written notice of any violation, or, to the Knowledge of Seller, is under investigation with respect to, or has been threatened to be charged with, any violation of, any Applicable Law that would reasonably be expected to have, individually or in the aggregate, a Material Adverse Effect.

(i) In-Licensees and Sublicensees.

(i) *Existing In-Licenses; No Other In-Licenses*. Except as set forth on Schedule 3.1(i), there are no In-Licenses (any In-License set forth on Schedule 3.1(i), an "***Existing In-License***"). A true, correct and complete copy of each Existing In-License has been provided to the Purchaser by Seller prior to the date hereof. Except as set forth on Schedule 3.1(i), Seller and the respective counterparty thereto have not made or granted any material amendment or waiver of any provision of any Existing In-License. The manufacture, importation, sale, offer for sale or use of the Product does not require Seller to obtain any In-License, in addition to the Existing In Licenses, in order to avoid or resolve any infringement or misappropriation of intellectual property rights or other rights of any other Person, except to the

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extent that such infringement or misappropriation is insignificant to the manufacture, importation, sale, offer for sale or use of the Product.

(ii) *Validity and Enforceability of the In-Licenses*. Each of the Existing In-Licenses is a valid and binding obligation of Seller, and to the Knowledge of Seller, the counterparty thereto. To the Knowledge of Seller, each of the Existing In-Licenses is enforceable against each counterparty thereto in accordance with its terms, except as may be limited by applicable Bankruptcy Laws or by general principles of equity (whether considered in a Proceeding in equity or at law). Seller has not received any written notice in connection with an Existing In-License challenging the validity, enforceability or interpretation of any provision of such agreement.

(iii) *No Liens or Assignments by Seller*. Except as set forth in Schedule 3.1(i), Seller has not, except for Permitted Encumbrances or as contemplated hereby, conveyed, assigned or in any other way transferred or granted any liens upon or security interests with respect to all or any portion of the Collateral.

(iv) *No Termination*. Seller has not (A) given written notice to a counterparty of the termination of any Existing In-License (whether in whole or in part) or any notice expressing any intention or desire to terminate any Existing In-License or (B) received from a counterparty thereto any written notice of termination of any Existing In-License (whether in whole or in part) or any written notice expressing any intention or desire to terminate any Existing In-License.

(v) *No Breaches or Defaults*. There is and has been no material breach or default under any provision of any Existing In-License either by Seller or, to the Knowledge of Seller, by the respective counterparty (or any predecessor thereof) thereto, and there is no event that upon notice or the passage of time, or both, would reasonably be expected to give rise to any breach or default either by Seller or, to the Knowledge of Seller, by the respective counterparty to such agreement.

(vi) *Payments Made*. Seller has made all material payments to the respective counterparty required under each Existing In-License as of the date hereof.

(vii) *No Assignments*. Seller has not consented to any assignment by the counterparty thereto of any of such counterparty's rights or obligations under any Existing In-License and, to the Knowledge of Seller, such counterparty has not assigned any of its rights or obligations under such Existing In-License to any Person.

(viii) *No Indemnification Claims*. Seller has not notified the respective counterparty to any Existing In-License or any other Person of any claims for indemnification under any Existing In-License nor has Seller received any claims for indemnification under any Existing In-License.

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(ix) *No Infringement*. Seller has not received any written notice from, or given any written notice to, any counterparty to any Existing In-License regarding any infringement of any of the Qsymia Patent Rights. To the Knowledge of Seller, but without inquiry, no Third Party is making, using, selling, offering for sale, importing or exporting anything in material violation of any of the Qsymia Patent Rights.

(j) Sublicenses; Out-Licenses. Except as set forth on Schedule 3.1(j), Seller has not entered into or executed a sublicense or other out-license with any other Person in respect of any Qsymia Product Rights (other than the Permitted Qsymia Product Rights).

(k) Third Party Agreements. The Third Party Agreements constitute all of the material agreements for the manufacture, supply, promotion and commercialization of the Product. Seller has delivered to Purchaser true, correct and complete copies of each Third Party Agreement.

(i) *Validity and Enforceability of the Third Party Agreements*. Each of the Third Party Agreements is a valid and binding obligation of Seller, and to the Knowledge of Seller, the counterparties thereto. To the Knowledge of Seller, the Third Party Agreements are enforceable against each of the parties thereto in accordance with their respective terms, except as may be limited by applicable Bankruptcy Laws or by general principles of equity (whether considered in a proceeding in equity or at law). The Seller has not received any written notice in connection with a Third Party Agreement challenging the validity, enforceability or interpretation of any provision of such agreement (except, solely with respect to interpretations, challenges in the ordinary course of business relating to immaterial provisions of such agreement).

(ii) *No Breaches or Defaults*. There is and has been no material breach or default under any provision of any Third Party Agreement either by Seller or, to the Knowledge of Seller, by the respective counterparty (or any predecessor thereof) thereto, and there is no event that upon notice or the passage of time, or both, would reasonably be expected to give rise to any material breach or default either by Seller or, to the Knowledge of Seller, by the respective counterparty to such agreement.

(iii) *Payments Made*. The Seller has made all material payments to the respective counterparty required under each Third Party Agreement as of the date hereof.

(iv) *Amendments or Waivers*. Seller and the respective counterparty thereto have not made or granted any material amendment or waiver of any provision of any Third Party Agreement.

(v) *No Indemnification Claims*. Seller has not notified the respective counterparty to each Third Party Agreement or any other Person of any claims for indemnification under any Third Party Agreement nor has Seller received any claims for indemnification under any Third Party Agreement.

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(l) Compliance.

(i) Seller is not in violation of, and to the Knowledge of the Seller, the Seller is not under investigation with respect to, nor has the Seller been threatened to be charged with or given notice of any violation of, any law or Judgment applicable to the Seller, which violation would reasonably be expected to materially affect the Seller's rights in or to any Qsymia Product Rights or Purchaser's rights with respect to Scheduled Quarterly Amounts hereunder (or, as applicable, the Quarterly Cap, subject to the terms and conditions herein).

(ii) Except as would not reasonably be expected to have a Material Adverse Effect, all applications, submissions, information and data related to the Product submitted or utilized as the basis for any request to any Governmental Entity by or on behalf of the Seller were true and correct in all material respects as of the date of such submission or request, and any updates, changes, corrections or modification to such applications, submissions, information or data required under applicable laws or regulations have been submitted in a timely manner to the necessary Governmental Entities.

(iii) Seller has not committed any act, made any statement or failed to make any statement that would reasonably be expected to provide a basis for the FDA or any other Governmental Entity to invoke its policy with respect to "Fraud, Untrue Statements of Material Facts, Bribery, and Illegal Gratuities", or similar policies, set forth in any applicable laws or regulations, except as would not reasonably be expected to have a Material Adverse Effect.

(m) Intellectual Property

(i) Schedule 3.1(m) contains a complete and accurate list of (A) all of the Patents included within the Qsymia Patent Rights and (B) all of the Qsymia Trademarks. Except as set forth on Schedule 3.1(m), Seller is the registered owner of all of the Qsymia Patent Rights. Schedule 3.1(m) specifies as to each listed patent or patent application (A) the jurisdictions by or in which each such Qsymia Patent Right has issued as a patent or a patent application has been filed, including the respective patent or application numbers, and (B) any other Person owning or having an interest in such Qsymia Patent Right, including the nature of such interest.

(ii) The Qsymia Patents Rights are the only Patents that are owned or controlled by Seller, or under which Seller is empowered to grant licenses, the subject matter of which is necessary in the development, manufacture, use, marketing, promotion, sale or distribution of the Product.

(iii) Except as set forth in Schedule 3.1(m), Seller has not received written notice of, and is not a party to, any pending, and to the Knowledge of Seller there are no threatened, litigations, interferences, reexaminations, oppositions or like procedures involving any of the Qsymia Patent Rights.

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(iv) All of the issued Patents within the Qsymia Patent Rights are in full force and effect and have not lapsed, expired or otherwise terminated. Seller has not received any written notice relating to the lapse, expiration or other termination of any of the issued patents within the Qsymia Patent Rights, or alleging that, and Seller has not received any written legal opinion that alleges that, an issued patent within any of the Qsymia Patent Rights is invalid or unenforceable.

(v) Seller has not received any written notice that there is any, and, to the Knowledge of Seller, there is no, Person who is or claims to be an inventor under any of the Qsymia Patent Rights who is not a named inventor thereof.

(vi) Seller has not and, to the Knowledge of Seller, no counterparty to an Existing In-License has received any written notice of any claim by any Person challenging inventorship or ownership of, the rights of Seller in and to, or the patentability, validity or enforceability of, any of the Qsymia Patent Rights, or asserting that the development, manufacture, importation, sale, offer for sale or use of the Product infringes or will infringe such Person's patents or other intellectual property rights.

(vii) To the Knowledge of Seller, the discovery, development, manufacture, importation, sale, offer for sale or use of the Product, has not and will not, infringe, violate or misuse any patent or other intellectual property rights owned by any Third Person that is not licensed to the Seller under an Existing In-License Agreement. ***

(viii) Seller owns the entire right, title, and interest in, to and under the Qsymia Trademarks, including all goodwill pertaining thereto, the right to conduct business under the Qsymia Trademarks, the right to license others under the Qsymia Trademarks, and all rights to sue, counterclaim and collect damages and payments for claims of past, present and future infringements, unfair competition or misappropriations thereof, and all income, royalties, damages and payments now or hereafter due or payable with respect to the Qsymia Trademarks.

(ix) The Qsymia Trademarks are not subject to any Encumbrance created by, through, or under Seller or any other Person, other than the Permitted Encumbrances.

(x) Seller has not purported to transfer or assign any of the Qsymia Trademarks to any Person, and Seller has not executed any agreement, document or other instrument in conflict herewith.

(xi) To Seller's Knowledge, all Qsymia Trademarks that have been registered with the PTO or other Governmental Authority are currently in compliance in all material respects with all Applicable Law (including the timely post-registration filing of affidavits of use and incontestability and renewal applications or similar documents), and are valid and enforceable.

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(xii) To the Knowledge of Seller, no Qsymia Trademark has been or is now involved in any opposition, invalidation or cancellation Proceeding and, to Seller's Knowledge, no such action is threatened with respect to any of the Qsymia Trademarks.

(xiii) To the Knowledge of Seller, no Person has infringed or otherwise violated, or is infringing or otherwise violating, any of the Qsymia Patent Rights or the Qsymia Trademarks, except to the extent such violation or infringement does not or cannot, reasonably be expected to have a Material Adverse Effect.

(xiv) Seller, and to Seller's Knowledge the counterparty to each In-License, has paid all maintenance fees, annuities and like payments required as of the date hereof with respect to any of the Qsymia Patent Rights.

(n) Supply and Manufacturing. To the Knowledge of Seller, the development, testing, manufacturing, production, storage, packaging, labeling and release to the market of Product is (i) in compliance with the final release quality specifications in effect for the Product and (ii) in compliance in all material respects with Applicable Law. To the Knowledge of Seller, no manufacturer of Product has received or is currently subject to a Form 483, with respect to the manufacture of Product. To the Knowledge of Seller, as of the date hereof, the Seller reasonably expects to have, as of the date of the launch of the Product, sufficient quantities of Product and of a sufficient quality to satisfy Seller's then-estimated demand for Product in the U.S.

(o) No Brokers Fees. Neither Seller nor any of its Affiliates has retained any Person to whom any brokerage commission, finder's fee or other like payment is or will be due in connection with this Agreement or the other Transaction Documents to which Seller is a party or the consummation of the transactions contemplated hereby or thereby.

(p) Subordination. The claims and rights of Purchaser created by any Transaction Document in, to and under the Purchased Receivables are not subordinated to any creditor of Seller or any other Person or Governmental Authority (other than any Permitted Encumbrance imposed by operation of any Applicable Law).

(q) UCC Representations and Warranties. Seller's exact legal name is, and has always been "VIVUS, Inc.". The principal place of business and principal executive offices of Seller where it keeps its books and records relating to the Qsymia Product Rights is, as has been for the preceding five (5) years, located at 1172 Castro Street, Mt. View, California 94040. Seller's Delaware organizational identification number is 2624559 and its Federal Employer Identification Number is 94-3136179.

(r) No Material Liabilities. Except as disclosed on the most recent Unaudited Financial Statements filed with the Securities and Exchange Commission on Form 10-Q or the most recent Audited Financial Statements filed with the Securities and Exchange Commission on Form 10-K, in each case, pursuant to the Securities and Exchange Act of 1934, as amended, there are no material Liabilities of Seller relating to or affecting the Purchased

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Receivables or the Additional Collateral of any kind whatsoever, whether accrued, contingent, absolute, determined, determinable or otherwise, and there is no existing condition or set of circumstances which could reasonably be expected to result, individually or in the aggregate, in any such Liability or in a Material Adverse Effect. Without limiting the generality of the foregoing, as specified in the label for Product, as reported during the clinical trials for Product and as spontaneously reported to the Seller or the FDA, there have been and will continue to be serious adverse events related to use of Product indicating that Product may pose and may continue to pose a significant hazard to humans; however, to the Knowledge of Seller, no material Liabilities have resulted from these reports to date.

(s) No Encumbrances; No Indebtedness.

(i) Without limiting the generality of any of the representations or warranties of Seller to Purchaser herein, no Encumbrance exists on the Collateral (other than Permitted Encumbrances).

(ii) Except as disclosed on the most recent Form 10-K, including the Audited Financial Statements and notes thereto, filed with the Securities and Exchange Commission pursuant to the Securities and Exchange Act of 1934, as amended, Seller is not a party to or otherwise bound by any contract, agreement, commitment or instrument that provides for the incurrence by Seller of Indebtedness in an aggregate principal amount in excess of $5,000,000.

(t) REMS Modification. Seller has delivered to Purchaser true and complete copies of all material documentation and materials in its possession which have been provided to or received from the FDA or any other Governmental Authority as part of or otherwise related to the REMS Modification submission to the FDA. Seller has not received any written notice (whether from the FDA or any other Governmental Authority) that the REMS Modification will or will not be approved.

(u) Disclosure. Seller has delivered or made available to Purchaser true and complete copies of each agreement, data, contract or other document or information (other than data and information of a general economic or industry nature) that is referred to in this Agreement or that has been requested in writing by Purchaser. To the Knowledge of Seller, no representation or warranty by Seller contained in this Agreement or any other Transaction Document (other than in respect of information of a general economic or industry nature) contains when made or certified any untrue statement of a material fact or omits to state any material fact necessary in order to make any statement contained herein or therein not misleading in any material respect at such time in light of the circumstances under which such representation or warranty was made (it being recognized by the Purchaser that any projections and forecasts provided by or on behalf of the Seller are based on good faith estimates and assumptions believed by the Seller to be reasonable as of the date of the applicable projections or assumptions, subject to uncertainties and contingencies, many of which are beyond the control of the Seller and that actual results during the period or periods covered by any such

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projections and forecasts may differ from projected or forecasted results); provided that, for clarity, this representation and warranty has no effect on any other representation or warranty by Seller contained in this Agreement or any other Transaction Document.

3.2 REPRESENTATIONS AND WARRANTIES OF PURCHASER. Purchaser represents and warrants to Seller, as of the Effective Date and, in the event the Tranche B Election is made, then as of the Tranche B Closing Date, as follows:

(a) Organization. Purchaser is a Cayman Islands exempted limited partnership, duly formed and validly existing under the laws of the Cayman Islands.

(b) Authorization. Purchaser has all necessary power, right and authority and all licenses, authorizations, consents and approvals of all Governmental Authorities required to carry on its business as it is presently carried on by Purchaser, to enter into, execute and deliver this Agreement and the other Transaction Documents to which it is a party and to perform all of the covenants, agreements, and obligations to be performed by Purchaser

hereunder and under the Transaction Documents to which it is a party. This Agreement and the other Transaction Documents to which it is a party have been duly executed and delivered by Purchaser and each constitutes Purchaser's valid and binding obligation, enforceable against Purchaser in accordance with its respective terms, subject to bankruptcy, insolvency, reorganization or similar laws affecting the rights of creditors generally and to equitable principles.

(c) No Conflicts. Neither the execution and delivery of this Agreement or any other Transaction Documents by Purchaser nor the performance or consummation of this Agreement or any other Transaction Documents to which it is a party or the transactions contemplated hereby or thereby by Purchaser will contravene or conflict with, result in a Breach or violation of, constitute a default or accelerate the performance under (with due notice or lapse of time or both), in any respect, the terms of: (i) to Purchaser's Knowledge, any Applicable Law; (ii) any material contract, agreement, or other arrangement to which Purchaser is a party or by which Purchaser or any of its assets is bound or committed; or (iii) the applicable organizational or constitutional documents of Purchaser.

(d) No Consent. Other than the filing of any documentation contemplated by Sections 4.7 and 4.8, no consent, approval, license, order, authorization, registration, declaration or filing with any Governmental Authority or any other Person is required by Purchaser in connection with the execution and delivery by Purchaser of this Agreement or the other Transaction Documents to which it is a party, the performance by Purchaser of its obligations under this Agreement and any other Transaction Document to which it is a party or the consummation by Purchaser of any of the transactions contemplated hereby or thereby.

(e) No Brokers Fees. Neither Purchaser nor any of its Affiliates has retained any Person to whom any brokerage commission, finder's fee or other like payment is or will be due in connection with this Agreement or the other Transaction Documents to which Purchaser is a party or the consummation of the transactions contemplated hereby or thereby.

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(f) No Litigation. There is no Proceeding against Purchaser, at law or in equity which challenges, or may have the effect of preventing, delaying, making illegal or otherwise interfering with, any of the transactions contemplated by any of the Transaction Documents.

(g) Financing. Purchaser has sufficient cash on hand or binding and enforceable commitments to provide it with funds sufficient to satisfy its obligations to pay the Purchase Price. Purchaser has no reason to believe, and has not been provided with any notice (whether written or otherwise), that any of the Persons providing the commitments referred to above are unable or are not required or do not intend, for any reason, to satisfy their obligations under such commitments. Purchaser acknowledges that its obligations under this Agreement are not contingent on obtaining financing.

(h) Tax Status. Purchaser is a foreign disregarded entity that is wholly owned by a foreign partnership, in each case for United States federal income tax purposes.

(i) Other Aspects of Purchaser's Status. None of Purchaser, the foreign partnership that wholly owns Purchaser, or any direct partner in such foreign partnership is (i) a "10-percent shareholder" of Seller within the meaning of Sections 871(h)(3) and 881(c)(3)(B) of the Code, (ii) a "bank" within the meaning of Section 881(c)(3)(A) of the Code, or (iii) a "controlled foreign corporation" within the meaning of Section 881(c)(3)(C) of the Code.

3.3 NO GUARANTEES. The Parties acknowledge and agree that (a) Purchaser is assuming all market risk associated with Product and, as such, will have no recourse against Seller or any of Seller's Affiliates based on the failure of the sales of Product to meet its or any other Person's projections, and (b) nothing in this Agreement shall be construed to constitute a guarantee by Seller regarding the commercial viability or economic potential of any Product in the marketplace.

3.4 DISCLAIMER OF WARRANTIES. EXCEPT AS EXPRESSLY SET FORTH IN THIS AGREEMENT OR ANY OTHER TRANSACTION DOCUMENT, EACH PARTY EXPRESSLY DISCLAIMS, WAIVES, RELEASES, AND RENOUNCES ANY WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY OF MERCHANTABILITY, NONINFRINGEMENT OR FITNESS FOR A PARTICULAR PURPOSE.

ARTICLE 4

COVENANTS OF SELLER; SECURITY INTEREST

Seller covenants and agrees with Purchaser that for the duration of the Term, Seller will perform the obligations set forth below:

4.1 SELLER'S RESPONSIBILITIES.

(a) Seller will use Commercially Reasonable Efforts to pursue the Funded

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Activities.

(b) Without limiting the generality of clause (a) above, the Seller will, each Calendar Quarter, use Commercially Reasonable Efforts to allocate a sufficient level of resources (both monetary and personnel) for the promotion and marketing of Product in the Territory.

(c) Seller agrees to use Commercially Reasonable Efforts to fund the expenses associated with the discovery, development and commercialization of Product, including the Funded Activities.

(d) With respect to the Product, Seller will use Commercially Reasonable Efforts to provide, or cause to be provided, a sufficient and consistent supply of such Product or the active pharmaceutical ingredient in such Product, as applicable.

(e) With respect to the performance of this Agreement and the activities contemplated hereby, Seller will, and will cause its Affiliates to, comply with all Applicable Law, except where compliance therewith is contested in good faith by appropriate proceedings or is not reasonably expected to result in a Material Adverse Effect.

(f) Seller will, and will cause its Affiliates to, use Commercially Reasonable Efforts to maintain the Regulatory Approvals and all other FDA, FFDCA and other Governmental Authority approvals, including complying with any and all requirements for post-approval follow-up studies and information reporting, except where the failure to maintain the Regulatory Approvals and other Governmental Authority approvals is not reasonably expected to result in a Material Adverse Effect.

(g) Seller will, and will cause its Affiliates to, use Commercially Reasonable Efforts to maintain its relationships with Third Person manufacturers and suppliers; provided, however, that notwithstanding the foregoing, Seller is permitted to terminate its relationships with Third Person manufacturers and suppliers in its sole discretion provided that such termination is not reasonably expected to result in a Material Adverse Effect.

(h) Seller will, and will cause its Affiliates to, use Commercially Reasonable Efforts to obtain consents from any licensee or sublicensee of Qsymia Patent Rights necessary to provide Purchaser, directly or indirectly, with copies of royalty reports delivered by such licensee or sublicensee to Seller.

(i) Seller will, and will cause its Affiliates to, use Commercially Reasonable Efforts to obtain approval for the REMS Modification. For the avoidance of doubt, so long as Seller and its Affiliates use such Commercially Reasonable Efforts, the ultimate failure to obtain the REMS Modification shall not be deemed a breach of this Section 4.1(i).

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4.2 INTELLECTUAL PROPERTY MATTERS.

(a) Seller shall promptly inform Purchaser of any infringement by a Third Person of any Qsymia Patent Right that would reasonably be expected to adversely affect in any material respect Product. Seller shall provide to Purchaser a copy of any written notice of any such infringement of any Qsymia Patent Rights delivered or received by the Seller, as well as copies of material correspondence related thereto, as soon as practicable and in any event not more than *** following such delivery or receipt.

(b) Seller shall promptly inform Purchaser by written notice of the initiation of an Enforcement Action regarding any infringement by a Third Person of any Qsymia Patent Right that would reasonably be expected to adversely affect in any material respect Product.

(c) If the Seller recovers monetary damages from a Third Person in an action brought for such Third Person's infringement of any of the Qsymia Patent Rights, where such damages, whether in the form of judgment or settlement, result from such infringement of such Qsymia Patent Rights, such recovery will be allocated first to the reimbursement of any expenses incurred by the Seller or a Permitted Partner in such litigation, and any remaining amounts that are not awarded as a multiple of compensatory damages for willful infringement will be treated as Net Sales of the Product. All costs and expenses (including attorneys' fees and expenses) incurred by a Party hereto in connection with any Enforcement Action shall be borne by such Party.

(d) With respect to the Qsymia Patent Rights, Seller will, and will cause its Affiliates to, use Commercially Reasonable Efforts to (i) prosecute each pending patent application and (ii) maintain, keep in full force and effect and seek available patent term extensions for each such Patent.

(e) With respect to the Qsymia Trademarks, Seller will, and will cause its Affiliates to, use Commercially Reasonable Efforts to (i) prosecute each pending trademark application and (ii) maintain, keep in full force and effect and seek available trademark term extensions for each such trademark.

(f) Notwithstanding Seller's obligations in Sections 4.2(d) and (e), Seller may decline to prosecute or maintain any Qsymia Patent Right or any Qsymia Trademark that (i) in Seller's reasonable discretion, is no longer necessary or useful for the development, manufacture, sale or commercialization of Product; provided that such failure to prosecute or maintain such Qsymia Patent Right or Qsymia Trademark would not reasonably be expected to result in a Material Adverse Effect and (ii) Seller may only decline to prosecute or maintain such Patent if Seller satisfies the Patent Abandonment Requirements.

4.3 COMMERCIALIZATION OF THE PRODUCT. Seller hereby agrees to use its Commercially Reasonable Efforts to take, or cause to be taken, all actions and to do, or cause to be done, all things reasonably necessary to maximize Net Sales of the Product and Commercialize the Product.

4.4 RESTRICTIVE COVENANTS. Seller will not, nor shall it permit any Subsidiary of

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the Seller to, without the prior written consent of Purchaser:

(a) incur, create, issue, assume, Guaranty, suffer to exist or otherwise become liable for or with respect to, or become responsible for, the payment or performance of, contingently or otherwise, whether present or future, Indebtedness in an amount at any time outstanding greater than the sum of EBITDA for the four (4) full Calendar Quarters immediately preceding such incurrence, creation, issuance, assumption, Guarantee, existence, liability or responsibility, other than Permitted Indebtedness**;**

(b) declare or pay any cash dividend or make any cash distribution on its capital stock (other than (i) dividends and distributions by a Subsidiary to another Subsidiary or the Seller and (ii) the repurchase of capital stock issued to employees, directors or officers upon the death, disability or termination of employment of such person), unless, following the payment of any such cash dividend or distribution Seller's cash and cash equivalents are in excess of $150,000;

(c) amend, restate, supplement or otherwise modify its certificate of incorporation or bylaws (or other organizational or constitutional documents) in any respect except for such amendments, restatements, supplements or modifications that: (i) do not adversely affect in any material respect the interests of Purchaser under this Agreement or in the Collateral and (ii) could not reasonably be expected to have a Material Adverse Effect;

(d) create, grant or suffer to exist any Encumbrance on any of the Collateral other than as required under this Agreement and other than Permitted Encumbrances;

(e) subject to the Patent Abandonment Requirements, abandon Qsymia Patent Rights; or

(f) commit to do or engage in any of the foregoing.

4.5 RELEVANT INFORMATION. In addition to, and not in limitation of, the other provisions of this Agreement, Seller will provide Purchaser with written notice as promptly as practicable (and in any event within ***) after obtaining Knowledge of any of the following:

(a) the occurrence of a Default or an Event of Default;

(b) that any representation or warranty made by Seller in this Agreement or any other Transaction Document or in any certificate delivered to Purchaser pursuant hereto or thereto that is qualified by materiality shall prove to be untrue, inaccurate or incomplete on the date as of which made, or that any representation or warranty made by Seller in this Agreement or any other Transaction Document that is not qualified by materiality shall prove to be untrue, inaccurate or incomplete in any material respect on the date as of which made;

(c) any event, occurrence or development that would reasonably be expected, individually or in the aggregate, to result in a Material Adverse Effect;

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(d) the occurrence of a Change of Control;

(e) any information reasonably requested by Purchaser to determine whether a Promotion and Marketing Failure or Retail Pharmacy Failure has occurred; or

(f) any official written communication from the FDA relating to the REMS Modification through the earlier of (i) the date on which the Seller announces publicly that the REMS Modification is available and (ii) December 31, 2013.

4.6 TRUE SALE. Purchaser and Seller intend and agree that the sale, conveyance, assignment and transfer of the Purchased Receivables shall constitute a true sale by Seller to Purchaser of the Purchased Receivables that is absolute and irrevocable and that provides Purchaser with the full benefits and detriments of ownership of the Purchased Receivables, and neither Purchaser nor Seller intends the transactions contemplated hereunder to be a financing transaction, borrowing or a loan from Purchaser to Seller, except as provided in Section 2.4(d). Each Party further agrees that it will treat the sale of the Purchased Receivables as a sale of an "account" in accordance with the UCC. Seller disclaims any ownership interest in the Purchased Receivables upon execution of this Agreement and each of Seller and Purchaser waives any right to contest or otherwise assert that this Agreement is other than a true, absolute and irrevocable sale and assignment by Seller to Purchaser of the Purchased Receivables under Applicable Law, which waiver will be enforceable against the applicable Party in any bankruptcy, insolvency or similar proceeding relating to such Party, except to the extent required by GAAP or the rules of the SEC. Seller authorizes and consents to Purchaser filing, including with the Secretary of State of the State of Delaware, one or more UCC financing statements (and continuation statements with respect to such financing statements when applicable) or other instruments and notices, in such manner and in such jurisdictions as in Purchaser's determination may be necessary or appropriate to evidence the purchase, acquisition and acceptance by Purchaser of the Purchased Receivables hereunder and to perfect and maintain the perfection of Purchaser's ownership in the Purchased Receivables and the security interest in the Purchased Receivables granted by Seller to Purchaser pursuant to Section 4.7; provided, however, that Purchaser will provide Seller with a reasonable opportunity to review any such financing statements (or similar documents) prior to filing and the description of the collateral identified in any such financing statement shall be limited to the "Collateral" as defined herein. For greater certainty, Purchaser will not file this Agreement in connection with the filing of any such financing statements (or similar documents). For sake of clarification, the foregoing statements in this Section 4.6 shall not bind either party regarding the reporting of the transactions contemplated hereby for GAAP or SEC reporting purposes.

4.7 PRECAUTIONARY SECURITY INTEREST IN PURCHASED RECEIVABLES. Without limiting Section 4.8 and as set forth in Section 4.6, it is the intent and expectation of both Seller and Purchaser that the sale, conveyance, assignment and transfer of the Purchased Receivables be a

true, irrevocable and absolute sale by Seller to Purchaser for all purposes. Notwithstanding the foregoing, in an abundance of caution to address the possibility that, notwithstanding that Seller and Purchaser expressly intend and expect for the sale, conveyance, assignment and

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transfer of the Purchased Receivables hereunder to be a true and absolute sale and assignment for all purposes, in the event that such sale and assignment will be characterized as a loan or other financial accommodation and not a true sale or such sale will for any reason be ineffective or unenforceable as such, as determined in a judicial, administrative or other proceeding (any of the foregoing being a "***Recharacterization***"), then this Agreement will be deemed to constitute a security agreement under the UCC and other Applicable Law. For this purpose and without being in derogation of the intention of Seller and Purchaser that the sale of the Purchased Receivables will constitute a true sale thereof, effective as of the Tranche A Closing Date, Seller does hereby grant to Purchaser a continuing security interest of first priority in all of Seller's right, title and interest in, to and under the Purchased Receivables, whether now or hereafter existing, and any and all "proceeds" thereof (as such term is defined in the UCC), in each case, for the benefit of Purchaser as security for the prompt and complete payment of a loan deemed to have been made in an amount equal to the Purchase Price actually paid to Seller together with the performance when due of all of Seller's obligations now or hereafter existing under this Agreement and the other Transaction Documents, which security interest will, upon the filing of a duly prepared financing statement in the appropriate filing office and to the extent the Purchased Receivables constitute an asset and not an obligation of Seller, be perfected and prior to all other Encumbrances thereon (other than Permitted Encumbrances) to the extent such security interest can be perfected under the UCC by the filing of a financing statement in the appropriate filing office. Purchaser will have, in addition to the rights and remedies which it may have under this Agreement, all other rights and remedies provided to a secured creditor after default under the UCC and other Applicable Law, which rights and remedies will be cumulative. Seller hereby authorizes Purchaser, as secured party, to file the UCC financing statements contemplated by Section 4.6. In the case of any Recharacterization, each of Seller and Purchaser represents and warrants as to itself that each remittance of payments of the Scheduled Quarterly Amount, in respect of the payments of the Scheduled Quarterly Amount or any other payment owed by Seller to Purchaser under this Agreement, will have been in payment of a debt incurred by Seller in the ordinary course of business or financial affairs of Seller and Purchaser, and made in the ordinary course of business or financial affairs of Seller and Purchaser.

4.8 SECURITY INTEREST IN ADDITIONAL COLLATERAL; REMEDIES.

(a) Seller hereby grants to Purchaser a security interest in all of Seller's right, title and interest in, to and under the Additional Collateral, to secure the prompt and complete payment and performance when due of all obligations of Seller hereunder and under the other Transaction Documents owing to the Purchaser, which security interest will, upon the filing of a duly prepared financing statement in the appropriate filing office (and the filing of the Patent Security Agreement with the PTO), be perfected and prior to all other Encumbrances thereon (other than the Permitted Encumbrances).

(b) Seller will notify Purchaser in writing at least *** (or such shorter period of time as may be agreed to by Purchaser) prior to any change in, or amendment or alteration to, (i) its legal name, (ii) its form or type of organizational structure or jurisdiction of organization (including its status as a corporation organized under the laws of the State of Delaware), or (iii)

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its Federal Employer Identification Number or state organizational identification number. Seller agrees not to effect or permit any such change referred to above unless all filings have been made under the UCC or otherwise that are required in order for Purchaser to continue at all times following such change to have a valid, legal and perfected Encumbrance (prior and superior in right and interest to any other Person (other than Permitted Encumbrances)) in all the Collateral.

(c) Without limiting the generality of Section 7.4(a), Seller will execute any and all further documents, financing statements, agreements and instruments, and take all further action that Purchaser may reasonably request, in order to grant, create, preserve, enforce, protect and perfect the validity and priority of the security interests and other Encumbrances created by this Agreement in the Collateral. Without limiting the foregoing, Seller will do or cause to be done all acts and things that Purchaser from time to time may reasonably request, to assure and confirm that Purchaser holds duly created and enforceable and perfected Encumbrances upon the Collateral (including any property or assets that are acquired or otherwise become Collateral after the date of this Agreement), in each case, as contemplated by, and with the lien priority required under, this Agreement. Nothwithstanding the foregoing, this Section 4.8(c) shall not obligate the Seller to otherwise undertake collateral perfection or protection obligations not otherwise required under the Transaction Documents (it being understood that perfection obligations with respect to Collateral that is perfected by delivery or control shall only be as expressly required pursuant to other provisions of this Agreement or the Transaction Documents, and, except as otherwise expressly provided in the Transaction Documents, actions with respect to Collateral that is not subject to perfection under the UCC or by filing a Patent Security Agreement with the PTO shall not be required unless reasonably requested by Purchaser, including such actions in jurisdictions other than the United States or a State thereof).

(d) Upon the request of Purchaser at any time after the occurrence and during the continuance of an Event of Default, Seller will permit Purchaser or any advisor, auditor, consultant, attorney or representative acting for Purchaser, upon reasonable notice to Seller and during normal business hours, to make extracts from and copy the books and records of Seller (and its Affiliates, as applicable) relating to the Collateral, and to discuss any matter pertaining to the Collateral with the officers and employees of Seller (and its Affiliates, as applicable).

(e) Unless in connection with (i) the occurrence of a Change of Control (for which Purchaser shall be paid in accordance with Section 4.12), (ii) a Permitted Partnering Agreement, or (iii) a Permitted Action, Seller will not, and will cause its Affiliates not to (A) directly or indirectly, sell, transfer, assign, lease, license, sublicense, convey or otherwise directly or indirectly dispose of any of the Collateral or any interest therein or (B) except

for the security interest in the Collateral granted to Purchaser, cause or suffer to exist or become effective any Encumbrance of any kind, other than a Permitted Encumbrance, on or with respect to any of the Collateral or any interest therein, or, in each case, enter into any agreement to do any of the foregoing.

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(f) Upon the occurrence and during the continuance of an Event of Default, Purchaser will have in any jurisdiction in which enforcement hereof is sought, in addition to all other rights and remedies granted in this Agreement, at law or in equity (including as set forth in Section 4.8(m)) with respect to the Collateral, the rights and remedies of a secured party under the UCC (whether or not in effect in the jurisdiction where such rights are exercised) or other Applicable Law.

(g) Seller agrees that, upon the occurrence and during the continuance of an Event of Default, Purchaser will have the right, subject to Applicable Law and subsection (n) below, to sell or otherwise dispose of all or any part of the Collateral, at public or private sale, for cash, upon credit or for future delivery as Purchaser shall deem appropriate. Each purchaser at any such sale shall hold the property sold absolutely, free from any claim or right on the part of Seller.

(h) Purchaser will give Seller not less than *** prior written notice of the time and place of any such proposed sale. Any such notice will (i) in the case of a public sale, state the time and place fixed for such sale, (ii) in the case of a private sale, state the day after which such sale may be consummated, (iii) contain the information specified in Section 9-613 of the UCC, (iv) be authenticated and (v) be sent to the parties required to be notified pursuant to Section 9-611(c) of the UCC; provided that, if Purchaser fails to comply with this sentence in any respect, its liability for such failure shall be limited to the liability (if any) imposed on it as a matter of law under the UCC. Seller agrees that such written notice will satisfy all requirements for notice to Seller that are imposed under the UCC or other Applicable Law with respect to the exercise of Purchaser's rights and remedies hereunder upon default. Purchaser will not be obligated to make any sale or other disposition of any Collateral if it shall determine not to do so, regardless of the fact that notice of sale or other disposition of such Collateral shall have been given. Purchaser may, without notice or publication, adjourn any public or private sale or cause the same to be adjourned from time to time by announcement at the time and place fixed for sale, and such sale may, without further notice, be made at the time and place to which the same was so adjourned.

(i) Any such public sale will be held at such time or times within ordinary business hours and at such place or places as Purchaser may fix and state in the notice of such sale. At any sale or other disposition following the occurrence and during the continuance of an Event of Default, the Collateral, or portion thereof, to be sold may be sold in one lot as an entirety or in separate parcels, as Purchaser may (in its sole and absolute discretion) determine. If any of the Collateral is sold, leased, or otherwise disposed of by Purchaser on credit, the obligations secured by the security interests granted herein shall not be deemed to have been reduced as a result thereof unless and until payment in full is received thereon by Purchaser.

(j) At any such public (or, to the extent permitted by Applicable Law, private) sale made pursuant hereto, Purchaser may bid for or purchase, free (to the extent permitted by Applicable Law) from any right of redemption, stay, valuation or appraisal on the part of Seller, the Collateral or any part thereof offered for sale, and Purchaser may make

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payment on account thereof by using any or all of the obligations secured by the security interests granted herein as a credit against the Purchase Price actually paid to Seller, and Purchaser may, upon compliance with the terms of sale, hold, retain and dispose of such property without further accountability to Seller therefor.

(k) As an alternative to exercising the power of sale herein conferred upon it, Purchaser may, upon the occurrence and during the continuance of an Event of Default, proceed by a suit or suits at law or in equity to foreclose upon the Collateral and, subject to subsection (n) below, to sell the Collateral or any portion thereof pursuant to a judgment or decree of a court or courts having competent jurisdiction or pursuant to a proceeding by a court-appointed receiver.

(l) To the extent permitted by Applicable Law, Seller hereby waives all rights of demand, redemption, stay, valuation and appraisal that Seller now has or may at any time in the future have under any rule of law or statute now existing or hereafter enacted.

(m) Without limiting the generality of Section 4.8(f), upon the occurrence and during the continuance of an Event of Default, at the sole election of the Purchaser (and automatically and without any notice to Seller, upon the upon the occurrence and during the continuance of an Event of Default described in clause (a) or (e) of the definition thereof), the Outstanding Payment Amount, will be due and payable to Purchaser (except as set forth in Section 4.8(n) below). Presentment, demand, protest or notice of any kind are hereby expressly waived. Further, if an Event of Default shall occur and be continuing, Purchaser may, subject to any restrictions set forth in this Section 4.8, foreclose or otherwise realize upon the Collateral in such portions or in full as Purchaser sees fit in its sole discretion.

(n) Without limiting the generality of the foregoing, if there is an occurrence and during the continuance of an Event of Default described in subsection (e) of that definition (a Bankruptcy Event), and if there is a sale or other disposition of all or any part of the Collateral by Purchaser pursuant to subsection (g) or subsection (k) above, then, in such case, Purchaser hereby agrees to accept from the proceeds of such a sale or other disposition an amount equal to the Outstanding Payment Amount.

4.9 IN-LICENSES.

(a) Seller shall act in a commercially reasonable manner with respect to its obligations under each of the In-Licenses and shall not take any action or forego any action that would reasonably be expected to constitute a material breach thereof. Promptly, and in any event within ***, after receipt of any written notice from a counterparty to such In-License or its Affiliates of an alleged material breach under any In-License, Seller shall give notice thereof to the Purchaser, including delivering the Purchaser a copy of such written notice. To the extent commercially reasonable, Seller shall undertake efforts to cure any material breaches by it under any In-License and shall give written notice to the Purchaser upon curing any such breach. Promptly, and in any event within *** following Seller's notice to a counterparty to any material In-License of an alleged material breach under such In-License, Seller shall give notice

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thereof to the Purchaser, including delivering the Purchaser a copy of such written notice. Notwithstanding the foregoing, Seller may terminate any In-License other than the Najarian Agreement that, in Seller's reasonable discretion, is no longer necessary or useful for the development, manufacture, sale or commercialization of Product.

(b) Seller shall promptly (and in any event within ***) provide the Purchaser with (i) executed copies of each new material In-License, (ii) executed copies of each material amendment, supplement, modification or waiver of any provision of an In-License and (iii) copies of all material reports, documents, and other materials provided by the counterparty to each In-License to Seller to the extent that the foregoing relate to Net Sales of Product.

(c) Seller shall provide Purchaser with written notice following any counterparty's material breach of its obligations under any material In-License.

(d) Seller shall provide the Purchaser with written notice following the termination of any material In-License.

4.10 THIRD PARTY AGREEMENTS.

(a) Seller shall act in a commercially reasonable manner with respect to its obligations under each of the Third Party Agreements and shall not take any action or forego any action that would reasonable be expected to constitute a material breach thereof. Promptly, and in any event within ***, after receipt of any written notice from any of the parties thereto or their Affiliates of an alleged material breach by Seller under a Third Party Agreement, Seller shall give notice thereof to the Purchaser, including delivering the Purchaser a copy of such written notice. To the extent commercially reasonable, Seller shall undertake efforts to cure any material breaches by it under any Third Party Agreements and shall give written notice to the Purchaser upon curing any such breach. Notwithstanding the foregoing, Seller may terminate any Third Party Agreement that, in Seller's reasonable discretion, is no longer necessary or useful for the development, manufacture, sale or commercialization of Product.

(b) Promptly (and in any event within ***) after Seller becomes aware of, or comes to believe in good faith that there has been, a material breach of any Third Party Agreement by the counterparty thereto, Seller shall provide notice of such breach to the Purchaser. In addition, Seller shall provide to the Purchaser a copy of any written notice of material breach or alleged material breach of any material Third Party Agreement delivered by Seller to the counterparty thereto within *** following such delivery.

(c) Seller shall promptly (and in any event within ***) provide the Purchaser with (i) executed copies of any material agreement meant to replace or supersede the services being provided under a Third Party Agreement and (ii) executed copies of each material amendment, supplement, modification or waiver of any provision of a Third Party Agreement.

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(d) Seller shall provide the Purchaser with written notice following the termination of any Third Party Agreement.

4.11 PARTNERING AGREEMENTS. Seller may, in its sole discretion and without the prior consent of or notice to Purchaser, enter into a Permitted Partnering Agreement.

4.12 CHANGE OF CONTROL. Upon the consummation of a Change of Control, automatically and without any notice to Seller, an amount equal to the Outstanding Payment Amount as of the date of the consummation of such Change of Control will be due and payable to Purchaser on the consummation of such Change of Control. Presentment, demand, protest or notice of any kind are hereby expressly waived.

4.13 PROMOTION AND MARKETING OF PRODUCT. Upon the occurrence of a Promotion and Marketing Failure on or prior to the second anniversary of the Effective Date, at the sole election of Purchaser, the Promotion and Marketing Payment Amount will be due and payable to Purchaser within *** after the expiration of the applicable cure period.

4.14 RETAIL PHARMACY MINIMUM. Upon the occurrence of a Retail Pharmacy Failure, at the sole election of Purchaser, the Tranche B Outstanding Payment Amount will be due and payable to Purchaser within *** after December 31, 2014. For the avoidance of doubt, the occurrence of a Retail Pharmacy Failure shall in no way negate or impact the continued payment of the Tranche A Scheduled Quarterly Amounts.

ARTICLE 5

CONFIDENTIALITY

5.1 DEFINITION OF CONFIDENTIAL INFORMATION. For purposes of this Agreement, the term ***"Confidential Information"*** of a Party means any information furnished by or on behalf of such Party to the other Party or its Affiliates (whether written or oral, or in electronic or other form, and whether furnished before or after the date of this Agreement) concerning, or related in any way, directly or indirectly, to this Agreement and the subject thereof, the Purchased Receivables, Product, the Qsymia Product Rights and the Excluded Assets, including, without limitation, (a) any license, sublicense or other agreements involving or relating in any way, directly or indirectly, to the Purchased Receivables, Product or the Qsymia Product Rights, including the In-Licenses and the Third Party Agreements, and (b) any documents, reports, notices, requests or correspondence furnished pursuant to this Agreement. Without limiting the generality of the foregoing, all Quarterly Reports will be deemed the Confidential Information of Seller. Notwithstanding the foregoing, a Party's Confidential Information will not include information that, in each case as demonstrated by written documentation or other competent evidence: was (i) already known to the receiving Party, other than under an obligation of confidentiality, at the time of disclosure; (ii) was generally available to the public or otherwise part of the public domain at the time of its disclosure to the receiving Party; (iii) became generally available to the public or otherwise part of the public domain after its disclosure and other than through any act or omission of the receiving Party in breach of this Agreement; (iv)

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was subsequently lawfully disclosed to the receiving Party by a Third Person having no obligation of which the receiving Party is aware to the disclosing Party or its Affiliates; or (v) is independently developed by the receiving Party without the benefit of Confidential Information of the disclosing Party.

5.2 OBLIGATIONS. Except as authorized in this Agreement or except upon obtaining the other Party's prior written permission to the contrary, each Party agrees that during the Term and for *** thereafter it will: (a) maintain in confidence, and not disclose to any Person, the other Party's Confidential Information; (b) not use the other Party's Confidential Information for any purpose, except as contemplated in this Agreement; and (c) protect the other Party's Confidential Information in its possession by using the same degree of care as it uses to protect its own Confidential Information (but no less than a reasonable degree of care).

Notwithstanding anything to the contrary in this Agreement, a Party will be entitled to injunctive relief to restrain the Breach or threatened Breach by the other Party of this Article 5 without having to prove actual Damages or threatened irreparable harm. Such injunctive relief will be in addition to any rights and remedies available to the aggrieved Party at law, in equity, and under this Agreement for such Breach or threatened Breach.

5.3 PERMITTED DISCLOSURES.

(a) Permitted Persons. A Party may disclose the other Party's Confidential Information, without the other Party's prior written permission, to:

(i) its and its Affiliates' members, trustees, managers, directors, employees, partners, agents, consultants, attorneys, accountants, shareholders, investors, banks and other financing sources, and permitted assignees, purchasers, transferees or successors-in-interest under Section 7.3 in each case, who need to know such Confidential Information to provide financing to the Party or to assist the Party in evaluating the transactions contemplated hereby or in fulfilling its obligations or exploiting its rights hereunder (or to determine their interest in providing such financing or assistance) and who are, prior to receiving such disclosure, bound by written or professional confidentiality and non-use obligations no less stringent than those contained herein; or

(ii) permitted assignees, purchasers, transferees, or successors-in-interest (or potential assignees, purchasers, transferees, or successors-in-interest) under Section 7.3 who need to know such Confidential Information in connection with such assignment, sale, or transfer (or potential assignment, sale, or transfer) and who are bound by written or professional confidentiality and non-use obligations no less stringent than those contained herein.

(b) Legally Required. A Party may disclose the other Party's Confidential Information, without the other Party's prior written permission, to any Person to the extent such disclosure is necessary to comply with Applicable Law, applicable stock exchange requirements, or an order or subpoena from a court of competent jurisdiction; provided that the compelled Party, to the extent it may legally do so, will give reasonable advance notice to the

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other Party of such disclosure and, at such other Party's reasonable request and expense, the compelled Party will use its reasonable efforts to secure confidential treatment of such Confidential Information prior to its disclosure (whether through protective orders or otherwise). Notwithstanding the foregoing, if a Party receives a request from an authorized representative of a Tax authority for a copy of this Agreement, that Party may provide a copy of this Agreement to such Tax authority representative without advance notice to, or the permission or cooperation of, the other Party.

5.4 TERMS OF AGREEMENT. Except to the extent allowed under Section 5.3 or as otherwise permitted in accordance with this Section 5.4, neither Party will make any public announcements concerning this Agreement or the terms hereof, without the prior written consent of the other Party and

each Party agrees that it will each treat the contents and terms of this Agreement and the consideration for this Agreement as Confidential Information of the other Party. Consistent with Section 5.3(b), Purchaser and Seller agree to use reasonable efforts to provide the other with a copy of any required SEC or other filing regarding this Agreement or its terms to review prior to filing and to consider any comments of the other Party in good faith, and to the extent either Party has to file or disclose this Agreement with the SEC, such Party will consider in good faith the other Party's comments with respect to confidential treatment of this Agreement's terms and will redact this Agreement in a manner allowed by the SEC to protect sensitive terms, and will be permitted to file this Agreement, as so redacted, with the SEC. For purposes of clarity, each Party is free to discuss with Third Persons the information regarding this Agreement and Parties' relationship disclosed in such SEC filings and any other authorized public announcements.

ARTICLE 6

TERM AND TERMINATION

6.1 TERM OF AGREEMENT; TERMINATION. This Agreement will commence as of the Effective Date and will continue until all of Purchaser's right to receive any payments on account of the Purchased Receivables set forth in this Agreement and all other amounts to which Purchaser may be entitled to receive as payment hereunder have expired, unless earlier terminated pursuant to the mutual written agreement of the Parties (the ***"Term"***). Upon expiration or earlier termination of the Term, this Agreement shall terminate.

6.2 TERMINATION OF SECURITY INTEREST. Immediately upon termination of this Agreement pursuant to Section 6.1, (i) all Encumbrances on the Collateral granted to the Purchaser pursuant to this Agreement and the other Transaction Documents shall automatically be released, without delivery of any instrument or performance of any act by any Person, (ii) Seller shall be permitted, and is hereby authorized, to terminate any financing statement which has been filed pursuant to the Transaction Documents, and (iii) Purchaser shall execute and deliver to Seller, at Seller's sole cost and expense, all releases and other documents as Seller shall reasonably request to evidence any such release.

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6.3 SURVIVAL. Notwithstanding anything to the contrary in this Article 6, the following provisions shall survive termination of this Agreement: Sections 2.1(g), 2.3, 2.4, 3.3, 3.4, Article 5 (Confidentiality), this Section 6.3, Article 7 (Miscellaneous) and Annex A (to the extent necessary for the interpretation of any surviving provisions). Termination of this Agreement shall not relieve any Party of liability in respect of breaches of this Agreement by any Party on or prior to termination.

ARTICLE 7

MISCELLANEOUS

7.1 ENTIRE AGREEMENT. This Agreement (including the Bill of Sale and this Agreement's other exhibits and schedules) sets forth all the covenants, promises, agreements, warranties, representations, conditions and understandings between and among the Parties and supersede and terminate all prior agreements and understandings between or among the Parties relating to the subject matter hereof. There are no covenants, promises, agreements, warranties, representations, conditions or understandings, either oral or written, between the Parties other than as set forth in this Agreement (including the Bill of Sale and this Agreement's other exhibits and schedules).

7.2 AMENDMENTS. This Agreement may be amended or supplemented only by a written agreement signed by an authorized officer of each Party (or, with respect to any Party that is a trust, its trustee).

7.3 BINDING AGREEMENT; SUCCESSORS AND ASSIGNS. The terms, conditions and obligations of this Agreement will inure to the benefit of and be binding upon the Parties hereto and their respective permitted successors and assigns thereof. Neither this Agreement nor any rights or obligations hereunder may be sold, assigned, hypothecated or otherwise transferred in whole or in part by any Party, by operation of law or otherwise, without the prior written consent of the other Party and compliance with Section 2.4 hereunder; provided, however, that without the applicable prior written consent, but subject to the terms of, and compliance with, Section 2.4 and Article 5, Purchaser may sell, assign, hypothecate or otherwise transfer all or any part of the Purchased Receivables to any one or more Persons, and provided, further, that no assignment of the Purchased Receivables shall be effective as against Seller unless and until written notice of the assignment is provided to Seller. Seller shall keep a complete and accurate record of all such assignments.

7.4 FURTHER ASSURANCES.

(a) Subject to Section 4.8(c), Seller and Purchaser covenant and agree, at any time or from time to time after the Tranche A Closing Date, to execute and deliver such other documents, certificates, agreements, instruments and other writings and to take such other actions as may be necessary or desirable, or reasonably requested by the other Party, in each case, without further consideration but at the expense of Seller, in order to vest and maintain in Purchaser good and marketable title in, to and under the Purchased Receivables free and clear of

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any and all Encumbrances (other than Permitted Encumbrances), and to consummate the other transactions contemplated hereby, including the perfection under the applicable UCC (or any comparable law) of all applicable jurisdictions in the United States and maintenance of perfection of Purchaser's

ownership interest in the Purchased Receivables, the back-up security interest in the Purchased Receivables granted by Seller to Purchaser pursuant to Section 4.7 and the security interest in the Additional Collateral granted by Seller to Purchaser pursuant to Section 4.8.

(b) During the Term, Purchaser will hold in trust for the benefit of Seller any over-payment of Scheduled Quarterly Amounts received by Purchaser and identified as such in the audit report described in Section 2.3(c) until such funds, if any, are paid to Seller pursuant to Section 2.3(c).

7.5 COUNTERPARTS AND FACSIMILE EXECUTION. This Agreement may be executed in two or more counterparts, each of which will be an original, but all of which together will constitute one and the same instrument. To evidence the fact that it has executed this Agreement, a Party may send a copy of its executed counterpart to the other Parties by facsimile or other electronic transmission. In such event, such Party will forthwith deliver to the other Parties the counterpart of this Agreement executed by such Party.

7.6 INTERPRETATION. When a reference is made in this Agreement to Articles, Sections or Exhibits, such reference will be to an Article, Section or Exhibit to this Agreement unless otherwise indicated. The words "include," "includes," and "including" when used herein will be deemed in each case to be followed by the words "without limitation" and will not be construed to limit any general statement which it follows to the specific or similar items or matters immediately following it. The headings and captions in this Agreement are for convenience and reference purposes only and will not be considered a part of or affect the construction or interpretation of any provision of this Agreement. Unless specified otherwise, all statements of, or references to, monetary amounts in this Agreement are in U.S. dollars. Provisions that require that a Party or the Parties "agree," "consent," or "approve" or the like will require that such agreement, consent or approval be specific and in writing, whether by written agreement, letter, approved minutes or otherwise. Words of any gender include the other gender. Neither Party hereto will be or be deemed to be the drafter of this Agreement for the purposes of construing this Agreement against one Party or any other.

7.7 WAIVER. Any term or condition of this Agreement may be waived at any time by the Party that is entitled to the benefit thereof, but no such waiver will be effective unless set forth in a written instrument duly executed by or on behalf of the Party waiving such term or condition. No waiver by any Party of any term or condition of this Agreement, in any one or more instances, will be deemed to be or construed as a waiver of the same or any other term or condition of this Agreement on any future occasion.

7.8 RELATIONSHIP OF THE PARTIES. The Parties acknowledge and agree that the relationship between Purchaser and Seller under this Agreement is intended to be that of buyer

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and seller, and nothing in this Agreement is intended to be construed so as to suggest that either Purchaser or Seller (except as expressly set forth herein) is obligated to provide, directly or indirectly, any advice, consultations or other services to the other Party. The Parties further acknowledge and agree that Purchaser is purchasing the Purchased Receivables solely in its capacity as an investor. Each Party is an independent contractor relative to the other Party under this Agreement, and this Agreement is not a partnership agreement and nothing in this Agreement will be construed to establish a relationship of co-partners or joint venturers between the Parties. Seller will have no responsibility for the hiring, termination or compensation of Purchaser's employees or for any employee benefits for such employee and Purchaser will have no responsibility for the hiring, termination or compensation of Seller's or any of its Affiliate's employees or for any employee benefits of such employee. No employee or representative of Seller or any of Seller's Affiliates will have any authority to bind or obligate Purchaser and no employee or representative of Purchaser will have any authority to bind or obligate Seller, for any sum or in any manner whatsoever. No employee or representative of Seller or any of Seller's Affiliates will have any authority to create or impose any contractual or other Liability on Purchaser without Purchaser's prior written approval and no employee or representative of Purchaser will have any authority to create or impose any contractual or other Liability on Seller without Seller's prior written approval.

7.9 NOTICES. All notices, consents, waivers, requests and other communications hereunder will be in writing and will be delivered in person, sent by overnight courier (e.g., Federal Express) to following addresses of the Parties:

If to Purchaser:

c/o BioPharma Secured Investments III Holdings Cayman LP
c/o Walkers Corporate Services Limited
Walker House
87 Mary Street, George Town
Grand Cayman KY1-9005
Cayman Islands

Tel.No.: +1 (212) 883-2296
Attention: Pedro Gonzalez de Cosio

with a copy (which will not constitute notice) to:

Pharmakon Advisors LP
110 East 59th Street, #3300
New York, NY 10022
Attention: Pedro Gonzalez de Cosio
Telephone: +1 (212) 883-2296

Akin Gump Strauss Hauer& Feld LLP
One Bryant Park
New York, NY 10036-6745
Attention: Geoffrey E. Secol
Telephone: +1 (212) 872-8081

If to Seller:

Vivus, Inc.
1172 Castro Street
Mountain View, CA 94040
Attention: Timothy E. Morris, Senior Vice President, Chief Financial Officer
John L. Slebir, Vice President, General Counsel
Telephone: +1 (650) 934-5200

with copies (which will not constitute notice) to:
Hogan Lovells LLP
525 University Avenue, Suite 400
Palo Alto, CA 94301
Attention: Jon Layman
Telephone: +1 (650) 463-4024

and

Hogan Lovells LLP
100 International Drive, Suite 2000
Baltimore, MD 21202
Attention: Asher M. Rubin
Telephone: +1 (410) 659-2777

or to such other address or addresses as Purchaser or Seller may from time to time designate by notice as provided herein. Any such notice will be deemed given when actually received.

7.10 GOVERNING LAW; SUBMISSION TO JURISDICTION; WAIVER OF JURY TRIAL.

(a) THIS AGREEMENT AND ANY PROCEEDING ARISING OUT OF OR RELATING TO THIS AGREEMENT OR THE TRANSACTIONS CONTEMPLATED HEREBY (WHETHER IN CONTRACT, TORT OR OTHERWISE) WILL BE GOVERNED BY, AND CONSTRUED, INTERPRETED AND ENFORCED IN ACCORDANCE WITH THE INTERNAL SUBSTANTIVE LAWS OF THE STATE OF NEW YORK, WITHOUT GIVING EFFECT TO THE PRINCIPLES OF CONFLICTS OF LAW THEREOF OTHER THAN SECTION 5-1401 OF THE GENERAL OBLIGATIONS LAW OF THE STATE OF NEW YORK, AND THE OBLIGATIONS, RIGHTS AND REMEDIES OF THE PARTIES HEREUNDER WILL BE DETERMINED IN ACCORDANCE WITH SUCH LAWS.

(b) ANY PROCEEDING WITH RESPECT TO THIS AGREEMENT OR ANY OTHER TRANSACTION DOCUMENT WILL BE BROUGHT IN THE COURTS OF THE STATE OF NEW YORK LOCATED IN THE BOROUGH OF MANHATTAN, THE

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CITY OF NEW YORK OR OF THE UNITED STATES OF AMERICA FOR THE SOUTHERN DISTRICT OF NEW YORK, AND EACH PARTY HEREBY ACCEPTS FOR ITSELF AND IN RESPECT OF ITS RESPECTIVE PROPERTY, GENERALLY AND UNCONDITIONALLY, THE EXCLUSIVE JURISDICTION OF THE AFORESAID COURTS.

(c) EACH PARTY HEREBY IRREVOCABLY WAIVES, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, TRIAL BY JURY IN ANY ACTION OR DISPUTE ARISING OUT OF OR RELATING TO THIS AGREEMENT OR THE TRANSACTIONS CONTEMPLATED HEREBY (WHETHER IN CONTRACT, TORT OR OTHERWISE).

(d) EACH PARTY HEREBY IRREVOCABLY WAIVES ANY OBJECTION, INCLUDING ANY OBJECTION TO THE LAYING OF VENUE OR BASED ON THE GROUNDS OF FORUM NON CONVENIENS, WHICH IT MAY NOW OR HEREAFTER HAVE TO THE BRINGING OF ANY SUCH ACTION OR PROCEEDING IN SUCH RESPECTIVE JURISDICTIONS.

(e) EACH PARTY IRREVOCABLY CONSENTS TO THE SERVICE OF PROCESS OF ANY OF THE AFOREMENTIONED COURTS IN ANY SUCH ACTION OR PROCEEDING BY THE SENDING OF COPIES THEREOF BY FEDERAL EXPRESS OR OTHER OVERNIGHT COURIER COMPANY, TO SUCH PARTY AT ITS ADDRESS SPECIFIED BY SECTION 7.9, SUCH SERVICE TO BECOME EFFECTIVE FOUR (4) DAYS AFTER DELIVERY TO SUCH COURIER COMPANY.

(f) NOTHING HEREIN WILL AFFECT THE RIGHT OF ANY PARTY TO SERVE PROCESS IN ANY OTHER MANNER PERMITTED BY LAW.

7.11 DISPUTE RESOLUTION. In the event of an alleged breach of a provision of this Agreement by a Party hereto, the Party alleging such breach or challenging the audit report, as applicable, shall notify the other Party promptly in writing. Such notice shall include a brief description of the

alleged breach or challenged portion of the audit report, including damages sought or estimated, to the extent actually known or reasonably capable of estimation. The Parties hereto shall then meet at a mutually acceptable time and location within thirty (30) days of the date such notice was delivered and shall attempt to negotiate a resolution in good faith. If a resolution is not reached within *** of the date of the original notice, then either Party may commence litigation in accordance with Section 7.10.

7.12 EQUITABLE RELIEF. Each of the Parties hereto acknowledges that each other Party may have no adequate remedy at law if a Party fails to perform any of its obligations under this Agreement in any material respect. In such event, the Parties agree that, in addition to any other rights the Parties may have (whether at law or in equity), in the event of any material Breach or threatened material Breach by any Party of any covenant, obligation or other provision set forth in this Agreement, any non-Breaching Party will be entitled (in addition to any other remedy that may be available to it) to seek (a) a decree or other of specific performance or

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mandamus to enforce the observance and performance of such covenant, obligation or other provision, and (b) an injunction restraining such material Breach or threatened material Breach.

7.13 NO THIRD-PARTY BENEFICIARIES. All rights, benefits and remedies under this Agreement are solely intended for the benefit of the Parties (including their permitted successors and assigns), and no other Person other than the Parties will have any rights whatsoever to (a) enforce any obligation contained in this Agreement, (b) seek a benefit or remedy for any Breach of this Agreement, or (c) take any other action relating to this Agreement under any legal theory, including but not limited to, actions in contract, tort (including but not limited to negligence, gross negligence and strict liability), or as a defense, set-off or counterclaim to any action or claim brought or made by the Parties (or any of their permitted successors and assigns).

7.14 SEVERABILITY. If any provision hereof should be held invalid, illegal or unenforceable in any jurisdiction, the Parties will negotiate in good faith a valid, legal and enforceable substitute provision that most nearly reflects the original intent of the Parties and all other provisions hereof will remain in full force and effect in such jurisdiction and will be liberally construed in order to carry out the intentions of the Parties as nearly as may be possible. Such invalidity, illegality or unenforceability will not affect the validity, legality or enforceability of such provision in any other jurisdiction. Nothing in this Agreement will be interpreted so as to require a Party to violate any Applicable Law.

7.15 EXPENSES.

(a) Upon (i) the Tranche A Closing or (ii) the failure by Seller to consummate the transactions contemplated by this Agreement on or before the Tranche A Closing Date, where Purchaser is, in good faith, ready, willing and able to consummate the transactions contemplated by this Agreement, Seller (in either case) shall be responsible for all reasonable and documented out-of-pocket legal costs and expenses related hereto incurred by Purchaser, subject to a cap of $300,000.00 (the "***Expense Cap***"). Upon the Tranche B Closing, if any, Seller shall be responsible for all reasonable and documented out-of-pocket legal costs and expenses incurred by Purchaser relating to the Tranche B Transaction; provided that the aggregate of all such expenses to be paid by Seller pursuant to this Section 7.15(a) for both the Tranche A Transaction and Tranche B Transaction shall not exceed the Expense Cap. Notwithstanding the foregoing, if Purchaser fails to consummate the transactions contemplated by this Agreement on or before the Tranche A Closing Date where Seller is, in good faith, ready, willing and able to complete the transactions contemplated by this Agreement, Seller shall not be responsible for any of Purchaser's legal expenses related to the transactions contemplated by this Agreement (unless the transactions contemplated by this Agreement are subsequently consummated).

(b) In any Proceeding between the Parties arising out of or involving this Agreement or any other Transaction, the prevailing party will be entitled to recover, in addition to any other relief awarded, all expenses it incurs in that Proceeding, including reasonable attorneys' fees and expenses.

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[Signature Page Follows]

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IN WITNESS WHEREOF, the Parties hereto have executed this Agreement as of the Effective Date.

PURCHASER:

BIOPHARMA SECURED INVESTMENTS III HOLDINGS

CAYMAN LP

By: Pharmakon Advisors, LP, its investment manager

By: Pharmakon Management I, LLC, its general partner

By: /s/ Pedro Gonzalez de Cosio

Name: Pedro Gonzalez de Cosio

Title: Managing Member

SELLER:

VIVUS, INC.

By: /s/ Leland F. Wilson

Name: Leland F. Wilson

Title: Chief Executive Officer

[Signature Page to Purchase and Sale Agreement]

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ANNEX A

DEFINED TERMS

"Accounting Firm" has the meaning set forth in Section 2.3(b).

"Additional Collateral" means all of Seller's right, title and interest in, to and under the following property, whether now owned or hereafter acquired, wherever located:

(a) all Qsymia Product Rights and all of Seller's rights and privileges with respect thereto;

(b) all Regulatory Approvals;

(c) all Supporting Obligations (as such term is defined in the UCC) in respect of the foregoing and all collateral security and guarantees given by any Person with respect to any of the foregoing;

(d) all of Seller's books and records relating to any and all of the foregoing;

(e) all contractual rights of Seller under any Permitted Partnering Agreement to receive payment of Net Sales; and

(f) all Proceeds (as such term is defined in the UCC) and products of and to any and all of the foregoing;

provided, however, that, "Additional Collateral" shall not include any general intangible, permit, lease, license, contract or other instrument of Seller included in items (D) through (H) of the definition of Qsymia Product Rights (or any of Seller's books and records relating thereto, or any Proceeds and products thereof and thereto), if, and only to the extent, the grant of a security interest in such general intangible, permit, lease, license, contract or other instrument in the manner contemplated by this Agreement, under the terms thereof or under Applicable Law, is prohibited and would result in the termination thereof or give the other Persons party thereto the right to terminate, accelerate or otherwise alter Seller's rights, title and interests thereunder (including upon the giving of notice or the lapse of time or both); provided, further, that (i) any such limitation described above on the security interests granted hereunder shall only apply to the extent that any such prohibition could not be rendered ineffective pursuant to the UCC or any other Applicable Law (including Bankruptcy Laws) or principles of equity and (ii) in the event of the termination or elimination of any such prohibition or the requirement for any consent contained in any Applicable Law, general intangible, permit, lease, license, contract or other instrument, to the extent sufficient to permit any such general intangible, permit, lease, license, contract or other instrument of Seller (and the books and records relating thereto and the Proceeds and products thereof and thereto) to become Additional Collateral hereunder, or upon the granting of any such consent, or waiving or terminating any requirement for such consent, a security interest in such general intangible, permit, lease, license, contract or other instrument (and the books and records relating thereto and the Proceeds and products thereof and thereto)

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shall be automatically and simultaneously granted hereunder and shall be included as Additional Collateral hereunder.

"Affiliate" means, with respect to an entity, any business entity controlling, controlled by, or under common control with such entity, but only so long as such control exists. For the purposes of this definition, ***"controlling"***, ***"controlled"***, and ***"control"*** mean the possession, directly (or indirectly through one or more intermediary entities), of the power to direct the management or policies of an entity, including through ownership of 50% or more of the voting securities of such entity (or, in the case of an entity that is not a corporation, ownership of 50% or more of the corresponding interest for the election of the entity's managing authority).

"Applicable Law" means, with respect to any Person, all provisions of (a) all constitutions, statutes, laws, rules, regulations, ordinances and orders of Governmental Authorities, (b) any authority, consent, approval, license, permit (or the like) or exemption (or the like) of any Governmental Authority, and (c) any orders, decisions, judgments, writs and decrees issued or entered by any Governmental Authority; in each case, applicable to such Person or any of its properties or assets.

"Audited Financial Statements" has the meaning set forth in Section 2.2(c).

"Bankruptcy Event" means, with respect to Seller, the occurrence of any of the following:

(a) Seller will voluntarily commence any case, proceeding or other action (i) under any existing or future law of any jurisdiction, domestic or foreign, relating to bankruptcy, insolvency, reorganization, relief of debtors or the like, seeking to have an order for relief entered with respect to it, or seeking to adjudicate it bankrupt or insolvent, or seeking reorganization, arrangement, adjustment, winding-up, liquidation, dissolution, composition or other relief with respect to it or its debts, or (ii) seeking appointment of a receiver, trustee, custodian or other similar official for it or for all or any portion of its assets, or Seller will make a general assignment for the benefit of its creditors;

(b) there will be commenced against Seller any case, proceeding or other action of a nature referred to in clause (a) above that remains undismissed or undischarged for a period of *** from the commencement thereof; or

(c) there will be commenced against Seller any case, proceeding or other action seeking issuance of a warrant of attachment, execution, distraint or similar process against all or any substantial portion of its assets, which results in the entry of an order or decree for any such relief that will not have been vacated, discharged, stayed or satisfied pending appeal for *** from the entry thereof.

"Bankruptcy Laws" means, collectively, bankruptcy, insolvency, reorganization, moratorium, fraudulent conveyance, fraudulent transfer or other similar laws affecting the enforcement of creditors' rights generally.

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"Bill of Sale" means the Bill of Sale attached hereto as **Exhibit A**.

"Breach" of a representation, warranty, covenant, agreement, obligation or other provision will be deemed to have occurred if there is or has been any inaccuracy in or breach of, or any failure to comply with or perform, such representation, warranty, covenant, agreement, obligation or other provision, and ***"Breach"*** will be deemed to refer to any such inaccuracy, breach or failure.

"Bring-Down Certificate" has the meaning set forth in Section 1.7(a).

"Business Day" means any day that is not a Saturday, Sunday or other day on which commercial banks in New York City are authorized or required by Applicable Law to remain closed.

"Calendar Quarter" means the 3-month period ended March 31, June 30, September 30 or December 31, as applicable.

"Calendar Year" means the 12-month period from January 1 through December 31.

"Change in Law" means any change in, or repeal, withdrawal, adoption or issuance of, any statute, law, rule, regulation, ordinance, order, decision, decree, judgment or ruling of any Governmental Authority that affects the applicability of any withholding Tax with respect to payments to Purchaser hereunder.

"Change of Control" means:

(a) the acquisition at any time by a "person" or "group" (as such terms are used in Sections 13(d) and 14(d)(2) of the Securities Exchange Act of 1934, as in effect on the Effective Date (the "***Exchange Act***")) who or which are the beneficial owners (as defined in Rule 13(d)-3 under the Exchange Act), directly or indirectly, of securities representing more than 50% of the combined voting power in the election of directors of the then outstanding securities of Seller or any successor of Seller;

(b) consummation of any assignment, transfer, sale or disposition of all or substantially all of the assets related to Product;

(c) consummation of any merger, consolidation, or statutory share exchange to which Seller is a party, as a result of which the Persons who were stockholders immediately prior to the effective date of the merger, consolidation or share exchange shall have beneficial ownership of less than 50% of the combined voting power in the election of directors of the surviving corporation;

(d) consummation by Seller of any sale or disposition, directly or indirectly, of any of the Collateral or any interest therein to any Third Person, including by operation of law or otherwise, except as permitted under this Agreement (including as permitted under the Patent Abandonment Requirements);

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(e) consummation by Seller of any sale or disposition, directly or indirectly, of any rights to or interest in any Product to any Third Person, including by operation of law or otherwise, that adversely affects Purchaser's right to receive any Scheduled Quarterly Amount (or, as applicable, the Quarterly Cap, subject to the terms and conditions herein); or

(f) the grant by Seller or any of its Affiliates at any time during the Payment Period to a Third Person of a license to market, offer for sale and sell Product in the U.S.

Notwithstanding the foregoing, a Permitted Partnering Agreement and a Permitted Action shall not constitute a Change of Control.

"Code" means the U.S. Internal Revenue Code of 1986, as amended.

"Collateral" means the Additional Collateral and, in the event of a Recharacterization, the Additional Collateral plus the Purchased Receivables.

"Commercialization" means any and all activities directed to the manufacture, distribution, marketing, detailing, promotion, selling and, outside of the United States, securing of reimbursement of Product. When used as a verb, "Commercialize" shall mean to engage in Commercialization.

"Commercially Reasonable Efforts" means those commercially reasonable efforts and resources consistent with the usual practices of Seller in pursuing the development, manufacturing or Commercialization of a biologic or pharmaceutical product or therapy owned or licensed by it, with similar product characteristics, which is at a similar stage of research, development or Commercialization, taking into account efficacy, safety, proprietary position of the product or therapy, including patent and regulatory exclusivity, regulatory structure involved including anticipated or approved labeling and anticipated or approved post-approval requirements, present and future market and commercial potential including competitive market conditions and probability of the profitability of the product or therapy in light of pricing and reimbursement issues, and all other relevant factors including technical, legal, scientific and/or medical factors and the unique nature of Product to be developed, manufactured or Commercialized under this Agreement.

"Confidential Information" has the meaning set forth in Section 5.1.

"Damages" means any loss, damage, Liability, claim, demand, settlement amount, judgment, award, fine, penalty, Tax, fee (including any reasonable legal fee, expert fee, accounting fee or advisory fee), charge, cost (including any reasonable cost of investigation and court cost) or expense of any nature.

"Default" means any event that, with the giving of notice or the lapse of time, or both, would become an Event of Default.

"EBITDA" means, for such period determined on a consolidated basis in accordance with GAAP, net profit or loss plus (without duplication and to the extent deducted in determining

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net profit or loss) (a) interest expense net of interest income, (b) provision for income taxes and (c) depreciation, amortization and stock-based compensation and other similar non-cash expenses; provided that, to the extent included in EBITDA and without duplication, the following shall be excluded: (i) extraordinary gains and losses and unusual or non-recurring income or charges, (ii) currency translation gains and losses related to currency remeasurements of Indebtedness and (iii) fair value non-cash gains or losses of swaps, derivatives or similar arrangements.

"Effective Date" has the meaning set forth in the Preamble.

"EMEA" means the European Medicines Agency or any successor agency thereto.

"Encumbrance" means any lien, charge, security interest, mortgage, option, pledge, assignment or any other encumbrance of any Person of any kind whatsoever.

"Enforcement Action" means any Proceeding brought, or assertion made, by Seller (whether as plaintiff or by means of counterclaim) against any Third Person relating to arising out of any infringement, misuse or misappropriation by such Third Person of any Qsymia Patent Rights.

"Event of Default" means each of the following events or occurrences:

(a) failure of Seller to deliver or cause to be delivered to Purchaser any (i) Scheduled Quarterly Amount or Quarterly Cap, as applicable, (ii) the Promotion and Marketing Payment Amount following a Promotion and Marketing Failure or (iii) the Tranche B Outstanding Payment

Amount following a Retail Pharmacy Failure, in each case, when and as such payment is due and payable in accordance with the terms of this Agreement and such failure is not cured within *** after written notice thereof is given to Seller by Purchaser;

(b) failure of Seller to deliver any of the deliverables to Purchaser in accordance with Section 2.2 and such failure is not cured within *** after written notice thereof is given to Seller by Purchaser;

(c) a Promotion and Marketing Failure occurring after the second anniversary of the Effective Date;

(d) Breach of the covenants in Section 4.4(a) (or, solely as it relates thereto, Section 4.4(e)) and such Breach is not cured within *** of the occurrence of such Breach; provided, however, that in the event such Breach relates to Seller exceeding a limitation on Permitted Indebtedness as set forth in subsection (k) of the definition of "Permitted Indebtedness" and Seller has notified Purchaser in writing that it plans to pay the Outstanding Payment Amount, then it shall not be considered an Event of Default if Seller pays in full the Outstanding Payment Amount to Purchaser within *** of the date Seller exceeded such limitation (if Seller does not pay the Outstanding Payment Amount in full within ***, then it shall be an Event of Default on *** following the date of Seller exceeding such limitation and there shall be no additional cure period).

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(e) Seller becomes subject to a Bankruptcy Event; and

(f) Purchaser shall fail to have a first-priority perfected security interest under the applicable UCC (or any comparable law) of all applicable jurisdictions in the United States in any of the Additional Collateral, subject only to Permitted Encumbrances, and such first-priority perfected security interest is not restored within *** after written notice thereof is given to Seller by Purchaser, other than in connection with a Licensing Transaction.

"Existing In-License" has the meaning set forth in Section 3.1(i).

"Excluded Assets" means collectively (a) the Qsymia Product Rights, subject to Section 4.8, (b) any Retained Receivables, (c) any reimbursements, milestone payments, fees, indemnification, damages, awards, settlement payments, compensation, interest, consideration or right of payment of any kind related to Product that is due to Seller other than as set forth herein, and (d) all other assets of Seller.

"Expense Cap" has the meaning set forth in Section 7.15(a).

"FDA" means the United States Food and Drug Administration and any successor entity thereto.

"FFDCA" means the Federal Food, Drug, and Cosmetic Act.

"Fixed Tranche B Date" has the meaning set forth in Section 2.1(a)(ii).

"Funded Activities" means any and all activities, efforts and services performed in furtherance of the research, discovery, development, commercialization and exploitation of Product, including the purchase of materials, general and administrative expenses, corporate infrastructure and corporate overhead.

"GAAP" means United States generally accepted accounting principles applicable to Seller or any licensee of Seller, consistently applied throughout Seller's or Seller's licensee's organization.

"Governmental Authority" means the government of the United States, any other nation or any political subdivision thereof, whether state or local, and any agency, authority (including supranational authority), instrumentality, regulatory body, court, central bank or other Person exercising executive, legislative, judicial, taxing, regulatory or administrative powers or functions of or pertaining to government.

"Guaranty" of any Person means any obligation, contingent or otherwise, of such Person (a) to pay any Liability of any other Person or to otherwise protect, or having the practical effect of protecting, the holder of any such Liability against loss (whether such obligation arises by virtue of such Person being a partner of a partnership or participant in a joint venture or by agreement to pay, to keep well, to purchase assets, goods, securities or services or to take or pay, or otherwise) or (b) incurred in connection with the issuance by a Third Person of a Guaranty of

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any Liability of any other Person (whether such obligation arises by agreement to reimburse or indemnify such Third Person or otherwise). The word ***"Guarantee"*** when used as a verb has the correlative meaning.

"Improvements" means any improvement, invention or discovery relating to the composition, manufacture, use or sale of a Product, an active ingredient therein, the formulation of such Product, or a derivative of any of the foregoing.

"Indebtedness" of any Person means (a) any obligation of such Person for borrowed money, (b) any obligation of such Person evidenced by a bond, debenture, note or other similar instrument, (c) any obligation of such Person to pay the deferred purchase price of property or services, except a trade account

payable that arises in the ordinary course of business, (d) any obligation of such Person as lessee under a capital lease, (e) any Mandatorily Redeemable Stock of such Person, (f) any repurchase obligation of such Person to purchase securities or other property that arises out of or in connection with the sale of the same or substantially similar securities or property by such Person (excluding any such obligation to the extent the obligation can be satisfied by the issuance of capital stock other than Mandatorily Redeemable Stock), (g) any non-contingent obligation of such Person to reimburse any other Person in respect of amounts paid under a letter of credit, bank guarantee or similar instrument issued by such other Person, (h) any Indebtedness of others secured by an Encumbrance on any asset of such Person and (i) any Indebtedness of others Guaranteed by such Person.

"In-License" means any license or other agreement between Seller or any of its Affiliates and any Third Person pursuant to which Seller or any of its Affiliates obtains a license, a right, a covenant not to sue or similar grant of rights, or an option to obtain any such grants of rights, to any Qsymia Product Right that is necessary for the research, development, use or Commercialization of the Product.

"Judgment" means any judgment, order, writ, injunction, citation, award or decree of any nature.

"Knowledge" means, (a) when referring to Seller, the actual knowledge of Seller's "Named Executive Officers" (as defined in Item 402 of Regulation S-K (17 CFR 229.402), as amended from time to time), and (b) when referring to Purchaser, the actual knowledge of any management-level employee of Purchaser or any of its Affiliates.

"Liability" of any Person means (in each case, whether with full or limited recourse) any indebtedness, liability, obligation, covenant or duty of or binding upon, or any term or condition to be observed by or binding upon, such Person or any of its assets, of any kind, nature or description, direct or indirect, absolute or contingent, due or not due, contractual or tortious, liquidated or unliquidated, whether arising under contract, Applicable Law, or otherwise, whether now existing or hereafter arising, and whether for the payment of money or the performance or non-performance of any act.

"Make-Whole Premium" means, for each Payment Date, an amount equal to the applicable Scheduled Quarterly Amount of the preceding Payment Date (which, for the

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avoidance of doubt, shall include the aggregate of all accrued and unpaid Make-Whole Premiums) less the actual payment of the Scheduled Quarterly Amount made to Purchaser of the preceding Payment Date, multiplied by 1.03.

"Mandatorily Redeemable Stock" means, with respect to any Person, any share of such Person's capital stock to the extent that it is (a) redeemable, payable or required to be purchased or otherwise retired or extinguished (other than capital stock to the extent redeemable in exchange for capital stock that is not Mandatorily Redeemable Stock, at the option of the issuer of such capital stock, or capital stock issuable under the Rights Plan), or convertible into any Indebtedness or Mandatorily Redeemable Stock of such Person, (i) at a fixed or determinable date, whether by operation of a sinking fund or otherwise, (ii) at the option of any Person other than such Person or (iii) upon the occurrence of a condition not solely within the control of such Person, such as a redemption required to be made out of future earnings, in the case of each of clauses (i) through (iii), on or prior to the end of the Term or (b) convertible into shares of such Person's capital stock described in subsection (a) above.

"Marketing Approval" means the approval of an NDA by the FDA necessary for the Commercialization of a pharmaceutical product in the United States (or, in a country other than the United States, the equivalent necessary approval(s) by applicable Governmental Entities for Commercialization of a pharmaceutical product in such country).

"Material Adverse Effect" means a material adverse effect on: (a) the validity or enforceability of any of the Transaction Documents; (b) the back-up security interest granted pursuant to Section 4.8; (c) the security interest granted pursuant to Section 4.9; (d) the right or ability of Seller to grant any of the rights or perform any of its obligations under any of the Transaction Documents or to consummate any of the transactions contemplated thereby; (e) the rights and remedies of Purchaser under any of the Transaction Documents; (f) the right of Purchaser to receive a Scheduled Quarterly Amount payment or the timing, amount or duration of such payment of the Scheduled Quarterly Amount (or, as applicable, the Quarterly Cap, subject to the terms and conditions herein); (g) the Purchased Receivables or any of Purchaser's right, title and interest therein, thereto and thereunder; or (h) Seller's title to or control of, or the validity or enforceability of, any of the Qsymia Patent Rights (subject to the Patent Abandonment Requirements) or Qsymia Trademarks.

"Najarian Agreement" means that certain Assignment Agreement, dated as of October 16, 2001, by and between Thomas Najarian, M.D. and Seller.

"NDA" means a new drug application (as such term is used under the FFDCA), or other applicable pharmaceutical approval submission to the FDA for Marketing Approval (or, in a country other than the U.S., the equivalent necessary submissions to the applicable Governmental Entity for Marketing Approval).

"Net Sales" means the aggregate, gross amount invoiced for sales of Product or any other obesity agent developed or marketed by Seller or its Affiliates by or on behalf of Seller or its Affiliates or any licensee of Seller or Seller's Affiliates to a Third Person in an arms-length

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transaction (excluding any sales among Seller, its Affiliates and any licensee of Seller or Seller's Affiliates) less the following amounts, to the extent actually incurred or accrued, related to such Product:

(a) reasonable and customary rebates, chargebacks, cash, quantity, trade and similar discounts, credits and allowances and other price reductions reasonably granted, allowed, incurred or paid in so far as they are applied to sales of such Product;

(b) reasonable and customary credits, allowances, discounts, rebates and chargebacks in so far as they are applied to sales of such Product, including, without limitation, any of the foregoing taken upon rejection, return or recall of such Product;

(c) reasonable and customary freight and insurance costs incurred with respect to the shipment of such Product to customers, in each case if charged separately and invoiced to the customer;

(d) duties, surcharges and other governmental charges in connection with the sales of such Product to any Third Person, to the extent borne by the Seller;

(e) sales, use, value-added, excise and other similar taxes (excluding income taxes), as adjusted for rebates and refunds, imposed in connection with the sales of such Product to any Third Person, to the extent such taxes are not paid by the Third Person; and

(f) any other expenses directly related to the distribution and sale of Product that are allowed by GAAP, provided that such expenses are reasonable and taken in good faith.

With respect to sales of Product invoiced in U.S. dollars, Net Sales shall be determined in U.S. dollars. With respect to sales of Product invoiced in a currency other than U.S. dollars, Net Sales shall be determined by translating the currencies at which the sales are made into U.S. dollars, at rates of exchange determined by calculating the quarterly business day average of the published rates of exchange for such non-U.S. dollar currencies as quoted by the Wall Street Journal.

Net Sales shall not include transfers of Products for use in the clinical trials (excluding post-Marketing Approval studies), development purposes, compassionate use purposes or samples, and no payment shall be due hereunder with respect to such transfers.

Notwithstanding the foregoing, a Net Sale shall be determined at all times in accordance with GAAP, except that, with respect to sales of Product by licensee that is a non-U.S. Person, a Net Sale by such licensee shall be determined in accordance with the generally accepted accounting principles applicable to, and required by Applicable Law to be used by, such licensee.

"Outstanding Payment Amount" means, as of any date, an amount equal to the sum of all (a) Tranche A Outstanding Payment Amounts and (b) Tranche B Outstanding Payment Amounts.

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"Party" or ***"Parties"*** has the meaning set forth in the Preamble.

"Patents" means all patents and patent applications existing as of the Effective Date and all patent applications filed or patents issued hereafter, including any continuation, continuation-in-part, division, provisional or any substitute applications, any patent issued with respect to any of the foregoing patent applications, any reissue, reexamination, renewal or patent term extension or adjustment (including any supplementary protection certificate) of any such patent, and any confirmation patent or registration patent or patent of addition based on any such patent, and all foreign counterparts of any of the foregoing.

"Patent Abandonment Requirements" means, with respect to any Patent that Seller desires to (i) decline to prosecute or maintain or (ii) abandon, Seller shall be required to first replace such Patent with a Patent that (A) similarly relates to the development, manufacture, use, marketing, promotion, sale or distribution of Product and (B) has a term of protection no shorter in duration than such Patent.

"Patent Security Agreement" means the Patent and Trademark Security Agreement attached hereto as **Exhibit B.**

"Payment Period" means the period of time commencing on March 31, 2014 and ending on the earlier of the Payoff Date and March 31, 2018.

"Payoff Date" has the meaning set forth in Section 2.1(d).

"Permitted Action" means:

(a) the sale, transfer, assignment, license, sublicense, abandonment or disposal of, or the failure to maintain or prosecute, any Permitted Qsymia Product Rights that, in Seller's reasonable discretion, is no longer necessary or useful for the development, manufacture, sale or commercialization of Product; provided that such action does not, and would not reasonably be expected to, result in a Material Adverse Effect;

(b) the license or sublicense of any Permitted Qsymia Product Rights in the ordinary course of business that is reasonably necessary in Seller's discretion to maximize Net Sales of the Product and/or Commercialize the Product; provided that such action (i) does not, and would not reasonably be expected to, result in a Material Adverse Effect and (ii) would not constitute a licensing, co-promotion, joint venture, partnering or similar agreement or arrangement with a Third Person for the purpose of securing promotional and/or marketing resources for Product that would not qualify as a Permitted Partnering Agreement;

(c) the surrender or waiver of contractual rights with respect to Permitted Qsymia Product Rights in the ordinary course of business; provided that such action does not, and would not reasonably be expected to, result in a Material Adverse Effect;

(e) the settlement, release or surrender of tort or other potential or actual litigation claims relating to Permitted Qsymia Product Rights in the ordinary course of business; provided

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that such action does not, would not reasonably be expected to, result in a Material Adverse Effect;

(f) the grant of Permitted Encumbrances; and

(g) any other action by Seller otherwise permitted or required under this Agreement.

"Permitted Encumbrances" means:

(a) Encumbrances created in favor of Purchaser pursuant to this Agreement;

(b) inchoate Encumbrances for Taxes not yet delinquent or Encumbrances for Taxes which are being contested in good faith and by appropriate proceedings and for which adequate reserves have been established in accordance with GAAP;

(c) Encumbrances in respect of property of Seller imposed by Applicable Law which were incurred in the ordinary course of business and do not secure Indebtedness for borrowed money, such as carriers', warehousemen's, distributors', wholesalers', materialmen's and mechanics' liens and other similar Encumbrances arising in the ordinary course of business and which do not in the aggregate materially detract from the value of the property of Seller and do not materially impair the use thereof in the operation of the business of Seller;

(d) Encumbrances (i) imposed by Applicable Law or deposits made in connection therewith in the ordinary course of business in connection with workers' compensation, unemployment insurance and other types of social security legislation, (ii) incurred in the ordinary course of business to secure the performance of tenders, statutory obligations (other than excise Taxes), surety, stay, customs and appeal bonds, statutory bonds, bids, leases, government contracts, trade contracts, performance and return of money bonds and other similar obligations (exclusive of obligations for the payment of borrowed money) or (iii) arising by virtue of deposits made in the ordinary course of business to secure liability for premiums to insurance carriers imposed by Applicable Law or deposits made in connection therewith in the ordinary course of business in connection with workers' compensation, unemployment insurance and other types of social security legislation;

(e) Encumbrances, consisting of the rights of licensors or licensees, existing on the date of this Agreement or granted or created in the ordinary course of business after the date of this Agreement, in each such case pursuant to a license permitted hereunder;

(f) Encumbrances on cash collateral securing reimbursement obligations under letters of credit;

(g) normal and customary rights of setoff upon deposits of cash in favor of banks or other depository institutions; and

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(h) Encumbrances securing judgments, awards or orders for payment of money (i) under $1,000,000, in the aggregate, (ii) covered by third-party insurance, or (iii) that are stayed, bonded or discharged within sixty (60) days.

"Permitted Indebtedness" means:

(a) Indebtedness in respect of capital leases or otherwise incurred to acquire equipment and capital assets;

(b) Indebtedness with respect to surety and performance bonds and similar obligations arising in the ordinary course of business;

(c) Indebtedness consisting of the endorsement of negotiable instruments for deposit or collection or similar transactions in the ordinary course of business;

(d) intercompany Indebtedness among Seller and its Subsidiaries;

(e) Indebtedness incurred in connection with corporate credit cards issued by companies or financial institutions in the ordinary course of business;

(f) Indebtedness in respect of letters of credit, bank guarantees and similar instruments issued for the account of Vivus and its Subsidiaries in the ordinary course of business supporting obligations under (A) workers' compensation, unemployment insurance and other social security laws and (B) bids, trade debt, leases, statutory obligations, surety and appeal bonds, performance bonds and obligations of a like nature;

(g) Indebtedness consisting of the financing of insurance premiums in the ordinary course of business;

(h) customer advances or deposits received in the ordinary course of business;

(i) Indebtedness in respect of netting services, overdraft protections, payment processing, automatic clearinghouse arrangements, arrangements in respect of pooled deposit or sweep accounts, check endorsement guarantees, and otherwise in connection with deposit accounts or cash management services;

(j) inventory or receivable financings in an aggregate principal amount at any time outstanding not to exceed 75% of the value of such inventory or receivables;

(k) (i) up to $250,000,000 aggregate face value at any time outstanding, in unsecured Indebtedness with a maturity date after September 30, 2018 and not redeemable at the option of the holder before September 30, 2018 (other than nominal amortization requirements not to exceed 1% per annum of the initial aggregate principal amount of such Indebtedness, excess cash flow and/or extraordinary receipts offer or repayment provisions, customary offers to repurchase such Indebtedness upon a change of control, asset sales (or casualty or condemnation events) or "fundamental change" and other than settlement upon conversion of convertible indebtedness)

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(the "***Initial Unsecured Debt***"); and

(ii) additional unsecured Indebtedness with a maturity date after December 31, 2019 and not redeemable at the option of the holder before December 31, 2019 (other than nominal amortization requirements not to exceed 1% per annum of the initial aggregate principal amount of such indebtedness, excess cash flow and/or extraordinary receipts offer or repayment provisions, customary offers to repurchase such Indebtedness upon a change of control, asset sales (or casualty or condemnation events) or "fundamental change" and other than settlement upon conversion of convertible indebtedness) (the "***Incremental Unsecured Debt***"); provided that the aggregate principal amount of Incremental Unsecured Debt at any time outstanding shall not exceed the lesser of (A) the trailing 12 months Net Sales, less $350,000,000, and (B) $250,000,000 (for the avoidance of doubt, the total aggregate principal amount of the Initial Unsecured Debt and the Incremental Unsecured Debt at any time outstanding shall not exceed $450,000,000);

(l) Indebtedness incurred to finance acquisitions or to finance the purchase, construction or other acquisition of manufacturing capacity; provided, that Purchaser shall have given its prior consent to any such incurrence, not to be unreasonably withheld or delayed (it being agreed that it shall not be unreasonable for Purchaser to take into account its economic interest in receiving Scheduled Quarterly Amounts in considering whether to give or withhold such consent);

(m) Indebtedness acquired in connection with any acquisition where such Indebtedness (i) existed on the date of the consummation of such acquisition, (ii) was not incurred in contemplation of such acquisition, and (iii) is not at any time secured by assets of Seller and its Subsidiaries other than those acquired in such acquisition; provided, that Purchaser shall have given its prior consent to the incurrence of any such Indebtedness, not to be unreasonably withheld or delayed (it being agreed that it shall not be unreasonable for Purchaser to take into account its economic interest in receiving Scheduled Quarterly Amounts in considering whether to give or withhold such consent);

(n) Indebtedness which may be deemed to exist in connection with agreements providing for indemnification, severance arrangements, purchase price adjustments, earnouts, stay bonuses and similar obligations in connection with the acquisition or disposition of assets;

(o) Indebtedness outstanding on the Effective Date;

(p) obligations (contingent or otherwise) existing or arising under any hedging transaction, provided that such obligations are (or were) entered into by Vivus or any of its Subsidiaries in the ordinary course of business for the purpose of directly mitigating risks associated with liabilities, commitments, investments, assets, or property held or reasonably anticipated by Vivus and any of its Subsidiaries, or changes in the value of securities issued by Vivus and any of its Subsidiaries, and not for purposes of speculation;

(q) Guaranties of Permitted Indebtedness;

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(r) Indebtedness incurred pursuant to this Agreement and the other Transaction Documents;

(s) Indebtedness that is recourse only to Seller's or any of its Subsidiary's right, title and interest in and to any or all of the patents and trademarks covering the manufacture and use of STENDRA™ (avanafil), which, for the avoidance of doubt, shall not include any of the Collateral and shall otherwise be non-recourse; and

(t) extensions, refinancings and renewals of indebtedness described in clauses (k), (l), (m), (o), and (s) above; provided that the principal amount of each such extension, refinancing or renewal does not exceed the original principal amount of the indebtedness being extended, refinanced or renewed (plus the sum of (A) accrued and unpaid interest and fees thereon and (B) customary fees and expenses relating to such extension, renewal, replacement or refinancing) or the terms thereof are not modified to impose materially more burdensome terms upon Vivus and any of its Subsidiaries, as the case may be.

"Permitted Partner" means a Third Person party to a Permitted Partnering Agreement with Seller.

"Permitted Partnering Agreement" means a licensing, co-promotion, joint venture, partnering or similar agreement or arrangement with a Permitted Partner for the purpose of securing promotional and/or marketing resources for Product that is expressly subject to the following conditions: (a) Seller shall continue to receive no less than twenty-five percent (25%) of Net Sales of Product and (b) the Permitted Partner covenants and agrees in writing to provide promotion and marketing efforts of Product in the Territory substantially similar to, and in any event no less in scope, degree or scale than, the promotional and marketing efforts undertaken by Seller hereunder.

"Permitted Qsymia Product Rights" means items (D) through (I) of the definition of "Qsymia Product Rights".

"Person" means any natural person, firm, corporation, limited liability company, partnership, joint venture, association, joint-stock company, trust, unincorporated organization, Governmental Authority or any other legal entity, including public bodies, whether acting in an individual, fiduciary or other capacity.

"Pharmakon" has the meaning set forth in Section 1.6.

"Proceeding" means any action, suit, claim, litigation, arbitration, mediation, proceeding (including any civil, criminal, administrative, investigative or appellate proceeding and any informal proceeding), prosecution, contest, hearing, inquiry, inquest, audit, examination or investigation commenced, brought, conducted or heard by or before, or otherwise involving, any Governmental Authority, any arbitrator or arbitration panel or any mediator.

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"Product" means Qsymia™ (phentermine and topiramate extended release) capsules (formerly known Qnexa®) and any derivative or Improvement thereof (for the avoidance of doubt, Product shall also include Qsiva™ as it relates to the European Union).

"Promotion and Marketing Failure" means the failure of Seller to use Commercially Reasonable Efforts in the promotion and marketing of Product in the Territory (i) during the period beginning on the Tranche A Closing Date and ending on December 31, 2013, and (ii) any Calendar Quarter thereafter, and such failure is not cured within *** after written notice thereof is given to Seller by Purchaser; provided that such cure must occur in the Calendar Quarter following receipt of such written notice for it to be effective.

"Promotion and Marketing Payment Amount" means an amount equal to all accrued and unpaid Scheduled Quarterly Amounts as of the date of payment (including any accrued and unpaid Make-Whole Premiums as of such date) plus a return on such Scheduled Quarterly Amounts equal to 12.75% per annum (compounded quarterly).

"PTO" means the United States Patent and Trademark Office.

"Purchase Price" has the meaning set forth in Section 1.2(a).

"Purchased Receivables" means (a) each payment of Scheduled Quarterly Amounts and (b) any Scheduled Quarterly Amount underpayments or other monetary recoveries resulting from an audit of Seller pursuant to Section 2.3 and (c) any interest on any amounts referred to in clauses (a) and (b) above payable by Seller to Purchaser pursuant to Section 2.5; in the case of clauses (a), and (b) above, irrespective of any amounts which may be payable by Seller or any of its Affiliates to Third Persons.

"Purchaser" has the meaning set forth in the Preamble.

"Qsymia Patent Rights" means (i) the Patents and patent applications listed in Schedule 3.1(m) (including any PCT and/or U.S. utility application claiming priority to such provisional application(s) that are filed on or before the one year conversion date of such application(s)); (ii) any patent or patent application that claims priority to, and is a divisional, continuation, reissue, renewal, reexamination, substitution or extension of, any patent application identified in (i); (iii) any patents issuing on any patent application identified in (i) or (ii), including any reissues, renewals, reexaminations, substitutions or extensions thereof; (iv) any claim of a divisional, continuation or continuation-in-part application or patent (including any reissues, renewals, reexaminations, substitutions or extensions thereof) that is entitled to the priority date of, and is directed specifically to subject matter specifically described in, at least one of the patents or patent applications identified in (i), (ii) or (iii); (v) any foreign counterpart (including PCTs) of any patent or patent application identified in (i), (ii) or (iii) or of the claims identified in (iv); and (vi) any supplementary protection certificates or similar patent term extensions of any patents and patent applications identified in (i) through (v).

"Qsymia Product Rights" means any and all of the following, as they exist throughout the world: (A) Qsymia Patent Rights; (B) rights in the Qysmia Trademarks; (C) regulatory

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filings, submissions and approvals related to Product; (D) unregistered trademarks, service marks, trade names, trade dress, logos, packaging design, slogans and Internet domain names, and registrations and applications for registration of any of the foregoing, in each case, as related to a Product; (E) copyrights in

both published and unpublished works, including without limitation all compilations, databases and computer programs, manuals and other documentation and all copyright registrations and applications, and all derivatives, translations, adaptations and combinations of the above, in each case, as related to a Product; (F) rights in know-how, trade secrets, confidential or proprietary information, research in progress, algorithms, data, databases, data collections, designs, processes, procedures, methods, protocols, materials, formulae, drawings, schematics, blueprints, flow charts, models, strategies, prototypes, techniques, and the results of experimentation and testing, including samples, in each case, as specifically related to a Product; (G) any and all other intellectual property rights and/or proprietary rights specifically relating to any of the foregoing; (H) claims of infringement and misappropriation against Third Parties relating to a Product; and (I) all contractual rights of Seller under the Third Party Agreements.

"Qsymia Trademarks" means the registered trademarks listed in Schedule 3.1(m).

"Quarterly Cap" has the meaning set forth in Section 2.1(b).

"Quarterly Reports" has the meaning set forth in Section 2.2(a).

"Recharacterization" has the meaning set forth in Section 4.7.

"Regulatory Approvals" means the New Drug Application, Abbreviated New Drug Application, Biologics License Application, or similar application which is required to be filed by Seller with the appropriate Governmental Authority (e.g., the FDA in the United States; the EMEA in Europe) to obtain approval to market a Product in the relevant jurisdiction and issued (or to be issued) in the name of Seller (or its Affiliates), and any amendments or supplements thereto.

"REMS Modification" means the Risk Evaluation and Mitigation Strategies Modification proposing to expand access to the Product through a network of certified retail pharmacies.

"Retail Pharmacy Failure" means the failure of Product to be available in at least *** certified retail pharmacy locations by December 31, 2014.

"Retained Receivables" means any and all amounts received by or payable to Seller by Affiliates or licensees of Seller that are attributable to sales of the Product that do not constitute Purchased Receivables.

"Rights Plan" means that certain Preferred Stock Rights Agreement, dated as of March 27, 2007, by and between Seller and Computershare Investor Services, LLC.

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"SEC" means the U.S. Securities and Exchange Commission and any successor entity thereto.

"Scheduled Quarterly Amounts" means (a) at any time prior to the Tranche B Closing, the Tranche A Scheduled Quarterly Amounts and (b) following the Tranche B Closing (if any), the Tranche A Scheduled Quarterly Amounts *plus* the Tranche B Scheduled Quarterly Amounts.

"Seller" has the meaning set forth in the Preamble.

"Subsidiary" means as to any Person, any corporation, partnership, limited liability company or other entity of which more than fifty percent (50%) of the outstanding capital stock having ordinary voting power to elect a majority of the board of directors (or equivalent governing body) or other managers of such corporation, partnership, limited liability company or other entity is at the time owned by (directly or indirectly) or the management is otherwise controlled by (directly or indirectly) such Person (irrespective of whether, at the time, capital stock of any other class or classes of such corporation, partnership, limited liability company or other entity shall have or might have voting power by reason of the happening of any contingency).

"Tax" means any present or future tax, levy, impost, duty, assessment, charge, fee, deduction or withholding of any nature and whatever called (including interest and penalties thereon and any additions thereto) by any Governmental Authority, on whomsoever and wherever imposed, levied, collected, withheld or assessed.

The ***"Term"*** of this Agreement will be as set forth in Section 6.1.

"Territory" means worldwide.

"Third Party Agreements" means the agreements set forth on Schedule 3.1(k).

"Third Person" means any Person other than the Parties or their respective Affiliates.

"Tranche A Amount" has the meaning set forth in Section 1.2(a)(i).

"Tranche A Closing" has the meaning set forth in Section 1.4.

"Tranche A Closing Date" has the meaning set forth in Section 1.4.

"Tranche A Transaction" has the meaning set forth in Section 1.2(a)(i).

"Tranche A Funding Payment" means one percent (1%) of the Tranche A Amount, or $500,000.

"Tranche A Outstanding Payment Amount" means, as of any date, an amount equal to the sum of all unpaid Tranche A Scheduled Quarterly Amounts (including any accrued and unpaid Make-Whole Premiums).

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"Tranche A Scheduled Quarterly Amount" has the meaning set forth in Section 2.1(a)(i).

"Tranche B Amount" has the meaning set forth in Section 1.2(a)(ii).

"Tranche B Transaction" has the meaning set forth in Section 1.2(a)(i).

"Tranche B Closing" has the meaning set forth in Section 1.4.

"Tranche B Closing Date" has the meaning set forth in Section 1.4.

"Tranche B Facility Payment" means one percent (1%) of the Tranche B Amount, or $600,000.

"Tranche B Final Amount" has the meaning set forth in Section 2.1(a)(ii).

"Tranche B Funding Payment" means one percent (1%) of the Tranche B Amount, or $600,000.

"Tranche B Outstanding Payment Amount" means, as of any date, an amount equal to the sum of all unpaid Tranche B Scheduled Quarterly Amounts (including any accrued and unpaid Make-Whole Premiums); provided, however, that if the Tranche B Closing has not occurred, then the Tranche B Outstanding Payment Amount shall be $0.

"Tranche B Scheduled Quarterly Amount" has the meaning set forth in Section 2.1(a)(ii).

"Transaction Documents" means, collectively, this Agreement, the Patent Security Agreement, the Bill of Sale, and any document, certificate or other instrument delivered in connection therewith.

"UCC" means the Uniform Commercial Code as in effect from time to time in the State of New York; provided, however, that, if, with respect to any financing statement or by reason of any provisions of law, the perfection or the effect of perfection or non-perfection of Purchaser's ownership interest in the Purchased Receivables, the back-up security interest granted pursuant to Section 4.7, or the security interest granted pursuant to Section 4.8 is governed by the Uniform Commercial Code as in effect in a jurisdiction of the United States other than the State of New York, then ***"UCC"*** shall mean the Uniform Commercial Code as in effect from time to time in such other jurisdiction for purposes of the provisions of this Agreement and any financing statement relating to such perfection or effect of perfection or non-perfection.

"Updated Disclosure Schedule" means an updated set of schedules to this Agreement, to be dated as of the Tranche B Closing Date, delivered to Purchaser pursuant to Section 1.7(b) of this Agreement and attached to the Bring-Down Certificate. Such Updated Disclosure Schedule shall include disclosure necessary to make the representations and warranties of Seller in Section 3.1 of this Agreement true and correct as of the date of the Tranche B Closing Date and to consist solely of information regarding circumstances, facts, events or conditions that have

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arisen, occurred or come into existence after the Effective Date of this Agreement; provided, however, that such Updated Disclosure Schedule shall not correct, supplement or amend the disclosures set forth in the schedules attached to the Agreement on the Effective Date for purposes of the representations and warranties made by the Company as of the Effective Date of this Agreement, but the disclosures contained in the Updated Disclosure Schedule shall be deemed to modify and qualify all representations and warranties made in this Agreement on and as of the Tranche B Closing Date with respect to the Tranche B Transaction.

"Up-Front Payments" means the Tranche A Funding Payment and the Tranche B Facility Payment.

"U.S." or ***"United States"*** means the United States of America, its 50 states, each territory thereof and the District of Columbia.

"Unaudited Financial Statements" has the meaning set forth in Section 2.2(b).

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EXHIBIT A

BILL OF SALE

THIS BILL OF SALE (this ***"Purchaser Bill of Sale"***) is made, entered into and effective this day of April, 2013, by and between by and between **VIVUS, INC.**, a Delaware corporation, and its permitted successors and assigns (***"Seller"***) and **BIOPHARMA SECURED INVESTMENTS III HOLDINGS CAYMAN LP**, a Cayman Islands exempted limited partnership, and its permitted successors and assigns (***"Purchaser"***). Capitalized terms used but not defined herein will have the meanings ascribed to such terms in that certain Purchase and Sale Agreement, dated as of March 25, 2013, by and between Seller and Purchaser (the ***"Purchase Agreement"***).

RECITALS

WHEREAS, Seller desires to sell, transfer, convey and assign to Purchaser, and Purchaser desires to purchase and accept from Seller, all of Seller's right, title and interest in, to and under the Purchased Receivables, on the terms and conditions set forth in the Purchase Agreement.

NOW, THEREFORE, in consideration of the premises and the mutual agreements contained herein and other good and valuable considerations, the receipt and adequacy of which are hereby acknowledged, the Parties hereto agree as follows:

1. Seller, by this Purchaser Bill of Sale, does hereby sell, transfer, convey, assign and deliver to Purchaser, and Purchaser does hereby purchase and accept, all of Seller's right, title and interest in, to and under the Purchased Receivables.

2. Seller hereby covenants that, at any time or from time to time after the date hereof, at Purchaser's reasonable request and without further consideration but at Purchaser's expense, Seller will execute and deliver to Purchaser such other instruments of sale, transfer, conveyance and assignment as Purchaser may reasonably deem necessary to sell, transfer, convey, assign and deliver to Purchaser, and to confirm Purchaser's title to, all of Seller's right, title and interest in, to and under the Purchased Receivables.

3. Seller represents, warrants and covenants that (a) it has absolute title to the Purchased Receivables free and clear of all Encumbrances (other than Permitted Encumbrances), (b) it has not made any prior sale, transfer, conveyance, assignment, grant or delivery of any Purchased Receivables, (c) it has the present lawful right, power and authority to sell, transfer, convey, assign and deliver the Purchased Receivables to Purchaser free and clear of all Encumbrances (other than Permitted Encumbrances), and (d) all action has been taken which is required for Seller to make this Purchaser Bill of Sale, and this Purchaser Bill of Sale is, a legal, valid and binding obligation of Seller.

4. This Purchaser Bill of Sale will be binding upon and inure to the benefit of Seller, Purchaser and their respective permitted successors and assigns under the Purchase Agreement,

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*** *Certain confidential information contained in this document, marked with three asterisks, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.*

for the uses and purposes set forth and referred to above, effective immediately upon its delivery to Purchaser.

5. (a) THIS PURCHASER BILL OF SALE AND ANY PROCEEDING ARISING OUT OF OR RELATING TO THIS PURCHASER BILL OF SALE OR THE TRANSACTIONS CONTEMPLATED HEREBY (WHETHER IN CONTRACT, TORT OR OTHERWISE) WILL BE GOVERNED BY, AND CONSTRUED, INTERPRETED AND ENFORCED IN ACCORDANCE WITH THE INTERNAL SUBSTANTIVE LAWS OF THE STATE OF NEW YORK, WITHOUT GIVING EFFECT TO THE PRINCIPLES OF CONFLICTS OF LAW THEREOF OTHER THAN SECTION 5-1401 OF THE GENERAL OBLIGATIONS LAW OF THE STATE OF NEW YORK, AND THE OBLIGATIONS, RIGHTS AND REMEDIES OF THE PARTIES HEREUNDER WILL BE DETERMINED IN ACCORDANCE WITH SUCH LAWS.

(b) ANY PROCEEDING WITH RESPECT TO THIS PURCHASER BILL OF SALE WILL BE BROUGHT IN THE COURTS OF THE STATE OF NEW YORK LOCATED IN THE BOROUGH OF MANHATTAN, THE CITY OF NEW YORK OR OF THE UNITED STATES OF AMERICA FOR THE SOUTHERN DISTRICT OF NEW YORK, AND EACH PARTY HEREBY ACCEPTS FOR ITSELF AND IN RESPECT OF ITS RESPECTIVE PROPERTY, GENERALLY AND UNCONDITIONALLY, THE EXCLUSIVE JURISDICTION OF THE AFORESAID COURTS.

(c) EACH PARTY HEREBY IRREVOCABLY WAIVES, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, TRIAL BY JURY IN ANY ACTION OR DISPUTE ARISING OUT OF OR RELATING TO THIS PURCHASER BILL OF SALE OR THE TRANSACTIONS CONTEMPLATED HEREBY (WHETHER IN CONTRACT, TORT OR OTHERWISE).

(d) EACH PARTY HEREBY IRREVOCABLY WAIVES ANY OBJECTION, INCLUDING ANY OBJECTION TO THE LAYING OF VENUE OR BASED ON THE GROUNDS OF FORUM NON CONVENIENS, WHICH IT MAY NOW OR HEREAFTER HAVE TO THE BRINGING OF ANY SUCH ACTION OR PROCEEDING IN SUCH RESPECTIVE JURISDICTIONS.

(e) EACH PARTY IRREVOCABLY CONSENTS TO THE SERVICE OF PROCESS OF ANY OF THE AFOREMENTIONED COURTS IN ANY SUCH ACTION OR PROCEEDING BY THE SENDING OF COPIES THEREOF BY FEDERAL EXPRESS OR OTHER OVERNIGHT COURIER COMPANY, TO SUCH PARTY AT ITS ADDRESS SPECIFIED BY SECTION 7.9 OF THE PURCHASE AGREEMENT, SUCH SERVICE TO BECOME EFFECTIVE FOUR (4) DAYS AFTER DELIVERY TO SUCH COURIER COMPANY.

(f) NOTHING HEREIN WILL AFFECT THE RIGHT OF ANY PARTY TO SERVE PROCESS IN ANY OTHER MANNER PERMITTED BY LAW.

6. Notwithstanding anything to the contrary contained in this Purchaser Bill of Sale, in the event of any conflict between the terms of this Purchaser Bill of Sale and the terms of the Purchase Agreement, the terms of the Purchase Agreement shall control.

7. This Purchaser Bill of Sale may be executed in any number of counterparts, each of which so executed will be deemed to be an original, but all of such counterparts will together constitute but one and the same instrument.

[Remainder of Page Intentionally Left Blank]

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IN WITNESS WHEREOF, the Parties hereto have executed this Purchaser Bill of Sale as of the day and year first written above.

SELLER:

VIVUS, INC.

By: _____

Name: Leland F. Wilson

Title: Chief Executive Officer

PURCHASER:

BIOPHARMA SECURED INVESTMENTS III HOLDINGS CAYMAN LP

By: Pharmakon Advisors, LP, its investment manager

By: Pharmakon Management I, LLC its general partner

By: _____

Name: Pedro Gonzalez de Cosio

Title: Managing Member

Signature Page to Purchaser Bill of Sale

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EXHIBIT B

PATENT SECURITY AGREEMENT

PATENT AND TRADEMARK SECURITY AGREEMENT

This Patent and Trademark Security Agreement (the "Security Agreement") is made the day of April, 2013, by and between **VIVUS, INC**., a Delaware corporation, and its permitted successors and assigns (the "Grantor") and **BIOPHARMA SECURED INVESTMENTS III HOLDINGS CAYMAN LP,** a Cayman Islands exempted limited partnership, and its permitted successors and assigns (the "Secured Party").

RECITALS

WHEREAS, reference is made to that certain Purchase and Sale Agreement ("the Agreement") dated as of March 25, 2013 (and as amended, supplemented, restated, or otherwise modified from time to time), by and between the Grantor and the Secured Party;

WHEREAS, pursuant to the Agreement, the Grantor granted to the Secured Party a security interest in regards to all of Grantor's right, title, and interest in, to, and under the Additional Collateral, whether now owned or hereafter acquired by the Grantor and all of Grantor's rights and privileges with respect thereto;

WHEREAS the Grantor and the Secured Party have agreed to execute all documents to perfect the security interest of the Secured Party in such Additional Collateral of the Grantor, perfected and prior to all other Encumbrances thereon (other than Permitted Encumbrances);

WHEREAS, in connection with the Agreement, the Grantor and the Secured Party have entered into this Security Agreement as of the date hereof (and as amended, supplemented, restated, or otherwise modified from time to time);

WHEREAS, the Grantor does hereby further acknowledge and affirm that the rights and remedies of the Secured Party with respect to the security interest in the Additional Collateral granted hereby are more fully set forth in the Agreement, the terms and provisions of which are incorporated by reference herein as if fully set forth herein.

WHEREAS, as a condition, among others, to the terms contemplated by the Agreement in regards to the Additional Collateral, the parties hereto execute this Security Agreement.

NOW THEREFORE, the parties hereto agree as follows:

1. Defined Terms. All capitalized terms used but not otherwise defined herein have the meanings ascribed to them, or incorporated by reference in, the Agreement.

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2. Grant of Security Interest. Pursuant to the terms of the Agreement, Grantor hereby grants a security interest in all of its right, title, and interest in, to, and under all of the following Additional Collateral:

(a) all Qsymia Product Rights set forth on Exhibit A to this Security Agreement and all of Grantor's rights and privileges with respect thereto;

(b) all Regulatory Approvals;

(c) all Supporting Obligations (as such term is defined in the UCC) in respect of the foregoing and all collateral security and guarantees given by any Person with respect to any of the foregoing;

(d) all of Grantors's books and records relating to any and all of the foregoing;

(e) all contractual rights of Grantor under any Permitted Partnering Agreement to receive payment of Net Sales; and

(f) all Proceeds (as such term is defined in the UCC) and products of and to any and all of the foregoing;

provided, however, that, "Additional Collateral" shall not include any general intangible, permit, lease, license, contract or other instrument of Grantor included in items (D) through (H) of the definition of Qsymia Product Rights (or any of Grantor's books and records relating thereto, or any Proceeds and products thereof and thereto), if, and only to the extent, the grant of a security interest in such general intangible, permit, lease, license, contract or other instrument in the manner contemplated by this Agreement, under the terms thereof or under Applicable Law, is prohibited and would result in the termination thereof or give the other Persons party thereto the right to terminate, accelerate or otherwise alter Grantor's rights, title and interests thereunder (including upon the giving of notice or the lapse of time or both); provided, further, that (i) any such limitation described above on the security interests granted hereunder shall only apply to the extent that any such prohibition could not be rendered ineffective pursuant to the UCC or any other Applicable Law (including Bankruptcy Laws) or principles of equity and (ii) in the event of the termination or elimination of any such prohibition or the requirement for any consent contained in any Applicable Law, general intangible, permit, lease, license, contract or other instrument, to the extent sufficient to permit any such general intangible, permit, lease, license, contract or other instrument of Grantor (and the books and records relating thereto and the Proceeds and products thereof and thereto) to become Additional Collateral hereunder, or upon the granting of any such consent, or waiving or terminating any requirement for such consent, a security interest in such general intangible, permit, lease, license, contract or other instrument (and the books and records relating thereto and the Proceeds and products thereof and thereto) shall be automatically and simultaneously granted hereunder and shall be included as Additional Collateral hereunder.

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3. Reference to the Agreement. This Security Agreement has been entered into by the Grantor and the Secured Party solely for purposes as contemplated by the Agreement. In the event of any inconsistency between any of the terms or provisions hereof and the terms and provisions of the Agreement, the terms and provisions of this Security Agreement shall govern.

4. Counterparts. This Agreement may be executed in two or more counterparts, each of which will be an original, but all of which together will constitute one and the same instrument. To evidence the fact that it has executed this Agreement, a Party may send a copy of its executed counterpart to the other Parties by facsimile or other electronic transmission. In such event, such Party will forthwith deliver to the other Parties the counterpart of this Agreement executed by such Party.

5. Governing Law. This Security Agreement shall be construed in accordance with and governed by the laws of the State of New York, without giving effect to the principles of conflicts of law thereof.

[Signature page follows]

IN WITNESS WHEREOF, the Secured Party and the Grantor have caused this Security Agreement to be duly executed by their respective officers thereunto duly authorized, as of the day and year first set forth above.

BIOPHARMA SECURED INVESTMENTS III HOLDINGS CAYMAN LP, as the Secured Party

By: Pharmakon Advisors, LP, its investment manager
By: Pharmakon Management I, LLC, its general partner

By: _____

Name: Pedro Gonzalez de Cosio

Title: Managing Member

VIVUS, INC., as the Grantor

By: _____

Name: Leland F. Wilson

Title: Chief Executive Officer

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EXHIBIT A

QSYMIA PRODUCT RIGHTS

"***Qsymia Patent Rights***" means (i) the Patents and patent applications listed in Schedule I below (including any PCT and/or U.S. utility application claiming priority to such provisional application(s) that are filed on or before the one year conversion date of such application(s)); (ii) any patent or patent application that claims priority to, and is a divisional, continuation, reissue, renewal, reexamination, substitution or extension of, any patent application identified in (i); (iii) any patents issuing on any patent application identified in (i) or (ii), including any reissues, renewals, reexaminations, substitutions or extensions thereof; (iv) any claim of a divisional, continuation or continuation-in-part application or patent (including any reissues, renewals, reexaminations, substitutions or extensions thereof) that is entitled to the priority date of, and is directed specifically to subject matter specifically described in, at least one of the patents or patent applications identified in (i), (ii) or (iii); (v) any foreign counterpart (including PCTs) of any patent or patent application identified in (i), (ii) or (iii) or of the claims identified in (iv); and (vi) any supplementary protection certificates or similar patent term extensions of any patents and patent applications identified in (i) through (v).

"***Qsymia Product Rights***" means any and all of the following, as they exist throughout the world: (A) Qsymia Patent Rights; (B) rights in the Qysmia Trademarks listed in Schedule II below; (C) regulatory filings, submissions and approvals related to Product; (D) unregistered trademarks, service marks, trade names, trade dress, logos, packaging design, slogans and Internet domain names, and registrations and applications for registration of any of the foregoing, in each case, as related to a Product; (E) copyrights in both published and unpublished works, including without limitation all compilations, databases and computer programs, manuals and other documentation and all copyright registrations and applications, and all derivatives, translations, adaptations and combinations of the above, in each case, as related to a Product; (F) rights in know-how, trade secrets, confidential or proprietary information, research in progress, algorithms, data, databases, data collections, designs, processes, procedures, methods, protocols, materials, formulae, drawings, schematics, blueprints, flow charts, models, strategies, prototypes, techniques, and the results of experimentation and testing, including samples, in each case, as specifically related to a Product; (G) any and all other intellectual property rights and/or proprietary rights specifically relating to any of the foregoing; (H) claims of infringement and misappropriation against Third Parties relating to a Product; and (I) all contractual rights of Seller under the Third Party Agreements.

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SCHEDULE I

LIST OF PATENTS

Title	Inventors	Country	Patent Number	App. Number	Pub. Number	Status	Filing Date
Combination Therapy for Effecting Weight Loss and Treating Obesity	Najarian	US	7,056,890	10/454,368	2004/0002462	Issued	6/3/03
		US	7,553,818	11/385,198	2006/0234950	Issued	3/20/06
		US	7,659,256	11/385,199	2006/0234951	Issued	3/20/06
		US	7,674,776	11/385,233	2006/0234952	Issued	3/20/06
		Australia	770068	200054896		Granted	6/14/00
		Canada	2,377,330	2377330		Granted	6/14/00
		Austria	1187603	00939884.3		Granted	6/14/00
		Belgium	1187603	00939884.3		Granted	6/14/00
		Cyprus	1187603	00939884.3		Granted	6/14/00
		Denmark	1187603	00939884.3		Granted	6/14/00
		Finland	1187603	00939884.3		Granted	6/14/00
		France	1187603	00939884.3		Granted	6/14/00
		Greece	1187603	00939884.3		Granted	6/14/00
		Germany	60035870	00939884.3		Granted	6/14/00
		Ireland	1187603	00939884.3		Granted	6/14/00
		Italy	1187603	00939884.3		Granted	6/14/00
		Luxembourg	1187603	00939884.3		Granted	6/14/00
		Monaco	1187603	00939884.3		Granted	6/14/00
		Netherlands	1187603	00939884.3		Granted	6/14/00

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Title	Inventors	Country	Patent Number	App. Number	Pub. Number	Status	Filing Date
		Portugal	1187603	00939884.3		Granted	6/14/00
		Spain	1187603	00939884.3		Granted	6/14/00
		Sweden	1187603	00939884.3		Granted	6/14/00
		Switzerland	1187603	00939884.3		Granted	6/14/00
		UK	1187603	00939884.3		Granted	6/14/00
		EPO		07011472.3		Pending	6/14/00
Compositions and Methods for Treating Sleep Apnea	Tam et al.	US		12/683,353	2010/0105765	Pending	1/6/10
"	Tam et al.	EPO		10184955.2	EP1825851	Pending	12/6/07
Combination Therapy for the Treatment of Sleep Apnea	Najarian	EPO			EP 2305226	Pending	9/30/10
Combination Therapy for the Treatment of Hypertension	Najarian	EPO		10184959.4	EP 2308481	Pending	9/30/10
Combination Therapy for the Treatment of Diabetes	Najarian	EPO		10184977.6	EP 2305227	Pending	9/30/10
Combination Therapy for the Treatment of Hyperlipidemia	Najarian	EPO		10184981.8	EP 2305228	Pending	9/30/10
Low Dose Topiramate/Phentermine Composition	Najarian et al.	EPO		12/481,540	2010/0215739	Pending	6/9/09

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Title	Inventors	Country	Patent Number	App. Number	Pub. Number	Status	Filing Date
and Methods of Use Thereof							
"		Australia		2009257572		Pending	6/9/09
"		Brazil		PI0914985-6		Pending	6/9/09
"		Canada		2727319		Pending	6/9/09
"		Chile		1365-2010		Pending	6/9/09
"		China		200980130379.5		Pending	6/9/09
"		EPO		09763479.4		Pending	6/9/09
"		India		6898/CHENP/2010		Pending	6/9/09
"		Israel		209874		Pending	6/9/09
"		Japan		2011-513646	JP2011522896A	Pending	6/9/09
"		Korea		10-2011-7000416		Pending	6/9/09
"		Mexico		MX/a/2010/013503		Pending	6/9/09
"		South Africa	2010/08839	2010/08839		Granted	6/9/09
Escalating Dosing Regimen for Effecting Weight Loss and Treating Obesity	Najarian et al.	US		12/481,548	2009/0304785	Pending	6/9/09
"		Australia		2009257573		Pending	6/9/09
"		Brazil		PI0914991-0		Pending	6/9/09
"		Canada		2727313		Pending	6/9/09
"		Chile		1366-2010		Pending	6/9/09
"		China		200980130444.4		Pending	6/9/09
"		EPO		09763480.2		Pending	6/9/09
"		India		6897/CHENP/2010		Pending	6/9/09

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Title	Inventors	Country	Patent Number	App. Number	Pub. Number	Status	Filing Date
“		Israel		209875		Pending	6/9/09
“		Japan		2011-513647	JP2011522897A	Pending	6/9/09
“		Korea		10-2011-7000417		Pending	6/9/09
“		Mexico		MX/a/2010/013505		Pending	6/9/09
“		South Africa	2010/08840	2010/08840		Granted	6/9/09

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SCHEDULE II

LIST OF TRADEMARKS

Country	Trademark	App. Number/ Date	Reg. Number/ Date	Class	Description of Services	Status	Next Renewal Date
US	QSYMIA	85656775 6/20/2012	4295224 2/26/2013	IC 005. US 006 018 044 046 051 052.	Pharmaceutical preparations for the treatment of obesity, to facilitate weight loss and weight control, to suppress appetite and lower the threshold for satiety.	Registered	2/26/2023
European Community	QSYMIA	011405198 12/7/2012		IC 005	Pharmaceutical preparations for the treatment of obesity, to facilitate weight loss and weight control, to suppress appetite and lower the threshold for satiety.	Pending	
International-Madrid Protocol	QSYMIA	A0033230 6/20/2012	1146156 2/7/2013	IC 005	Pharmaceutical preparations for the treatment of obesity, to facilitate weight loss and weight control, to suppress appetite and lower the threshold for satiety.	Registered	12/14/2022
Canada	QSYMIA	1606513 12/13/2012		IC 005	Pharmaceutical preparations for the treatment of obesity, to facilitate weight loss and	Pending	

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					weight control, to suppress appetite and lower the threshold for satiety		

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SCHEDULE 3.1(g)

Litigation

1. *Kovtun v. Vivus, Inc. et al*, Case No. CV10-4957 PJH, filed in the U.S. District Court, Northern District of California, as disclosed and described in the most recent Form 10-K filed by Seller with the Securities and Exchange Commission.

2. *Turberg v. Logan, et al*, Case No. CV10-05271 PJH, filed in the U.S. District Court, Northern District of California, as disclosed and described in the most recent Form 10-K filed by Seller with the Securities and Exchange Commission.

3. *In re Vivus, Inc. Derivative Litigation*, Master File No. 11 0 CV188439, filed in the California Superior Court, Santa Clara County, as disclosed and described in the most recent Form 10-K filed by Seller with the Securities and Exchange Commission.

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SCHEDULE 3.1(i)

Existing In-Licenses

1. The Najarian Agreement.

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SCHEDULE 3.1(j)

Sublicenses and Out-Licenses

1. ***

2. Qsymia™ Risk Evaluation and Mitigation Strategy (REMS) Certified Pharmacy Services Agreement, effective August 30, 2012, between CuraScript, Inc. and Seller.

3. Qsymia™ Risk Evaluation and Mitigation Strategy (REMS) Certified Pharmacy Services Agreement, effective August 27, 2012, between CVS Pharmacy, Inc. and Seller.

4. Certified Pharmacy Services Agreement, effective September 17, 2012, by and between Kaiser Foundation Health Plan, Inc. and Seller.

5. Qsymia™ Risk Evaluation and Mitigation Strategy (REMS) Certified Pharmacy Services Agreement, effective September 1, 2012, between Walgreens Mail Service, Inc. and Seller.

6. Qsymia™ Risk Evaluation and Mitigation Strategy (REMS) Certified Pharmacy Services Addendum to Supplier Agreement, effective November 30, 2012, between Wal-Mart Stores, Inc. and Seller.

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SCHEDULE 3.1(k)

Third Party Agreements

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SCHEDULE 3.1(m)

Intellectual Property

1. Patents included within the Qsymia Patent Rights:

Title	Inventors	Country	Patent Number	App. Number	Pub. Number	Status	Filing Date
Combination Therapy for Effecting Weight Loss and Treating Obesity	Najarian	US	7,056,890	10/454,368	2004/0002462	Issued	6/3/03
		US	7,553,818	11/385,198	2006/0234950	Issued	3/20/06
		US	7,659,256	11/385,199	2006/0234951	Issued	3/20/06
		US	7,674,776	11/385,233	2006/0234952	Issued	3/20/06

		Australia	770068	200054896		Granted	6/14/00
		Canada	2,377,330	2377330		Granted	6/14/00
		Austria	1187603	00939884.3		Granted	6/14/00
		Belgium	1187603	00939884.3		Granted	6/14/00
		Cyprus	1187603	00939884.3		Granted	6/14/00
		Denmark	1187603	00939884.3		Granted	6/14/00
		Finland	1187603	00939884.3		Granted	6/14/00
		France	1187603	00939884.3		Granted	6/14/00
		Greece	1187603	00939884.3		Granted	6/14/00
		Germany	60035870	00939884.3		Granted	6/14/00
		Ireland	1187603	00939884.3		Granted	6/14/00
		Italy	1187603	00939884.3		Granted	6/14/00
		Luxembourg	1187603	00939884.3		Granted	6/14/00
		Monaco	1187603	00939884.3		Granted	6/14/00
		Netherlands	1187603	00939884.3		Granted	6/14/00
		Portugal	1187603	00939884.3		Granted	6/14/00
		Spain	1187603	00939884.3		Granted	6/14/00
		Sweden	1187603	00939884.3		Granted	6/14/00
		Switzerland	1187603	00939884.3		Granted	6/14/00
		UK	1187603	00939884.3		Granted	6/14/00
		EPO		07011472.3		Pending	6/14/00
Compositions and Methods for Treating Sleep Apnea	Tam et al.	US		12/683,353	2010/0105765	Pending	1/6/10
"	Tam et al.	EPO		10184955.2	EP1825851	Pending	12/6/07
Combination Therapy for the Treatment of	Najarian	EPO			EP 2305226	Pending	9/30/10

****Certain confidential information contained in this document, marked with three asterisks, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.*

Title	Inventors	Country	Patent Number	App. Number	Pub. Number	Status	Filing Date
Sleep Apnea							
Combination Therapy for the Treatment of Hypertension	Najarian	EPO		10184959.4	EP 2308481	Pending	9/30/10
Combination Therapy for the Treatment of Diabetes	Najarian	EPO		10184977.6	EP 2305227	Pending	9/30/10
Combination Therapy for the Treatment of Hyperlipidemia	Najarian	EPO		10184981.8	EP 2305228	Pending	9/30/10
Low Dose Topiramate/Phentermine Composition and Methods of Use Thereof	Najarian et al.	EPO		12/481,540	2010/0215739	Pending	6/9/09
"		Australia		2009257572		Pending	6/9/09
"		Brazil		PI0914985-6		Pending	6/9/09
"		Canada		2727319		Pending	6/9/09
"		Chile		1365-2010		Pending	6/9/09
"		China		200980130379.5		Pending	6/9/09
"		EPO		09763479.4		Pending	6/9/09
"		India		6898/CHENP/2010		Pending	6/9/09
"		Israel		209874		Pending	6/9/09
"		Japan		2011-513646	JP2011522896A	Pending	6/9/09
"		Korea		10-2011-7000416		Pending	6/9/09
"		Mexico		MX/a/2010/013503		Pending	6/9/09
"		South Africa	2010/08839	2010/08839		Granted	6/9/09
Escalating Dosing Regimen for Effecting	Najarian et al.	US		12/481,548	2009/0304785	Pending	6/9/09

****Certain confidential information contained in this document, marked with three asterisks, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.*

Title	Inventors	Country	Patent Number	App. Number	Pub. Number	Status	Filing Date
Weight Loss and Treating Obesity							
"		Australia		2009257573		Pending	6/9/09
"		Brazil		PI0914991-0		Pending	6/9/09
"		Canada		2727313		Pending	6/9/09
"		Chile		1366-2010		Pending	6/9/09
"		China		200980130444.4		Pending	6/9/09
"		EPO		09763480.2		Pending	6/9/09
"		India		6897/CHENP/2010		Pending	6/9/09
"		Israel		209875		Pending	6/9/09
"		Japan		2011-513647	JP2011522897A	Pending	6/9/09
"		Korea		10-2011-7000417		Pending	6/9/09
"		Mexico		MX/a/2010/013505		Pending	6/9/09
"		South Africa	2010/08840	2010/08840		Granted	6/9/09

2. Qsymia Trademarks:

Country	Trademark	App. Number / Date	Reg. Number / Date	Class	Description of Services	Status	Next Renewal Date
US	QSYMIA	85656775 6/20/2012	4295224 2/26/2013	IC 005. US 006 018 044 046 051 052.	Pharmaceutical preparations for the treatment of obesity, to facilitate weight loss and weight control, to suppress appetite and lower the threshold for satiety.	Registered	2/26/2023
European Community	QSYMIA	011405198		IC 005	Pharmaceutical	Pending	

		12/7/2012			preparations for the treatment of obesity, to facilitate weight loss and weight control, to suppress appetite and lower the threshold for satiety.		
International-Madrid Protocol	QSYMIA	A0033230 6/20/2012	1146156 2/7/2013	IC 005	Pharmaceutical preparations for the treatment of obesity, to facilitate weight loss and weight control, to suppress appetite and lower the threshold for satiety.	Registered	12/14/2022
Canada	QSYMIA	1606513 12/13/2012		IC 005	Pharmaceutical preparations for the treatment of obesity, to facilitate weight loss and weight control, to suppress appetite and lower the threshold for satiety	Pending	

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****Certain confidential information contained in this document, marked with three asterisks, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.*

MASTER SERVICES AGREEMENT

Between

Medpace Inc.
an Ohio Corporation
4620 Wesley Avenue
Cincinnati, Ohio 45212

("MEDPACE")

and

VIVUS, Inc.
a Delaware Corporation
1172 Castro Street
Mountain View, California 94040-2552

("VIVUS")

This MASTER SERVICES AGREEMENT (the "Agreement"), dated as of September 12, 2007 (the "Effective Date"), is between MEDPACE and VIVUS. MEDPACE and VIVUS are sometimes referred to herein individually as a "Party" and together as the "Parties".

RECITALS:

WHEREAS, VIVUS is in the business of developing and obtaining regulatory approval of the marketing and sale of pharmaceutical products and

WHEREAS, MEDPACE is engaged in the business of providing services related to the design and execution of clinical development programs involving drugs, biologics, and medical devices through engagement by its clients, the sponsors of clinical development programs, to perform such services; and

WHEREAS, VIVUS desires to engage MEDPACE to perform certain services ("Services") as set forth hereinafter in connection with certain clinical trials, all in accordance with and subject to the terms of this Agreement;

NOW, THEREFORE, in consideration of the premises and the mutual covenants and conditions hereinafter set forth, the Parties agree as follows:

1. **PROJECT SPECIFICATIONS**

1.1 MEDPACE hereby agrees to perform Services for VIVUS from time to time. The precise Services to be performed by MEDPACE shall be mutually agreed upon by the Parties and set forth in one or more task orders (each a "Task Order"), a form of which is attached hereto as Exhibit A. Each Task Order shall be signed by an authorized representative of each Party and shall include detailed information concerning a given project, including a description of the specific services to be provided ("Scope of Work"), project milestones and target completion dates ("Project Schedule"), a detailed budget ("Project Budget"), and a schedule of payments related to the Project Schedule and the Project Budget ("Payment Schedule"). Each Task Order shall contain a Transfer of Obligations list ("Transfer of Obligations") in conjunction with the relevant Task Order and consistent with the regulations set forth in 21 C.F.R. Section 312, Subpart D (Responsibilities of VIVUS and Investigators). Any responsibilities not specifically transferred in the Transfer of Obligations shall remain the regulatory responsibility of VIVUS. Each Task Order shall designate a Project Manager or other duly authorized representative authorized to make decisions on behalf of each Party with respect to the Services to be rendered under the Task Order.

2. PROJECT SCHEDULE

2.1. Each Task Order shall contain project timelines, milestones or target dates for completion of a project or a portion thereof, and all such schedules shall be reasonable for the Services to be provided. In all events, the Parties shall use their reasonable best efforts to comply with each Task Order.

2.2. If at any time either Party anticipates a delay in meeting the timelines for a given Task Order as set forth in its Project Schedule, either due to changes to the Services requested by VIVUS, or other causes (such as FDA approval of a competitor's NDA for the same drug, which may adversely affect patient enrollment), then the anticipating Party shall promptly notify the other Party in writing, specifying the reason for the delay and the anticipated effect upon the timelines, milestones or other deliverables.

3. CHANGE ORDERS

3.1. Any change in the details of a Task Order or the assumptions upon which the Task Order is based may require changes in the Project Budget, Payment Schedule or Project Schedule. Every such change shall require a written amendment to the Task Order (a "Change

Order"). Each Change Order shall detail the requested changes to the applicable task, responsibility, duty, budget, timeline or other matter. The Change Order will become effective upon the execution of the Change Order by both Parties, and the Change Order will specify the period of time within which MEDPACE must implement the changes. Both Parties agree to act in good faith and promptly when considering a Change Order requested by the other party but neither party is obligated to execute a Change Order. No Change Order shall become effective unless and until it is signed by both Parties. Any such changes that result in additional charges shall be reflected in the Change Order to the affected Task Order, Project Budget or Payment Schedule.

4. PROJECT BUDGET, PAYMENT SCHEDULE, AND TERMS

4.1. VIVUS agrees to pay MEDPACE for Services rendered pursuant to the Project Budget and Payment Schedules included in each Task Order.

4.2. VIVUS agrees to reimburse MEDPACE for reasonable pass-through expenses identified in the Task Order and incurred by MEDPACE in providing the Services in accordance with the relevant Task Order. All expenses billed to VIVUS by MEDPACE must be accompanied by appropriate documentary evidence, such as receipts or other documentation reasonably acceptable to VIVUS.

4.3. VIVUS shall mail payments to MEDPACE within 45 days after receipt of a written invoice and required supporting documentation as applicable. An annual interest rate of 12% will be applied to outstanding invoices greater than 45 days.

5. WARRANTIES AND REPRESENTATIONS:

5.1. Acknowledgements:

MEDPACE acknowledges that the Services to be provided hereunder are for the benefit of, and are subject to the direction of VIVUS. MEDPACE acknowledges that VIVUS is the beneficiary under the terms of this Agreement and each Task Order, and that VIVUS is entitled to enforce the provisions thereof.

5.2. Representations and Warranties of MEDPACE

5.2.1. MEDPACE represents and warrants that it is a corporation with its principal office and place of business at 4620 Wesley Avenue, Cincinnati, Ohio 45212, duly organized, validly existing and in good standing in its place of organization, and is in good standing in and duly qualified to do business.

5.2.2. MEDPACE warrants that the execution, delivery and performance of this Agreement and each Task Order has been validly authorized by all corporate action and this Agreement and each Task Order represents the valid binding agreement of MEDPACE enforceable in accordance with its terms. The execution, delivery and performance of this Agreement and each Task Order will not violate any organizational document governing MEDPACE, any agreement to which MEDPACE is a party, or any law or court or governmental order, holding or writ by which MEDPACE is bound. MEDPACE further warrants that it shall render the Services requested by VIVUS in accordance with high professional standards, consistent with Good Clinical Practices and Laboratory Regulations and with the standard of care customary in the contract research organization industry. MEDPACE shall complete all services in conformance with each approved Task Order, including each Project Schedule and Project Budget.

5.2.3. MEDPACE warrants that the personnel assigned to perform services rendered under this Agreement shall be qualified and professionally capable of performing the Services, shall be adequate to effectively perform the Services on the agreed upon schedule and shall devote such time as is necessary to perform the Services on such agreed upon schedule.

5.2.4. MEDPACE further warrants that it shall perform the Services in compliance with the terms of this Agreement, the terms of the Task Orders, and all applicable laws and regulations including, without limitation, the Federal Food, Drug and Cosmetic Act and the regulations promulgated pursuant thereto, and all future amendments during the term. MEDPACE further warrants that it shall make available to VIVUS, or to the responsible regulatory authority, relevant records, programs and data as may reasonably be requested by VIVUS or which is the subject of a Task Order. VIVUS shall have the right to monitor the operations of MEDPACE hereunder, and VIVUS representatives shall have the right to visit any of the facilities where MEDPACE is performing any of the Services and during such visits to inspect the work being done and materials used, to observe the procedures being followed, to examine the books, records and other data relevant to the Services. If any regulatory agency requests to inspect any books, records, data or facilities of

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MEDPACE relating to the Services, MEDPACE shall immediately notify VIVUS.

5.2.5. MEDPACE represents and warrants that there is no litigation, regulatory investigation or proceeding, administrative hearing or any other similar proceeding pending or to the best of its knowledge threatened against MEDPACE which could adversely affect MEDPACE's ability to perform the Services or which alleges a violation by MEDPACE of any law or regulation related to Services.

5.2.6. Obligation of MEDPACE

MEDPACE shall immediately notify VIVUS in writing if any of the representations or warranties contained in this Article 5 become untrue. MEDPACE shall correct or perform again any portion of the Services that fails to conform to any warranty set forth in this Article 5 without additional cost to VIVUS and within thirty (30) days of receipt of notice from VIVUS.

5.3. Representations and Warranties of VIVUS

5.3.1 VIVUS represents and warrants that it is a corporation with its principal office and place of business at 1172 Castro Street, Mountain View, California 94040-2552, duly organized, validly existing and in good standing in its place of organization, and is in good standing in and duly qualified to do business.

5.3.2 VIVUS warrants that the execution, delivery and performance of this Agreement and each Task Order has been validly authorized by all corporate action and this Agreement and each Task Order represents the valid binding agreement of VIVUS enforceable in accordance with its terms. The execution, delivery and performance of this Agreement and each Task Order will not violate any organizational document governing VIVUS, any agreement to which VIVUS is a party, or any law or court or governmental order, holding or writ by which VIVUS is bound.

5.3.3 VIVUS represents and warrants that there is no litigation, regulatory investigation or proceeding, administrative hearing or any other similar proceeding pending or to the best of its knowledge threatened against VIVUS which could adversely affect VIVUS's ability to perform under this Agreement or any Task Order or which alleges a violation by VIVUS of any law or regulation related to the subject matter of the Services rendered by MEDPACE hereunder.

5.3.4 Obligation of VIVUS

VIVUS shall immediately notify MEDPACE in writing if any of the representations or warranties contained in this Article 5 become untrue.

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6. TERMINATION

6.1 VIVUS may terminate this Agreement without cause immediately upon giving MEDPACE notice of such termination, provided such termination shall not in and of itself affect any then uncompleted Task Order.

6.2 VIVUS may terminate any Task Order without cause immediately upon giving MEDPACE notice of such termination. As soon as practicable, after receipt of such notice, the Parties shall cooperate in good faith to agree on a plan to expeditiously conclude activities with respect to such matter. MEDPACE shall transfer to VIVUS all case report forms, study files, and other data and information in any and all formats available, including electronic format and computer files and programs, in MEDPACE's possession.

6.3 MEDPACE may terminate a Task Order only if VIVUS has defaulted on its obligations thereunder and has not cured such default within 10 days after written notice if the default is the failure to pay MEDPACE any amount due thereunder or within 30 days after written notice in the event of any other default, upon giving VIVUS notice of such termination; provided, however, that such amounts are not in dispute. Should VIVUS dispute any amounts due, the undisputed portion will be paid in accordance with Section 4.5, and VIVUS and MEDPACE will work together in good faith to settle the disputed portion. Upon resolution, any amounts then owing will be paid within ten (10) days of reaching said resolution. As soon as practicable, after receipt of such notice, the Parties shall cooperate in good faith to agree on a plan to expeditiously conclude activities with respect to such matter.

MEDPACE shall transfer to VIVUS all case report forms, study files, and other data and information in any and all formats available, including electronic format and computer files and programs, in MEDPACE's possession.

6.4 In the event of any termination of a Task Order before completion, VIVUS agrees to pay MEDPACE for all Services rendered pursuant to the unfinished Task Order prior to such termination and any non-cancelable expenses incurred in connection with MEDPACE's performance of Services thereunder. As soon as reasonably practicable following receipt of a termination notice, MEDPACE shall submit an itemized accounting of Services performed, expenses incurred pursuant to performance of the Services, non-cancelable expenses incurred by MEDPACE relating to any unfinished Task Order, and payments received in order to determine a balance to be paid by either Party to the other. Such balance shall be paid within 30 days of receipt of such an itemized accounting by VIVUS.

7. COMMUNICATIONS

7.1 Any notice required or permitted under this Agreement shall be in writing and shall be deemed given if delivered personally, mailed by prepaid, first class, certified mail, return receipt requested, or sent by express courier service, to the

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Party to be notified at the addresses set forth below (or such other address as shall be designated by written notice); provided that all notices shall be effective upon receipt thereof:

If to MEDPACE:

Medpace, Inc.
4620 Wesley Avenue
Cincinnati, Ohio 45212
Attn: August J. Troendle
Telephone: (513) 579-9911 x2278

If to VIVUS:

VIVUS, Inc.
1172 Castro Street
Mountain View, CA 94040
Attn: Legal Affairs
Telephone: (650) 934-5652

8. CONFIDENTIALITY

8.1. VIVUS may provide confidential information to MEDPACE during the course of this Agreement. All information by VIVUS or its clients or data collected by MEDPACE for VIVUS during the course of performance of the Services is deemed to be the confidential information of VIVUS. MEDPACE shall not disclose confidential information to any third party, or use the confidential information for any purpose other than for the benefit of VIVUS, without the prior written consent of VIVUS.

8.1.1. MEDPACE shall ensure by binding written agreement that its employees, agents, and approved independent contractors involved in the Services shall comply with the provisions of Article 8 of this Agreement. MEDPACE shall disclose only confidential information to those of its employees, agents, and independent contractors who reasonably need to know the confidential information.

8.1.2. MEDPACE shall exercise due care, but no less than a reasonable degree of care, to prevent the unauthorized disclosure and use of confidential information associated with the Services.

8.2. MEDPACE Confidential Information.

VIVUS shall hold confidential all non-public information and materials furnished to it by MEDPACE pertaining to MEDPACE's business practices or pertaining to proprietary information of MEDPACE.

8.3. This confidentiality and nondisclosure provision shall not apply to:

Information which was known by the Party before the date hereof or which is independently discovered, after the date hereof, without the aid, application or use of the confidential information, as evidenced by written records;

Information which is in the public domain on the date hereof or subsequently becomes publicly available through no fault or action of the other Party; or

Information, which is disclosed to the Party by a third party authorized to disclose it.

8.3.1. If the receiving Party is requested to disclose the Confidential Information of the other Party or the substance of this Agreement in connection with a legal or administrative proceeding or otherwise to comply with a requirement under the law, the receiving party will give the disclosing Party prompt notice of such request so that the disclosing Party may seek an appropriate protective order or other remedy, or waive compliance with the relevant provisions of this Agreement. The disclosing Party must notify the receiving Party within 10 days that it intends to take action in response to the request for disclosure. If the disclosing Party seeks a protective order or other remedy, the receiving Party, at the disclosing Party's expense, will cooperate with and assist the disclosing Party in such efforts. Failure of the disclosing Party to intervene shall not relieve the obligations to maintain confidentiality except in so far as the receiving Party must comply with the terms of such process compelling disclosure.

9. RIGHTS IN PROPERTY

9.1. All materials, documents, data, software and information of every kind and description supplied to MEDPACE by VIVUS or any of VIVUS's clients, or prepared, developed, or generated by MEDPACE pursuant to this Agreement, (except for the pre-existing MEDPACE procedural manuals, personal data, methods, procedures, and policies) are and shall be the sole and exclusive property of VIVUS. Further, all data and information generated or derived by MEDPACE as the result of services performed by it under this Agreement shall be and remain the exclusive property of VIVUS. VIVUS shall have the right to make whatever use they deem desirable of any such materials, documents, data or software. MEDPACE shall not, without the prior written consent of VIVUS, publish, disseminate, or otherwise disclose to any third party any such property (except such disclosure as may be required by law), or use any such property for any purpose other than the performance of this Agreement. Any inventions or other intellectual property, including without limitation protectable copyrights and trademarks, that may evolve from the data and information described above or as the result of Services performed by MEDPACE under this Agreement shall belong to VIVUS and MEDPACE agrees to assign its rights in all such inventions and/or other intellectual property to VIVUS consistent with the obligations set forth in Article 10 below.

9.2. VIVUS acknowledges that all computer programs, software, applications, databases, proposals and other documentation generally used by MEDPACE and not directly related to, derived from or developed solely for VIVUS are the exclusive and confidential property of MEDPACE or the third parties from whom MEDPACE has secured the right of use. VIVUS agrees that any improvement, alteration or enhancement to MEDPACE systems, software, applications or processes which are developed or implemented during the course of any Services performed hereunder, without the use of any VIVUS data, information, materials or Confidential Information (or derivatives thereof), shall be the property of MEDPACE.

10. PATENT RIGHTS

10.1. MEDPACE shall disclose promptly to VIVUS any and all inventions, discoveries and improvements conceived or made by MEDPACE while providing such services to VIVUS pursuant to the Agreement and constituting a modification or extension of use relating to VIVUS's proprietary rights, and agrees to assign all its interest therein to VIVUS or its nominee; whenever requested to do so by VIVUS, MEDPACE shall execute any and all applications, assignments, or other instruments and give testimony which VIVUS shall deem necessary to apply for and obtain a patent in the United States of America and/or other applicable jurisdiction or of any foreign country or to protect otherwise VIVUS's interests and shall compensate MEDPACE for the time devoted to said activities and reimburse it for expenses incurred.

11. PUBLICITY

11.1. MEDPACE shall not make any public announcements concerning this Agreement or the subject matter hereof without the prior written consent of VIVUS.

11.2 VIVUS may not use MEDPACE's name, logo or trademark in any communication, release, notice or other publication without the express prior written consent of MEDPACE, except as required by SEC.

12. SECURITY AND DISPOSITION OF STUDY FILES

12.1. MEDPACE shall use commercially reasonable efforts, including, but not limited to, periodic backup of computer files, to prevent the loss or alteration of VIVUS's study data, Confidential Information, documentation, and correspondence. MEDPACE shall in all respects comply with any Food and Drug Administration regulations concerning the maintenance, creation and storage of records, including electronic records.

12.2. At appropriate time points or at completion of Services under a Task Order, MEDPACE shall transfer study materials, documents and correspondence to VIVUS. MEDPACE shall have the right to retain one copy of any study materials, documentation, and correspondence necessary solely to meet regulatory

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or MEDPACE's own internal audit requirements, so long as it continues to maintain the Confidentiality requirements of Article 8.

13. VIVUS OBLIGATIONS

13.1. VIVUS acknowledges that performance of the Services by MEDPACE will require the co-operative involvement of both Parties, and VIVUS hereby agrees to provide such assistance as may be reasonably necessary to enable MEDPACE to perform the Services.

14. INDEMNIFICATION

14.1 Indemnification by VIVUS

VIVUS agrees to indemnify, defend and hold harmless MEDPACE, and each officer, agent, employee and contractor of Medpace (Medpace and each such party, a "MEDPACE Indemnitee") from any and all liability, loss, expenses (including reasonable attorneys' fees) or damage such MEDPACE Indemnitee may suffer ("Damages") as the result of any claim, demand, cost or judgment against them arising out of the Services to be performed pursuant to each Task Order which arise, or are alleged to arise, except as follows:

(i) A Medpace Indemnitee shall not be entitled to indemnification hereunder to the extent such Damages are the result of the negligence or willful misconduct of such MEDPACE Indemnitee (provided all Medpace Indemnitees who are not negligent or guilty of willful misconduct causing such Damages shall still be entitled to the indemnification hereunder notwithstanding the negligence or willful misconduct of such other Medpace Indemnitee); or

(ii) A Medpace Indemnitee shall not be entitled to indemnification hereunder to the extent such Damages are the result of a breach of any applicable federal, state or local law or a material breach of this Agreement or any Task Order by such MEDPACE Indemnitee (provided all Medpace Indemnitees not in such breach causing such Damages shall still be entitled to the indemnification hereunder notwithstanding the breach of such other Medpace Indemnitee).

14.2 Indemnification by MEDPACE

MEDPACE agrees to indemnify, defend and hold harmless VIVUS, its affiliates, and their respective officers, agents and employees, from any and all liability, loss (including reasonable attorneys' fees) or damage any such party may suffer as the result of claims, demands, costs or judgments against them arising out of the Services to be performed pursuant to each Task Order which arise, or are alleged to, arise out of:

(i) The negligence or willful misconduct of MEDPACE; or

(ii) A breach of any applicable federal, state or local law or a material breach of this Agreement or any Task Order by MEDPACE.

15. LIMITATION OF LIABILITY

15.1. Notwithstanding the terms of Article 14 above, in no event shall VIVUS or MEDPACE be liable for any indirect, incidental, special, or consequential damages or lost profits arising out of the provision of services hereunder, even if the breaching party has been advised of the possibility of such damages unless the breaching party acted with willful misconduct in its performance of services hereunder.

16. INSPECTIONS AND AUDITS

16.1. VIVUS shall have the right, upon at least ten (10) days' prior written notice to MEDPACE, to examine the standard operating procedures, facilities, books, records, papers, files and documentation, including computer files, data bases and records, at MEDPACE's facilities and the facilities of clinical investigators contracted by MEDPACE to determine the adequacy of such records, to ensure the Services are being performed in accordance with the approved Task Orders and applicable regulations and/or to examine the financial records of MEDPACE as may be reasonably necessary to verify out-of-pocket expenses incurred during the performance of the Services. Such inspections and audits shall be conducted during normal business hours.

16.2. MEDPACE shall provide reasonable assistance, including making available members of its staff and providing access to all requested records, to facilitate such inspections and audits.

16.3. MEDPACE shall take all reasonable steps required by VIVUS to cure any deficiencies found in any audit, inspection or investigation.

17. DEBARMENT

17.1. MEDPACE hereby represents, warrants, and certifies that neither it nor any of its officers, directors, owners, principals or employees has been or will be at any relevant time hereunder debarred under Section 306 of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. §335a(a) or (b), or similar local law. In the event that any such party becomes debarred, MEDPACE shall notify VIVUS in writing immediately.

17.2. MEDPACE hereby represents, warrants, and certifies that it has not and shall not use in any capacity the services of any individual, corporation, partnership, or association which has been debarred under Section 306 of the Federal Food, Drug and Cosmetic Act, 21 U.S.C**.** §335a(a) or (b), or similar local law. In the event MEDPACE becomes aware of or receives notice of the debarment of any individual, corporation, partnership, or association providing services to

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MEDPACE, which relate to the Services being provided under this Agreement, MEDPACE shall notify VIVUS in writing immediately.

18. NON SOLICITATION

Neither Party and its affiliates shall during the term of this Agreement and for a period of twelve months following its termination, either directly or indirectly, hire any employee of the other Party with whom its comes into contact as a result of providing the Services, or recruit, solicit, or entice any such person to become employed by it or any affiliate and shall not approach any such employee for such purpose or encourage, authorize or approve the taking of such action by any other person. The Parties agree that any breach of this provision would cause irreparable harm and that in addition to any and all other available remedies injunctive relief, without the necessity of a bond or other security, shall be appropriate and available.

19. ENTIRE AGREEMENT

This Agreement contains the full understanding of the Parties with respect to the subject matter hereof and supersedes all existing agreements and all other oral, written or other communications between the Parties concerning the subject matter hereof. This Agreement shall not be amended, modified or supplemented in any way except in writing and signed by a duly authorized representative of VIVUS and MEDPACE.

20. GOVERNING LAW

This Agreement shall be governed by the laws of the State of California, without reference to conflicts of laws principles. In the event of breach or threatened breach, in addition to other remedies that may be available, Company shall have the right to seek specific performance and other injunctive and equitable relief, without the obligation to post bond or a security interest.

21. NO WAIVER

No waiver of any term, provision, or condition of this Agreement whether by conduct or otherwise in any one or more instances shall be deemed to be or construed as a further or continuing waiver of any such term, provisions, or conditions, or of any other term, provision, or condition of this Agreement.

22. INDEPENDENT CONTRACTOR

In fulfilling its obligations pursuant to this Agreement, each Party shall be acting as an independent contractor. Neither Party is granted any right or authority to assume or to create any obligation or responsibility, expressed or implied, on behalf of or in the name of the other Party.

23. FORCE MAJEURE

Neither Party shall be liable or deemed to be in default for any delay due to causes

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beyond the reasonable control of the Party, such as: war, acts or threats of terrorism, civil disorders, acts of God, or government action; provided, that the affected Party promptly notifies the other of the cause and its effects on the Services to be performed hereunder. Financial difficulty shall never be deemed a force majeure event.

24. SEVERABILITY

In the event any provision of this Agreement shall be determined to be void or unenforceable, the remaining provisions shall remain in full force and effect.

25. ASSIGNMENT

25.1 Except as set forth herein, neither Party shall assign this Agreement or any Task Order except with the express prior written consent of the other Party.

25.2 Notwithstanding anything contained herein: (i) a Party may assign this Agreement and/or any Task Order to any Affiliate, provided that the assigning Party remains fully liable for all liabilities and obligations under this Agreement and any such Task Order; and, (ii) a Party may assign this Agreement and/or any Task Order to a Successor.

25.3 As used herein, "Affiliate means in relation to a Party, any entity controlling such Party, controlled by such Party, or under common control with such Party; and "Successor" means any entity which acquires all or substantially all assets of a Party, or all or substantially all of the assets pertaining to the subject matter of this Agreement, or any entity into which a Party is merged.

26. SUBCONTRACTING

MEDPACE may subcontract any portion of the Services to any of its Affiliates hereunder without the prior written consent of VIVUS, provided MEDPACE remains liable for the performance of any such Subcontractor.

27. CONFLICTS BETWEEN AGREEMENTS

In the event that there is any conflict between the provisions of this Agreement and any duly executed Task Order, the duly executed Task Order (but not any attachment there to) shall control.

IN WITNESS WHEREOF, the Parties have executed this Agreement as of the date first set forth above.

MEDPACE, INC.

Signature: /s/ August Troendle

By: August Troendle
(Print Name)

Title: President

Date: 9/12/07

VIVUS

Signature: /s/ Wesley W. Day

By: Wesley W. Day
(Print Name)

Title: V.P., Clinical Development

Date: 9/7/07

EXHIBIT A

FORM OF TASK ORDER

MEDPACE Task Order Number:

MEDPACE Project Number:

This Task Order, dated , is between Medpace, Inc. (**"MEDPACE"**), and VIVUS, Inc. (**"VIVUS"**).

RECITALS:

WHEREAS, MEDPACE and VIVUS have entered into that certain Master Services Agreement dated (the "Master Services Agreement"); and

WHEREAS, pursuant to the Master Services Agreement, MEDPACE has agreed to perform certain Services in accordance with Task Orders from time to time entered into by the Parties and VIVUS and MEDPACE now desire to enter into such a Task Order; and

WHEREAS, MEDPACE and VIVUS desire that MEDPACE provide certain services with respect to (the **"**Study") for the study of the product (**"**Study Product") as set out in the Protocol Number: , which is attached hereto as Appendix 1;

NOW, THEREFORE, in consideration of the mutual covenants contained herein, the Parties hereby agree as follows:

1. Scope of Work: MEDPACE shall perform the services described in the Scope of Work, attached hereto as Appendix 2, in accordance with the Project Schedule, attached hereto as Appendix 3 and any other documents attached to and specifically referenced in this Task Order ("Services")

2. Compensation: For performance of these Services, VIVUS shall pay to MEDPACE an amount equal to the Project Budget set forth in Appendix 4, which amount shall be payable pursuant to the Payment Schedule set forth in Appendix 5.

3. Transfer of Obligations: Sponsor Obligations transferred to MEDPACE by VIVUS (consistent with the regulations set forth in 21 C.F.R. Section 312, Subpart D) are identified in Appendix 6.

4. MSA. The provisions of the Master Services Agreement are hereby expressly incorporated by reference into and made a part of this Task Order.

IN WITNESS WHEREOF, the Parties have hereunto signed this Task Order effective as of the day and year first written above.

MEDPACE, INC.

Signature: _____

By: _____
(Print Name)

Title: _____

Date: _____

SPONSOR

Signature: _____

By: _____
(Print Name)

Title: _____

Date: _____

List of Appendices:

Appendix 1: Protocol
Appendix 2: Scope of Work
Appendix 3: Project Schedule
Appendix 4: Project Budget
Appendix 5: Payment Schedule
Appendix 6: Transfer of Obligations

MEDPACE
VIVUS Task Order #01

EXHIBIT A

Qnexa OB-301 TASK ORDER

MEDPACE Task Order Number: 01

MEDPACE Project Number: VOB301

This Task Order, dated September 12, 2007, is between Medpace, Inc. (**"MEDPACE"**), and VIVUS, Inc. (**"VIVUS"**).

RECITALS:

WHEREAS, MEDPACE and VIVUS have entered into that certain Master Services Agreement dated September 12, 2007 (the "Master Services Agreement"); and

WHEREAS, pursuant to the Master Services Agreement, MEDPACE has agreed to perform certain Services in accordance with Task Orders from time to time entered into by the Parties and VIVUS and MEDPACE now desire to enter into such a Task Order; and

WHEREAS, MEDPACE and VIVUS desire that MEDPACE provide certain services with respect to a phase III, randomized, double-blind, parallel design study comparing multiple doses of VI-0521 to placebo and their single-agent phentermine and topiramate constituents for the treatment of obesity in adults (the **"**Study") for the study of the product VI-0521 (**"**Study Product") as set out in the Protocol Number: OB-301, which is attached hereto as Appendix 1;

NOW, THEREFORE, in consideration of the mutual covenants contained herein, the Parties hereby agree as follows:

1. Scope of Work: MEDPACE shall perform the services described in the Scope of Work, attached hereto as Appendix 2, in accordance with the Project Schedule, attached hereto as Appendix 3 and any other documents attached to and specifically referenced in this Task Order ("Services")

2. Compensation: For performance of these Services, VIVUS shall pay to MEDPACE an amount equal to the Project Budget set forth in Appendix 4, which amount shall be payable pursuant to the Payment Schedule set forth in Appendix 5.

3. Transfer of Obligations: Sponsor Obligations transferred to MEDPACE by VIVUS (consistent with the regulations set forth in 21 C.F.R. Section 312,

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Subpart D) are identified in Appendix 6.

4. MSA. The provisions of the Master Services Agreement are hereby expressly incorporated by reference into and made a part of this Task Order.

IN WITNESS WHEREOF, the Parties have hereunto signed this Task Order effective as of the day and year first written above.

MEDPACE, INC.

Signature: /s/ August J. Troendle

By: August J. Troendle
(Print Name)

Title: President

Date: September 12, 2007

SPONSOR

Signature: /s/ Wesley W. Day

By: Wesley W. Day
(Print Name)

Title: Vice President, Clinical Development

Date: September 10, 2007

List of Appendices:

Appendix 1: Protocol
Appendix 2: Scope of Work
Appendix 3: Project Schedule
Appendix 4: Project Budget
Appendix 5: Payment Schedule
Appendix 6: Transfer of Obligations

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CLINICAL PROTOCOL

A PHASE III, RANDOMIZED, DOUBLE-BLIND, PARALLEL-DESIGN STUDY COMPARING MULTIPLE DOSES OF VI-0521 TO PLACEBO AND THEIR SINGLE-AGENT PHENTERMINE AND TOPIRAMATE CONSTITUENTS FOR THE TREATMENT OF OBESITY IN ADULTS

Compound:	VI-0521
Compound Name (if applicable):	Phentermine plus Topiramate
US IND Number (if applicable):	***
Protocol Number:	OB 301
Phase:	3
Medical Monitor:	***
Sponsor:	VIVUS, Inc. 1172 Castro St. Mountain View, CA 94040 Tel: (650) 934-5200 Fax: (650) 934-5209
Version and Date:	***

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INTERNAL PROTOCOL APPROVAL

	Signature	**Date**
Craig Peterson Sr. Director, Clinical Research		
Wesley Day, Ph.D. VP, Clinical Development		
Jacqueline Dombroski, Ph.D. Sr. Director, Regulatory Affairs		
Ted Broman Sr. Director, Pharmaceutical Development		

PRINCIPAL INVESTIGATOR SIGNATURE

The signature below indicates that the principal investigator has read and understands the protocol and agrees to conduct the study in accordance with the protocol, applicable guidelines for Good Clinical Practices, the Declaration of Helsinki and all applicable regulatory guidelines and requirements. Please return one copy of this executed page to VIVUS, Inc.

Printed Name: _____

Signature: _____ Date: _____

Facility Name: _____

Address:

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PROTOCOL SYNOPSIS

Rationale:

VI-0521, a combination drug product containing phentermine hydrochloride and topiramate, has been shown in preliminary studies to result in weight loss over a prolonged period of time. These agents effect weight loss through different mechanisms, therefore, their concurrent use may provide greater efficacy than can be obtained with maximum tolerated doses of either agent alone. This study will confirm this combination drug effect by comparing weight loss associated with various doses of VI-0521, with both the individual phentermine and topiramate components comprising each combination, and with placebo.

Objectives:

The objective of this study is to evaluate the safety and efficacy of various doses of VI-0521 compared to both placebo, and the single-agent phentermine and topiramate components that comprise each combination dose. This study will provide confirmatory data to demonstrate that doses of VI-0521 have efficacy that is greater than placebo and each of the single-agent components that comprise the combination dose.

Trial Design:

In this prospective, randomized, double-blind, placebo-controlled study, eligible subjects will be randomly assigned to receive daily treatment with one of the following regimens:

***

Subjects will be enrolled at approximately *** study sites, with the intent of randomizing approximately 100 subjects into each of the *** treatment groups. The randomization will be stratified by ***.

Study treatment will consist of a 4-week titration period followed by 24 weeks of treatment. Clinic visits will occur at weeks 2 and 4 during the titration period, and subsequently every 4 weeks for the duration of treatment.

Study Subjects

Subjects included in this study will be adult men and women up to 70 years of age with BMI from *** inclusive. All female subjects who are of childbearing potential must agree to use adequate contraception, defined as a double barrier method, stable hormonal contraception plus single barrier, or tubal ligation. Major exclusions for this study include: type II diabetes; clinically significant cardiac disease; clinically significant hepatic, renal or pulmonary disease; clinically significant thyroid disease, as evidenced by signs, symptoms, or TSH >1.5 x ULN; history of bipolar disorder or psychosis, depression of moderate or greater severity, or presence or history of suicidal behavior or active suicidal ideation; obesity of known genetic or endocrine

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origin; recent history of weight instability, or recent participation in a formal weight loss program; history of glaucoma; and smoking cessation within 3 months prior to study enrollment.

Efficacy Endpoints:

The primary study endpoints will be based on the percent weight loss at week 28, calculated as ***, and the percentage of subjects achieving at least 5% weight loss at week 28. For subjects who discontinue treatment prior to study completion, every attempt will be made to have them return for week 28 evaluations. ***.

Secondary efficacy endpoints will include the proportion of subjects achieving 10% weight loss, change from baseline in waist circumference, and change from baseline in *** and *** at ***. As was done for the primary endpoints, subjects who discontinue prior to study completion ***.

Additional endpoints will include *** assessments of *** and ***, changes in primary and secondary outcomes over monthly intervals during the study, and Framingham 10-year risk assessments.

*** will also be evaluated. Data will be obtained using a multiple trough sampling scheme with samples collected at *** and *** from each subject. Effects of various cofactors including (but not limited to) ***, gender, race, ***, and age will be evaluated.

Safety Endpoints

Safety endpoints will include adverse events, ***. Adverse event assessments will include direct questions related to eye pain and *** will be assessed at each visit using the ***.

Statistical Methods:

Comparisons between treatments will be assessed using a *** with factors of *** and ***, and with ***. A step down multiple comparison procedure will be utilized to protect overall ***. For the first level of testing, the response to the *** will be compared to ***, and to ***. If each of these *** comparisons is significant at the *** for both of the co-primary endpoints, then this combination will be considered to have met requirements, and testing will continue to the second level, which will evaluate the *** compared to *** and ***. If all comparisons at the second level are met at the ***, differences in treatment effect between the *** and the ***, the ***, and the *** will be presented using ***.

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LIST OF ABBREVIATIONS

mU	Micro units
ACE	Angiotensin Converting Enzyme
***	***
***	***
***	***
BMI	Body Mass Index
***	***
***	***
***	***
CFR	Code of Federal Regulations
CNS	Central Nervous System
CO_2	Carbon Dioxide
CRF	Case Report Form
***	***
dL	deciliter
ECG	Electrocardiogram
eg	For example
FDA	Food and Drug Administration
***	***
HBsAg	Hepatitis B Surface Antigen
HCV	Hepatitis C Virus
HDL	High Density Lipoprotein
HIV	Human Immunodeficiency Virus
I-CAM	Intercellular Cell Adhesion Molecule
ICH-GCP	International Committee for the Harmonization of Good Clinical Practices
IEC	Independent Ethics Committee
IND	Investigational New Drug
IRB	Institutional Review Board
IVRS	Interactive Voice Response System
***	***
kcal	Kilocalorie
kg	Kilogram
***	***
LDL	Low Density Lipoprotein
LOCF	Last Observation Carried Forward
m	Meter
mg	Milligram
mL	Milliliter
mmHg	Millimeters of Mercury
NYHA	New York Heart Association
PAI-1	Plasminogen Activator Inhibitor 1
***	***
QoL	Quality of Life
RBP-4	Retinol Binding Protein 4
***	***
***	***
TSH	Thyroid Stimulating Hormone
UA	Urinalysis
***	***
V-CAM	Vascular Cell Adhesion Molecule

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WNL Within Normal Limits

1. INTRODUCTION

Phentermine hydrochloride is a synthetic sympathomimetic amine that is approved by the FDA for the short-term treatment of obesity.(1) The usual adult dosage of phentermine hydrochloride is *** administered either once daily or in divided doses. Topiramate is a sulfamate-substituted monosaccharide that is approved by the FDA for the treatment of partial onset seizures, primary generalized tonic-clonic seizures, seizures associated with Lennox-Gastaut syndrome, and for migraine headache prophylaxis. Topiramate has been shown to ***.(2) The recommended total daily dose of topiramate for treatment of seizures in adults is *** administered in two divided doses. The present study is being conducted to evaluate the combined use of phentermine at doses up to 15 mg/day, and topiramate at doses up to 92 mg/day for the treatment of obesity.

1.1. Background

It is estimated that approximately 129 million adults in the United States are clinically overweight or obese.(3) In recent years, there has been a dramatic increase in obesity in both children and adults.(4),(5) Results from the National Health and Nutrition Examination Survey showed an overall 32.2% prevalence of obesity during 2003-2004, with obesity increasing from 27.5% in 1999-2000 to 33.4% in 2003-2004 in men but remaining relatively unchanged in women (1999-2000, 33.4%; 2003-2004, 33.2%).(5)

Obesity is associated with numerous co-morbidities including dyslipidemia, coronary artery disease (CAD), hypertension, stroke and type 2 diabetes.(4),(6) Epidemiological data indicate that obesity is associated with increased mortality,(7) and a recent study of over 500,000 individuals concluded that excess body weight during midlife, including overweight, was associated with an increased risk of death.(8) A modest weight loss (5-10%) can result in a marked reduction in obesity-related metabolic and cardiovascular risk factors.(9),(10),(11) Diet, exercise and behavior modification are standard treatments for obesity, however most obese individuals do not achieve prolonged weight reduction without supplemental pharmacotherapy. Medications currently approved by FDA for weight loss are often poorly tolerated due to side effects and often fail to maximize long-term efficacy.(12)

Phentermine hydrochloride, a synthetic sympathomimetic amine, is an anorectic agent approved by the FDA as a short-term adjunct to a weight loss regimen based on exercise, behavior modification and caloric restriction. The mechanism of action of phentermine for weight loss is similar to that of other anorectic agents; it has peripheral sympathomimetic actions and stimulates the central nervous system.(1) It is postulated that ***, and there is a ***.(13),(14) Additionally, increased *** levels may result in a decrease in *** that may result in increased satiety and decreased appetite.

Topiramate, a sulfamate-substituted monosaccharide, is an antiepileptic agent indicated as adjunctive therapy for partial onset seizures, primary generalized tonic-clonic seizures, seizures associated with Lennox-Gastaut syndrome and for migraine headache prophylaxis.(2) The recommended total daily dose of topiramate for treatment of seizures in adults is ***

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administered in two divided doses; ***. Topiramate is known to ***.(2) Recent clinical studies have shown that topiramate may promote weight loss in ***.(15),(16),(17) However, the exact mechanism by which topiramate exerts its anorectic effect is unknown.

VI-0521 has been studied in a Phase 2, randomized, double-blind clinical trial of 200 otherwise healthy obese adults under an Investigator-Initiated IND.(18) In this study, subjects were randomized into 1 of 4 treatment groups: ***. Treatment was continued for ***. Weight loss among subjects treated with VI-0521 ***, compared to *** among *** among ***, and *** among ***. Subjects treated with VI-0521 *** than subjects in the other treatment groups. Significant decreases vs. *** and *** were also observed in subjects receiving VI-0521. Of the 200 subjects randomized, *** completed treatment to ***, and a *** completion rate was reported for subjects in the *** group. No deaths or serious adverse events were reported during the study and no significant changes in heart valve morphology were observed. The most commonly reported adverse events in subjects treated with VI-0521 were ***.

1.2. Rationale

VI-0521 is an investigational weight loss therapy that is a combination of two currently approved drugs, phentermine and topiramate. As such, VI-0521 represents a potential advance in the medical treatment of obesity since the two agents comprising this combination product effect weight loss through different mechanisms. Additionally, some of the expected side effects of the two drugs may be mitigated by complementary effects of the other. Thus, combining phentermine with topiramate may produce a similar or better adverse event profile compared to either of these agents individually. Topiramate therapy has been associated with ***. Due to the ***, it is mechanistically possible that ***. Thus, the dual mechanisms and low drug doses employed in VI-0521 may provide a safe and effective pharmacotherapy for the achievement and maintenance of weight loss in obese adults.

2. TRIAL OBJECTIVES

The primary objective of this trial is to demonstrate that two different dose levels of VI-0521, a fixed combination of phentermine and topiramate, result in weight loss that is greater than both placebo, and the single agent phentermine and topiramate constituents that comprise each combination dose. Additional study objectives are to evaluate the safety of combination doses compared to both placebo and their single-agent constituents.

3. TRIAL DESIGN

In this prospective, randomized, double-blind, placebo and single agent-controlled trial, subjects meeting the eligibility criteria will be randomly assigned (with equal probability) among the *** treatment groups described in Figure 1.

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***

Figure 1. Schematic representation of study design.

Subjects will be recruited at approximately *** study sites with the intent of randomizing 100 subjects into each of the *** treatment groups. The randomization schedule will be stratified by *** to ***.

The first 4 weeks of drug treatment will be a titration period, during which doses will be gradually increased at *** intervals until the specified dose is reached. The 4-week titration period will be followed by an additional 24 weeks of drug treatment at the assigned dose level. Clinic visits will occur at the end of weeks 2 and 4 during the titration period, and at 4-week intervals thereafter.

The primary efficacy endpoints for this trial will be based on the percent weight loss at week 28, calculated as ***, and the percentage of subjects achieving at least 5% weight loss at week 28. Secondary efficacy endpoints will include the percentage of subjects losing 10% of their body weight, reductions in waist circumference, and changes in ***. For each of these endpoints, statistical comparisons will evaluate differences between *** and ***, and between *** and the *** doses that comprise each combination. Additional efficacy variables will include *** of *** and ***, and changes in primary and secondary outcomes over monthly intervals during the trial, and Framingham 10-year risk assessments.(19)

*** will also be obtained, and effects of various cofactors including (but not limited to) ***, gender, race, ***, and age will be evaluated. ***.

Safety evaluations will include summaries of adverse events, ***.

4. SUBJECT SELECTION

This clinical trial can fulfill its objectives only if appropriate subjects are enrolled. The following eligibility criteria are designed to select subjects for whom protocol treatment is considered appropriate. All relevant medical and non-medical conditions should be taken into consideration when deciding whether this protocol is suitable for a particular subject.

4.1. Inclusion Criteria

To be eligible for enrollment into this trial, subjects must meet all of the following criteria. Specifically, subjects must:

1. Be adults 70 years of age or less with a BMI between ***;

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2. If females of child-bearing potential, be using adequate contraception, defined as double barrier methods, stable hormonal contraception plus single barrier, or tubal ligation. Females are considered to be of child-bearing potential unless they are at least 55 years of age with spontaneous amenorrhea for at least 12 months or have a documented FSH value of 40 IU/L or greater, or have had a hysterectomy or bilateral oophorectomy;

3. Provide written informed consent;

4. Be willing and able to comply with scheduled study visits, treatment plan, laboratory tests, and other study procedures;

4.2. Exclusion Criteria

Subjects presenting with any of the following will not be included in the trial:

1. Known allergy or hypersensitivity to phentermine or topiramate, or use of phentermine or topiramate for any indication within the past 3 months;

2. Weight gain or loss of greater than 5 kg, use of a very low-calorie diet, or participation in a formal weight loss program (investigational or otherwise) within the past 3 months (this includes: Weight Watchers and related dietary/lifestyle intervention programs; prepared food programs; prescribed or over-the-counter weight loss medications; dietary supplement or herbal preparations, teas, or tinctures intended for weight loss; or any supervised fast or very low calorie diet);

3. Obesity that is of a known genetic or endocrine origin;

4. History of eating disorders (eg. bulimia, binge eating disorder), drug abuse, or alcohol abuse (defined as >14 drinks per week) within the past year;

5. Previous bariatric surgery;

6. Smoking cessation within the previous 3 months or plans to quit smoking during study participation;

7. History of glaucoma or any past or present use of medications to treat increased intraocular pressure;

8. Clinically significant thyroid dysfunction as evidenced by signs or symptoms of hypothyroidism, a TSH > 1.5 x ULN, or use of thyroid hormone treatment that has not been stable for at least 3 months;

9. Use of chronic systemic glucocorticoid therapy, or any other steroid hormone therapy that has not been stable for at least 3 months;

10. Any history of bipolar disorder or psychosis, greater than one lifetime episode of major depression, current depression of moderate or greater severity (PHQ-9 score of 10 or more), presence or history of suicidal behavior or ideation with some intent to act on it, or antidepressant use that has not been stable for at least 3 months;

11. Diagnosis of type 2 diabetes by history, or as confirmed by a fasting blood glucose of 126 mg/dL or greater, or history of any antidiabetic medication use;

12. Stroke, myocardial infarction, life-threatening arrhythmia, or coronary re-vascularization within the past 6 months;

13. Unstable angina, NYHA class II-IV congestive heart failure, or known clinically significant cardiac valvulopathy;

14. Systolic blood pressure greater than 160 mmHg, or diastolic blood pressure greater than 100 mmHg;

15. Cholelithiasis within the past 6 months;

16. Any history of nephrolithiasis;

17. History of malignancy within the past 5 years other than basal or squamous cell carcinomas of the skin that have been completely excised, or cervical cancers that have been surgically removed;

18. Pregnancy, breastfeeding, or plans for pregnancy during the study period;

19. Use of any investigational medication or device for any indication within the last month;

20. Evidence of any clinically significant renal, hepatic, pulmonary, psychiatric, or other condition that, in the opinion of the investigator, would contraindicate the administration of study medications, interfere with study evaluations, or confound the interpretation of study results.

4.3. Randomization Criteria

The following additional criteria must be met prior to dispensing treatment to trial subjects:

1. Baseline physical examination, ECG, and laboratory findings with no abnormalities that are considered clinically significant by the principal investigator;

2. Laboratory values that are within the ranges specified below:

***

4.4. Life Style Guidelines

Prior to randomization, subjects will be counseled on how to reduce their caloric intake by 500 kcal/day, and on the importance of light daily exercise. In order to facilitate discussions between study subjects and research staff, subjects will complete a 24-hour dietary recall at their randomization visit, however, information provided as part of this exercise will be used only for discussions related to recommended dietary modification.

Subjects randomized into the study will also be advised to initiate a lifestyle change program utilizing the LEARN® Program for Weight Management. The LEARN® program is a 12-week program designed to aid in weight management by providing tools to facilitate lifestyle, attitude, relationship, nutrition and exercise changes. Each subject will be provided with a LEARN® manual and advised to read and implement the material as appropriate to their individual situation. Site personnel will be encouraged to discuss these materials with subjects at their regularly scheduled visits, however, no data will be collected to document the level of compliance with the program's dietary, lifestyle and/or exercise recommendations.

5. TRIAL TREATMENTS

5.1. Allocation to Treatment

Subjects will be assigned to study treatment using a centrally managed, computer-generated randomization schedule. This randomization will be stratified by gender, and will assign subjects among the *** treatment groups with equal probability.

To implement the randomization of subjects among treatment groups, each participating site will be pre-stocked with titration kits corresponding to each treatment group. When study subjects qualify for randomization at the appropriate study visit (see Section 6), site personnel will contact an Interactive Voice Response System (IVRS), either by telephone or through a designated website, and provide the requested information about the study subject. The randomization assignment will then be made, and the site will be instructed to dispense a specific kit number to the study subject. Additional kits will then be shipped to sites to replace those dispensed to subjects according to the randomization schedule. When subjects return for subsequent study visits, the IVRS system will be used to dispense treatment kits.

5.2. Breaking the Blind

Blinding of drug kits must not be broken during the study unless it considered necessary by the investigator for the management of an adverse event or other medical emergency. In the event of such medical emergency, the identity of the study treatment is obtained by contacting the IVRS. Should unblinding of any subject's treatment occur, VIVUS would be notified ***. Investigators are also required to ensure that any potential serious adverse events are reported according to the requirements outlined in Section 8.2, and to send a written report to VIVUS within *** days to

document the reason for unblinding. Should unblinding of any subject's treatment occur, the subject must discontinue trial participation.

5.3. Drug Supplies

5.3.1. Formulation and Packaging

Medications for this trial will consist of ***. Doses specified for each treatment group will be achieved by varying the *** added to each capsule. Regardless of the dosage assignment, all study treatments will be administered as a ***.

Clinical supplies will be manufactured for VIVUS by *** in accordance with current Good Manufacturing Practices. All clinical supplies will be labeled with information required by national and/or international regulations. Study drug will be packaged into 2 types of kits, titration kits for use during the first 4 weeks of study therapy when doses are being increased gradually to the final assigned dose, and treatment kits, for use once subjects have been titrated to their assigned dosage of medication. Titration kits consist of a ***. Each *** on the *** will be labeled with the *** and will contain capsules with the dose specified for that week of treatment, as outlined in Table 1.

Table 1. Dosage strengths by titration week for each treatment group.

		***			
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***

Titration kits will be labeled with the ***. *** will be labeled with the ***.

Treatment kits will consist of bottles, *** of study medication at the treatment dosages shown in Table 1. Each kit will contain a single bottle of capsules, will be labeled with the ***.

5.3.2. Preparation and Dispensing

Clinical supplies provided by the sponsor are to be dispensed only by or under the direct supervision of qualified investigators to subjects meeting the criteria for study entry and in accordance with this protocol. Assignment of specific drug kits to study subjects will require the use of the IVRS system, however, no other preparation of clinical supplies is required of the investigational staff.

5.3.3. Administration

Investigators will instruct subjects to take 1 capsule of study medication every morning. When dispensing titration kits, investigators should ensure that subjects understand that each card contains a 4-week supply of medication, and that the capsules must be taken ***.

5.3.4. ***

Should *** would cause subjects to consider ***, investigators may, at their discretion, ***. *** are possible with agreement from the medical monitor. Such events may or may not be related to trial treatment.

All subjects undergoing *** for ***may be *** based on discretion of the PI. If dosing has been ***, a new titration kit should be ordered through *** to ***. For shorter ***, subjects may ***. All subjects whose trial treatment has been *** will be encouraged to *** and to attend their regularly scheduled study visits.

5.3.5. Compliance

Subject compliance with trial medication will be assessed by ***, and *** should plan any corrective action necessary. Subjects who remain noncompliant with study dosing despite corrective actions by site personnel may be discontinued from the trial.

5.4. Drug Storage and Drug Accountability

All unused study drug must be stored in its packaging at room temperature in a dry, secure area. Access to drug storage areas should be limited to the investigator and staff involved with the study. All used and unused drug must be maintained at the study site, and made available for audit by VIVUS, Inc. personnel.

The investigator must maintain records documenting the amount, condition, and date of delivery of all study drug received from the Sponsor. In addition, all drug dispensed to study subjects during the course of the study must be ***. Subjects must be instructed to *** by each subject. No investigational drug, used or unused, may be discarded. All used and unused drug must be returned to the sponsor or designated representative upon completion of the study.

5.5. Concomitant Medication(s)

5.5.1. Excluded Medications

Subjects must not take the following medications during their participation in this trial:

- ***;
- ***;

- ***;
- ***;
- ***.

Although the need for any antidiabetic medications at screening would exclude subjects from trial participation, subjects who develop a need for these medications during the course of the trial need not be discontinued. Should antidiabetic medications be required by any trial subjects, it is recommended that *** be used initially, followed by *** and/or ***. ***, either alone or in combination with other medications, should be reserved for subjects who cannot achieve adequate control with other modes of treatment. *** are prohibited, and subjects requiring treatment with these medications must be discontinued from the trial. Subjects whose *** cannot be adequately controlled with the concomitant treatments allowed in this trial should be discontinued and referred back to their primary health care provider for further follow-up (see Section 6.3).

5.5.2. Other Restricted Medications

Subjects using *** must be on doses that have been stable for at least 3 months. For subjects who develop symptoms consistent with *** during the study, *** replacement may be initiated following appropriate diagnostic workup. Similarly, subjects whose needs for *** medications change may have these treatments added or changed as clinically indicated. In the event that subjects require any other changes in these medications, the Sponsor should be contacted regarding their continued eligibility.

All medications used for the treatment of *** associated with *** must be stable for at least 1 month prior to trial entry; however, adjustment of these medications during the trial is permitted if subjects' requirements for treatment change. For subjects whose ***, or who exhibit symptoms associated with *** during the trial, *** agents should be withdrawn or doses should be reduced. For this trial, it is recommended that *** be the first medications to be reduced or withdrawn followed by ***.

For subjects whose ***, *** therapy should be initiated with *** or ***. If these medications are already present, *** may be added.

Subjects whose *** cannot be adequately controlled with the concomitant treatments allowed in this trial should be discontinued and referred back to their primary health care provider for further follow-up (see Section 6.3).

5.5.3. Documentation of Concomitant Medication Use

All concomitant medications, including over-the-counter products and nutritional/herbal supplements, must be listed on the appropriate case report form at trial entry. Any changes in concomitant medication during the course of the trial must also be noted on the appropriate CRF.

6. TRIAL PROCEDURES

6.1. Schedule of Visits

A schedule of study activities by visit is shown in **Appendix 1**. A detailed list of activities conducted at each study visit is also described in the following section.

VISIT 1: Screening:

- Obtain written informed consent;
- Obtain medical history;
- Assess vital signs, weight, height, waist circumference, and BMI;
- Administer ***, and ***;
- Assess inclusion/exclusion criteria;
- Obtain blood and urine samples for laboratory analyses, and perform urine pregnancy test (female subjects of childbearing potential only);
- Schedule a follow-up visit in 2 weeks (±1 week).

VISIT 2: Randomization: Week 0:

- Perform urine pregnancy test (female subjects of childbearing potential only);
- Perform physical examination including ECG evaluation (can be done at any time between screening;
- If screening laboratory results and physical examination findings are acceptable, obtain randomization assignment through IVRS;
- Assess weight, waist circumference, and vital signs;
- Administer *** for *** and ***, and perform *** (see Section 7.4);
- Perform 24-hour dietary recall with subject and review lifestyle modifications;
- Dispense assigned titration kit and provide instructions for proper use;
- Assess adverse events (including eye pain), and changes in concomitant medications;

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- Schedule next follow-up visit in 2 weeks (±2 days).

VISIT 3: Titration: Week 2:

- Perform urine pregnancy test (female subjects of childbearing potential only);
- Assess weight, waist circumference, and vital signs;
- Administer *** and ***;
- Administer *** for *** and ***;
- Review lifestyle modifications with subject;
- Review assigned titration kit to assess medication use and treatment compliance. Re-dispense kit and provide proper instructions for continued use;
- Assess adverse events (including eye pain), and changes in concomitant medications;
- Schedule next follow-up visit in 2 weeks (±2 days).

VISIT 4: Titration: Week 4:

- Collect blood sample for laboratory tests (all subjects) and perform urine pregnancy test (female subjects of childbearing potential only);
- Assess weight, waist circumference, and vital signs;
- Administer *** and ***;
- Administer *** for *** and ***, and perform *** (see Section 7.4);
- Review lifestyle modifications with subject;
- Collect titration kit, assess treatment compliance, and perform drug accountability;
- Obtain treatment kit assignment through IVRS, dispense kit to subject, and provide proper instructions for use;
- Assess adverse events (including eye pain), and changes in concomitant medications;
- Schedule next follow-up visit in 4 weeks (±1 week).

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VISIT 5: Treatment: Week 8:

- Collect blood sample for laboratory tests (all subjects), and perform urine pregnancy test (female subjects of childbearing potential only);
- Assess weight, waist circumference, and vital signs;
- Administer *** and ***;
- Administer *** for *** and ***;
- Review lifestyle modifications with subject;
- Collect used treatment kit, assess treatment compliance, and perform drug accountability;
- Obtain treatment kit assignment through IVRS, dispense kit to subject, and provide proper instructions for use;
- Assess adverse events (including eye pain), and changes in concomitant medications;
- Schedule next follow-up visit in 4 weeks (±1 week).

VISIT 6: Treatment: Week 12:

- Perform urine pregnancy test (female subjects of childbearing potential only);
- Assess weight, waist circumference, and vital signs;
- Administer *** and ***;
- Administer *** for *** and ***;
- Review lifestyle modifications with subject;
- Collect used treatment kit, assess treatment compliance, and perform drug accountability;
- Obtain treatment kit assignment through IVRS, dispense kit to subject, and provide proper instructions for use;
- Assess adverse events (including eye pain), and changes in concomitant medications;
- Schedule next follow-up visit in 4 weeks (±1 week). Subjects should be reminded not to take their study medication on the morning of their next visit, but instead, to bring it to

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the visit with them, and take it after blood samples have been obtained. Subjects should also note the time of their last dose prior to the next visit.

VISIT 7: Treatment: Week 16

- Ensure that the previous dose of trial medications was taken between 20 and 28 hours ago, and obtain a *** blood sample for *** evaluations (if the previous dose of trial medications is outside this window, *** should be postponed for 1 day);
- Collect blood sample for laboratory tests (all subjects), and perform urine pregnancy test (female subjects of childbearing potential only);
- Assess weight, waist circumference, and vital signs;
- Administer *** and ***;
- Administer *** for *** and ***;
- Review lifestyle modifications with subject;
- Collect used treatment kit, assess treatment compliance, and perform drug accountability;
- Obtain treatment kit assignment through IVRS, dispense kit to subject, and provide proper instructions for use;
- Assess adverse events (including eye pain), and changes in concomitant medications;
- Schedule next follow-up visit in 4 weeks (±1 week).

VISIT 8: Treatment: Week 20:

- Perform urine pregnancy test (female subjects of childbearing potential only);
- Assess weight, waist circumference, and vital signs;
- Administer *** and ***;
- Administer *** for *** and ***;
- Review lifestyle modifications with subject;
- Collect used treatment kit, assess treatment compliance, and perform drug accountability;

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- Obtain treatment kit assignment through IVRS, dispense kit to subject, and provide proper instructions for use;
- Assess adverse events (including eye pain), and changes in concomitant medications;
- Schedule next follow-up visit in 4 weeks (±1 week).

VISIT 9: Treatment: Week 24:

- Perform urine pregnancy test (female subjects of childbearing potential only);
- Assess weight, waist circumference, and vital signs;
- Administer *** and ***;
- Administer *** for *** and ***;
- Review lifestyle modifications with subject;
- Collect used treatment kit, assess treatment compliance, and perform drug accountability;
- Obtain treatment kit assignment through IVRS, dispense kit to subject, and provide proper instructions for use;
- Assess adverse events (including eye pain), and changes in concomitant medications;
- Schedule next follow-up visit in 4 weeks (±1 week). Subjects should be reminded not to take their trial medication on the morning of their next visit, but instead, to bring it to the visit with them, and take it after blood samples have been obtained. Subjects should also note the time of their last dose prior to the next visit.

VISIT 10: End of Treatment: Week 28 (or early term):

- Ensure that the previous dose of trial medications was taken between 20 and 28 hours ago, and obtain a *** blood sample for *** evaluations (if the previous dose of trial medications is outside this window, *** should be postponed for 1 day);
- Collect blood and urine samples for laboratory tests (all subjects), and perform urine pregnancy test (female subjects of childbearing potential only);
- Assess weight, waist circumference, and vital signs;
- Administer ***, and ***;

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- Perform physical examination including ECG evaluation;
- Administer *** for *** and ***, and perform *** (see Section 7.4);
- Collect used treatment kit, assess treatment compliance, and perform drug accountability;
- Assess adverse events (including eye pain), and changes in concomitant medications;
- Ask End of Treatment Questions (see Section 7.5);
- Discontinue subject's trial participation.

6.2. Trial Period

For each subject, the trial period will begin when written informed consent is provided and will continue until Visit 10 (Week 28 or early termination) is completed. In certain instances, however, adverse event information may be required for events that occur after the trial period (see Section 8).

6.3. Subject Withdrawal

Subjects may withdraw from the trial at any time and for any reason. Additionally, the investigator must discontinue participation for any subject who:

- Experiences an adverse event that, based on the investigator's medical judgment, would jeopardize the subject's well being or prevent the safe completion of the study;
- Becomes pregnant;
- Requires other medical treatment that is excluded by the protocol;

- Has their treatment unblinded by the investigator;
- Is unwilling to comply with the provisions of the protocol.

Investigators must discontinue trial participation for all subjects if the Sponsor terminates the trial. Evaluations that would normally be performed upon trial completion should be made for all subjects who exit the trial prematurely. For subjects who have received ***, this includes obtaining appropriate samples for laboratory testing, and performing a physical examination (including ECG). Additionally, for all subjects who discontinue trial participation prematurely, investigators should make all reasonable attempts to schedule a clinic visit at week 28 to make a final weight assessment.

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If a subject does not return for a scheduled visit, every effort should be made to contact the subject. In any circumstance, every effort should be made to document subject outcome, if possible. The investigator should ***

If the subject withdraws from the trial and also withdraws consent for disclosure of future information, ***. ***.

7. ASSESSMENTS

7.1. Weight and Waist Measurement Assessments

Subjects should be weighed using a calibrated digital scale. The same scale should be used for each measurement and measurements should be evaluated by the same site personnel at each visit, whenever possible. Subject weights should be obtained, whenever possible, under the same conditions (no shoes, clothing of similar weight) that were employed at the first (screening) weighing. Subjects should be encouraged to complete their weigh-in visits in the morning and should be fasting prior to weigh-in.

Waist measurement will be performed using a measuring tape provided by VIVUS, Inc., and should be obtained by the same individual at each visit. To measure the waist circumference, locate the top of the right iliac crest, and place the measuring tape in a horizontal plane (parallel to the floor) around the abdomen at the level of the top of the iliac crest, as shown in Figure 2.

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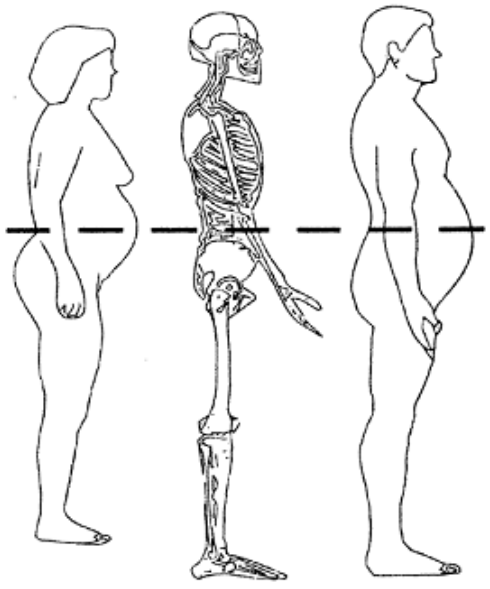

Figure 2. Measuring Tape Position for Waist Circumference Assessments

Ensure that the subject is relaxed. Ensure that the tape is snug but does not indent or compress the skin, and make the measurement at the end of a normal expiration.

7.2. Vital Signs

Vital signs including blood pressure, pulse rate, temperature, and respiration rate will be assessed at each study visit. All blood pressure measurements should be obtained after subjects have been resting in the seated position for at least ***. Pulse rate and respiratory rate measurements should be made by counting events (heartbeats or breaths) for a period of 30 seconds and multiplying these values by 2 to obtain the rates per minute. Whenever possible, the same person should do all of the assessments for a given subject.

7.3. Questionnaires

7.3.1. *

The *** that is to be completed ***, and ***. This questionnaire is designed to evaluate the ***.(20),(21) Because this instrument is intended to be completed ***. Site personnel must also ***. It is critical, therefore, that site personnel review questionnaires for completeness at the time they are initially filled out, and that any missing answers are completed before the ***.

7.3.2. *

The *** for the assessment of *** that will be completed ***, and at *** after the ***.(22),(23)

Because this instrument is intended to be completed ***, it is important that *** on this questionnaire in any way. Should subjects ***. Because this questionnaire assesses the ***. Site personnel, therefore, must carefully review questionnaires for completeness before ***, and assure that questionnaires are properly completed.

The *** is being used ***. Answers to the questionnaire may reveal evidence of ***, including the ***. It is the responsibility of the investigator to evaluate ***. The evaluation by the Investigator will be guided by the ***. Investigators should document any such problems ***. It is expected that any randomized ***.

7.3.3. *

The ***(24) is an ***. Each of the ***, and is answered on a yes/no basis. This assessment will be administered to all *** at *** in order to confirm the *** included in the treatment program. Subsequent *** evaluations will be done at *** after ***. All *** assessments must be administered by a trained staff member. If any test reveals ***, then test results must be confirmed by a physician investigator prior to ***.

7.4. *

*** will be assessed using the ***. The ***will be assessed at ***, and ***, and measures ***. Effects of trial treatment on *** will be based on observed changes in the ***.

7.5. *

*** assessments of *** and *** will be collected at ***. For the *** assessment, subjects will *** For the *** assessment, a ***

At the completion of study treatment (Visit 10), subjects will answer *** questions assessing ***. These questions are as follows:

. ***

. ***

. ***

7.6. Laboratory Tests

The following laboratory tests will be evaluated during this trial:

· Hematology tests, including hemoglobin, hematocrit, red blood cell count (RBC), total white blood cell count (WBC), WBC differential (neutrophils, lymphocytes, monocytes, eosinophils, basophiils) and platelet count, will be evaluated at screening and at Visit 10 (end of treatment or early exit);

- Fasting blood chemistries including: albumin, alkaline phosphatase, alanine transaminase (ALT), aspartate amino transferase (AST), blood urea nitrogen (BUN), serum calcium, serum chloride, serum sodium, carbon dioxide (CO2), creatinine (and estimated creatinine clearance), direct bilirubin, gamma-glutamyl transferase (GGT), glucose, lactate dehydrogenase (LDH), serum phosphorus, serum potassium, total bilirubin, total protein, and uric acid, will be evaluated at screening, Visit 4 (week 4), Visit 5 (week 8), Visit 7 (week 16), and Visit 10 (end of treatment or early exit);

- Lipid panel including total cholesterol, LDL cholesterol (LDL-C), HDL cholesterol (HDL-C), triglycerides, apolipoprotein A, apolipoprotein B-100, and Lp (a) will be evaluated at screening and Visit 10 (end of treatment or early exit). Visit 10 (end of treatment or early exit) results for apolipoprotein A, apolipoprotein B-100, and Lp (a) will be blinded to investigators and sponsor;

- Blood biomarkers including HgbA1c, C-reactive protein, adiponectin, retinol binding protein-4 (RBP-4), intercellular cell adhesion molecule (I-CAM), vascular cellular adhesion molecule (V-CAM), plasminogen activator inhibitor 1 (PAI-1) and fibrinogen, will be evaluated at screening and at Visit 10 (end of treatment or early exit). Visit 10 (end of treatment or early exit) results for all biomarkers with the exception of HgbA1c will be blinded to investigators and sponsor;

- Urine microalbumin, creatinine, and albumin/creatinine ratio will be evaluated at screening and at Visit 10 (end of treatment or early exit);

- Thyroid Stimulating Hormone (TSH) will be evaluated at screening;

- Serology testing for Hepatitis B surface antigen (HBsAg), Hepatitis C virus (HCV), and Human Immunodeficiency Virus (HIV) will be evaluated at screening;

- Urine drug screen for cannabinoids, cocaine, amphetamines, opiates, and phencyclidine will be evaluated at screening;

- Midstream UA with reflex microscopic evaluation will be evaluated at screening.

A certified central laboratory will be used for all of the above laboratory assessments.

In addition to the standard laboratory parameters described above, plasma samples will be obtained at Visit 7 (week 16) and Visit 10 (end of treatment or early exit) for the assessment of trough levels of phentermine and topiramate.

For women of childbearing potential, urine pregnancy tests will be performed locally at each visit.

7.7. Physical Examination

A complete physical examination will be performed at week 0 (Visit 2) and week 28 (Visit 10 or early withdrawal). The physical examination will consist of an examination of the following systems: general appearance, skin, eyes, ears, nose, throat, neck (including thyroid), lymph nodes, chest, heart (including any auscultated cardiac murmurs), abdomen, extremities, and neurologic.

7.8. Electrocardiograms (ECG)

Twelve-lead electrocardiographic studies will be obtained at week 0 (Visit 2) and the end of treatment (Visit 10 or early withdrawal). Studies will be evaluated for clinically significant abnormalities that would prevent entry into the study, and for clinically relevant changes between screening and end of treatment. Parameters including R-R, QRS, QT, QTc intervals will also be recorded.

8. ADVERSE EVENT REPORTING

8.1. Adverse Events

Adverse events (AEs) are defined as any untoward medical occurrences in subjects administered the trial treatment, whether or not they have a causal relationship to the treatment. All observed or volunteered adverse events regardless of suspected causal relationship to the investigational product must be reported as described in the following sections.

Study investigators must collect sufficiently detailed information to describe adverse events, their character, onset, severity, relationship to study treatment, and resolution or other outcomes. Descriptions of neurological or psychological adverse events should be consistent with standard diagnostic criteria and terminology (such as DSM-IV) rather than general reports of symptoms. Whenever possible, description under a unifying diagnosis should be used in preference to a list of multiple signs or symptoms. Any adverse event judged by the investigator to be causally related to study treatment must be followed and documented by the investigator until the events or their sequelae resolve or stabilize at a level acceptable to the investigator, and VIVUS concurs with that assessment. Investigators must also determine whether any adverse event meets the specific criteria for classification as a Serious Adverse Event (SAE; see Section 8.2), which requires immediate notification to VIVUS or its designated representative.

8.1.1. Severity Assessment

The investigator will assess the severity of all adverse events using the ***,***, or *** to describe the maximum intensity of each adverse event. For purposes of consistency, these intensity grades are defined as follows:

- ***;
- ***;
- ***.

Note the distinction between the severity and the seriousness of an adverse event. A *** is not necessarily a ***. For example, a headache may be *** but would not be classified as serious unless it met one of the criteria for ***.

8.1.2. Causality Assessment

Trial investigators are required to provide an assessment of causality, for all adverse events observed during this trial. This assessment will provide a determination of whether, in the investigators' judgment, there exists a reasonable possibility that the investigational product caused or contributed to an adverse event. For this assessment, investigators must categorize the causality as either "related" or "not related." For an adverse event to be considered "related" to the trial treatment, there should be evidence that the event follows a reasonable temporal sequence from the administration of trial treatment, or that the event follows a known response pattern to the drug. Causality would be further confirmed by improvement in an adverse event upon stopping the trial treatment, and reappearance of the event upon rechallenge.

8.1.3. Abnormal Test Findings

The criteria for determining whether an abnormal objective test finding should be reported as an adverse event are as follows:

- Test result is associated with accompanying symptoms, and/or
- Test result requires additional diagnostic testing or medical/surgical intervention, and/or
- Test result leads to a change in trial dosing or discontinuation from the trial, significant additional concomitant drug treatment, or other therapy, and/or
- Test result is considered by the investigator or sponsor to represent a clinically significant finding.

Merely repeating an abnormal test, in the absence of any of the above conditions, does not constitute an adverse event. Any abnormal test result that is determined to be an error does not require reporting as an adverse event.

8.2. Serious Adverse Events

As defined in the Code of Federal Regulations (21 CFR 312.32), a serious adverse event or serious adverse drug reaction is any untoward medical occurrence at any dose that:

- Results in death;
- Is life-threatening (immediate risk of death);
- Requires inpatient hospitalization or prolongation of existing hospitalization;
- Results in persistent or significant disability/incapacity;
- Results in congenital anomaly/birth defect.

Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious adverse drug experiences when, based on appropriate medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed above. Adverse events that, in the investigator's judgment, significantly jeopardized trial subjects or required medical or surgical intervention in order to prevent any of the outcomes listed above, should, therefore, be reported as serious adverse events.

8.2.1. Definition of Hospitalization

Adverse events reported from clinical trials that result in hospitalization or prolong an existing hospitalization are considered serious. Any initial admission (even if less than 24 hours) to a healthcare facility meets these criteria.

Outpatient ambulatory surgical procedures (same day surgeries) and routine emergency room treatment do not qualify as hospitalizations. Additionally, hospitalization in the absence of a precipitating, clinical adverse event is not in itself a serious adverse event. Examples include, but are not limited to:

- Admission for treatment of a preexisting condition not associated with the development of a new adverse event or with a worsening of the preexisting condition (eg, for work-up of persistent pre-treatment lab abnormality);

- Administrative admission (eg, for yearly physical exam);

- Optional admission not associated with a precipitating clinical adverse event (eg, for elective cosmetic surgery);

- Pre-planned treatments or surgical procedures should be noted in the baseline documentation for the entire protocol and/or for the individual subject.

Diagnostic and therapeutic non-invasive and invasive procedures, such as surgery, should not be reported as adverse events. However, the medical condition for which the procedure was performed should be reported if it meets the definition of an adverse event. For example, an acute appendicitis that begins during the adverse event reporting period should be reported as the adverse event, and the resulting appendectomy should be recorded as treatment of the adverse event.

8.3. Eliciting Adverse Event Information

The investigator is to report all directly observed adverse events and all adverse events spontaneously reported by the trial subject. In addition, trial subjects should be ***

Certain adverse events require prompt and specific action by the investigator in any clinical trial. The following sections describe additional requirements to ensure ***.

8.3.1. Eye Pain

At each visit, subjects will be queried regarding eye symptoms, *** Subject responses will be recorded as adverse events, where appropriate. If any subject reports eye pain and/or ***, the subject should be referred to ***. Treatment with study drug should be discontinued until the ***.

8.3.2. ***

All subjects will be screened for the presence and *** at *** and subsequently monitored at *** after the *** using a validated survey instrument *** designed for assessment of *** in a primary care setting. The *** is a *** module based directly on the diagnostic criteria for ***.

*** will also be assessed at *** and *** following the *** using the ***. Should this additional assessment indicate the presence ***. Any such event must be ***. Subjects must be ***.

Any *** must be ***.

8.4. Reporting Period

The reporting period for adverse events begins when the subject provides written informed consent and extends until *** after the last dose of the investigational product is administered, or until the subject is discontinued from the study, whichever is later. All adverse events that occur

during this period and are known to the investigator must be reported according to the requirements outlined in Section 8.5.

8.5. Reporting Requirements

All adverse events will be reported on the adverse event page(s) of the CRF. In addition, serious adverse events must also be reported on a separate Serious Adverse Event form. Where the same data are collected, the forms must be completed in a consistent manner. For example, the same adverse event term should be used on both forms. Adverse events should be reported using concise medical terminology on the CRFs as well as on the form for collection of serious adverse event information.

8.5.1. Serious Adverse Event Reporting Requirements

If a serious adverse event occurs, VIVUS is to be notified within 1 business day of awareness of the event by the investigator. In particular, if the serious adverse event is fatal or life-threatening, notification to VIVUS must be made immediately, irrespective of the extent of available adverse event information. This timeframe also applies to additional new information (follow-up) on previously forwarded serious adverse event reports.

***

For all serious adverse events, the investigator is obligated to pursue and provide information to VIVUS in accordance with the timeframes for reporting specified above. In addition, an investigator may be requested by VIVUS to obtain specific additional follow-up information in an expedited fashion. This information may be more detailed than that captured on the adverse event case report form. In general, this will include a description of the adverse event in sufficient detail to allow for a complete medical assessment of the case and independent determination of possible causality. Information on other possible causes of the event, such as concomitant medications and illnesses must be provided. In the case of a subject death, a summary of available autopsy findings must be submitted as soon as possible to VIVUS or its designated representative.

8.5.2. Non-Serious Adverse Event Reporting Requirements

Non-serious adverse events are to be reported on the adverse event CRFs, which are to be submitted to VIVUS.

8.5.3. ***

If any trial subject becomes or is found to be *** while receiving the investigational product, the investigator must discontinue trial treatment and submit this information to VIVUS on an ***.

The investigator will follow the *** and then notify VIVUS of the outcome. The investigator will provide this information as a follow up to the ***.

For reported ***. The status of an ***.

If *** meet the criteria for classification as serious adverse events ***, the investigator should follow the procedures for reporting serious adverse events. Similarly, any *** that are considered to be adverse events should be reported as such on the appropriate CRF, however, *** need not be reported as an adverse event if there is no associated adverse outcome.

For reporting purposes, *** should be reported as serious adverse events, but because the ***.

9. DATA ANALYSIS/STATISTICAL METHODS

9.1. Sample Size Determination

To demonstrate the efficacy of a combination therapy, the combination (phentermine and topiramate) must be superior to both of the individual components that comprise the combination and placebo, at ***. The projected sample size of this trial is determined by the anticipated mean difference between the *** and the ***. In a previously conducted VIVUS *** trial, *** had a ***, compared to ***. In this trial, the effect of the *** is roughly equal to ***. Assuming the weight reduction for ***, and the weight reduction for ***, then the estimated effect of *** would be ***. Similarly, the estimated effect for *** would be ***. The effect of the *** is estimated as ***. Therefore, the estimated sample size is based on detecting a mean difference of *** between the ***. The pooled standard deviation for percent change in body weight from this *** trial was approximately ***. With 100 subjects in each of the *** in this trial, the trial should have more than *** power to demonstrate that the *** is an effective combination.

9.2. Efficacy Analysis

9.2.1. Analysis of Primary Endpoint

The primary calculated endpoints for this trial are based on the percent weight loss at week 28, and the percentage of subjects with at least 5% weight loss at week 28. The percent weight loss at week 28 will be calculated as ***.

The primary subject population is the Intent to Treat (ITT) population that consists of all subjects who are randomized, receive at least 1 dose of trial treatment, and have at least 1 post-dosing trial assessment. For subjects who discontinue treatment prior to trial completion, every attempt will be made to have them return to the clinic at week 28 for final assessments, regardless of when they discontinued trial treatment. For subjects who ***.

The primary objective of the statistical test is to confirm that at least one of the proposed phentermine/topiramate combinations evaluated in this trial is an effective combination therapy

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for weight reduction. To demonstrate that a combination therapy is effective, it is necessary to show that a *** versus each *** comprising the ***, and *** versus ***, are all significant at the *** using ***. If any one of the *** does not reach the *** level for either of the co-primary endpoints, then the efficacy of that combination cannot be confirmed. A step-down multiple testing procedure will be used to control the overall type I error for this trial. The hypothesis that the *** is an effective combination therapy will be tested first. Once the efficacy of this *** is confirmed, then the efficacy of the *** will be tested using the same criteria. Comparisons between treatments for the endpoint of percent weight loss will be assessed using a *** model with factors of ***. Comparisons between treatment of the percentage of subjects with at least 5% weight loss at week 28 will be evaluated by ***.

Once the efficacy of both the *** has been confirmed, the difference in mean weight reduction between the *** therapies will be estimated. *** percent confidence intervals for the difference in mean percent body weight reduction between the two combination therapies will be derived.

9.2.2. Analysis of Secondary Endpoints

Secondary efficacy endpoints that are based on continuous data, including changes from baseline to week 28 in waist circumference and ***, will be evaluated in a manner similar to the primary endpoint. Categorical variables, including the proportion of subjects achieving 10% reductions in body weight at week 28 will be evaluated by ***. Analyses of secondary endpoints will also be based on the ITT population, and a step down strategy analogous to that used for the primary endpoint will be implemented to protect the overall alpha levels for these comparisons.

9.3. Analysis of Other Endpoints

Additional efficacy endpoints evaluated during this trial include *** of *** and ***, changes in primary and secondary outcomes over monthly intervals during the study, and Framingham 10-year risk assessments. The methodology for these comparisons will be similar to that used for primary and secondary endpoints.

*** will be obtained during this trial using a multiple trough sampling scheme, where samples are obtained from each subject at weeks 16 and 28 (or early exit). These data will be combined for analyses with data from other phase 3 trials that will utilize similar sampling schemes. *** will characterize *** for both drugs. The effects of various covariates including (but not limited to) ***, gender, race, *** and age will be evaluated.

9.4. Safety Analysis

Safety analyses will include tabular summaries of adverse event frequency, ***. Changes from baseline in *** evaluating *** will be summarized by treatment group using point estimates and *** confidence intervals. Since the proposed indication for the study medication is weight loss, summaries of total ***, which assesses ***, will also be presented to ensure that overall effects

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on *** are not driven exclusively by the study medication's known pharmacologic effect on appetite. Descriptive summaries of individual questionnaire items will also be presented.

9.5. Interim Analysis

No interim analyses are planned for this trial.

9.6. ***

***

10. QUALITY CONTROL AND QUALITY ASSURANCE

During trial conduct, VIVUS or its agent will conduct periodic monitoring visits to ensure that the protocol and GCPs are being followed. The monitors may review source documents to confirm that the data recorded on CRFs are accurate. The investigator and institution will allow VIVUS monitors or its agents and appropriate regulatory authorities direct access to all appropriate source documents to perform this verification.

The trial site and trial-related documents may be subject to review by the institutional review board (IRB)/independent ethics committee (IEC), and/or to quality assurance audits performed by VIVUS or its agents, and/or to inspection by appropriate regulatory authorities.

It is important that the investigator(s) and their relevant personnel are available during the monitoring visits and possible audits or inspections and that sufficient time is devoted to the process by the investigator and site personnel.

11. DATA HANDLING AND RECORD KEEPING

11.1. Case Report Forms / Electronic Data Record

As used in this protocol, the term case report form (CRF) should be understood to refer to either a paper form or an electronic data record or both, depending on the data collection method used in this trial.

A CRF is required and should be completed for each included subject. The completed original CRFs are the sole property of VIVUS and should not be made available in any form to third parties, except for authorized representatives of VIVUS or appropriate regulatory authorities, without written permission from VIVUS.

It is the investigator's responsibility to ensure completion and to review and approve all CRFs. CRFs must be signed by the investigator or by an authorized staff member. These signatures serve to attest that the information contained on the CRFs is complete and accurate. At all times, the investigator has final personal responsibility for the accuracy and authenticity of all clinical and laboratory data entered on the CRFs. Subject source documents are the physician's subject

records maintained at the trial site. In most cases, the source documents will be the hospital's or the physician's chart. In cases where the source documents are the hospital or the physician's chart, the information collected on the CRFs must match those charts.

In some cases, the CRF may also serve as the source document. In these cases, VIVUS and the investigator must prospectively document which items will be recorded in the source documents and for which items the CRF will stand as the source document.

11.2. Record Retention

To enable evaluations and/or audits from regulatory authorities or VIVUS, the investigator agrees to keep records, including the identity of all participating subjects (sufficient information to link records, eg, CRFs and hospital records), all original signed informed consent forms, copies of all CRFs, serious adverse event forms, source documents, and detailed records of treatment disposition. The records should be retained by the investigator according to ICH, local regulations, or as specified in the Clinical Study Agreement, whichever is longer.

If the investigator relocates, retires, or for any reason withdraws from the trial, VIVUS should be prospectively notified. The trial records must be transferred to an acceptable designee, such as another investigator, another institution, or to VIVUS. The investigator must obtain written permission from VIVUS before disposing of any records, even if retention requirements have been met.

12. ETHICS

12.1. Institutional Review Board (IRB)/Independent Ethics Committee (IEC)

Regulations require that an IRB/IEC oversee all investigational drug trials. This board or committee, the makeup of which must conform to local and regional regulations, will approve all aspects of the study, including the protocol, advertising, and the form used to obtain written informed consent from trial subjects, prior to initiation of the trial. It is the responsibility of the investigator to have prospective approval of the trial protocol, protocol amendments, informed consent forms, and other relevant documents, eg, advertisements, if applicable, from the IRB/IEC. All correspondence with the IRB/IEC should be retained in the Investigator File. Copies of IRB/IEC approvals should be forwarded to VIVUS. All correspondence with the IRB/IEC should be retained in the Investigator File and copies forwarded to VIVUS, Inc.

All amendments to the protocol must be reviewed and approved by VIVUS and the IRB/IEC prior to implementation. The only circumstance in which an amendment may be initiated prior to IRB/IEC approval is where the change is necessary to eliminate apparent immediate hazards to the subjects. In that event, the investigator must notify the IRB/IEC and VIVUS in writing within 5 working days after the implementation.

The investigator is responsible for obtaining annual (at a minimum) IRB/IEC renewal for the duration of the trial. The investigator is also responsible for keeping the IRB/IEC advised of the progress of the trial, and of any changes made to the protocol. Copies of these reports and documentation of all IRB/IEC action (extension or otherwise) must be forwarded to VIVUS.

12.2. Ethical Conduct of the Trial

The trial will be performed in accordance with the protocol, International Conference on Harmonization Good Clinical Practice guidelines, and applicable local regulatory requirements and laws.

12.3. Subject Information and Consent

The informed consent form and any changes to the informed consent form made during the course of the trial must be agreed to by VIVUS, Inc. and the IRB/IEC prior to its use and must be in compliance with all ICH-GCP, local regulatory requirements and legal requirements.

The investigator must ensure that each trial subject is fully informed about the nature and objectives of the trial and possible risks associated with participation and must ensure that the subject has been informed of his/her rights to privacy. The investigator will obtain written informed consent from each subject before any trial-specific activity is performed and should document in the source documentation that consent was obtained prior to enrollment in the trial. The original signed copy of the informed consent form must be maintained by the investigator and is subject to inspection by a representative of

VIVUS, Inc., their representatives, auditors, the IRB/IEC and/or regulatory agencies. A copy of the signed informed consent form will be given to the subject.

12.4. Disclosure of Data

Data generated by this trial must be available for inspection by the U.S. Food and Drug Administration (FDA), by the sponsor or a designate acting on behalf of the sponsor, by applicable foreign health authorities, and by the IRB or EC as appropriate. At a subject's request, medical information may be given to their personal physician or other appropriate medical personnel responsible for their welfare.

Subject medical information obtained during the course of this trial is confidential and disclosure to third parties other than those noted above is prohibited.

13. Regulatory Correspondence

The trial site and trial-related documents may be subject to review by the institutional review board IRB/IEC, and/or to quality assurance audits performed by VIVUS, Inc., and/or to inspection by the FDA and/or applicable foreign health authorities. The investigator will notify VIVUS, Inc. within *** working days following any FDA or other regulatory agency contact

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with the investigative site regarding this study. The investigator will provide VIVUS, Inc. with copies of all correspondence with the FDA or other regulatory agency which may affect the review of the current study (e.g., Form 483, Inspection Observations) or their qualification as an investigator in studies conducted by VIVUS, Inc. (e.g., warning letters).

14. Definition of end of trial (If Applicable)

The end of this trial is defined as the time when the last subject completes their last trial visit.

Additionally, data and materials that are required by the Sponsor before any trial site's activity can be considered completed include:

- All completed Case Report Forms, appropriately signed by the investigator;
- All laboratory findings, clinical data, and special test results collected during the trial period;
- Completed drug accountability and investigational materials return records;
- Statement of outcome for any serious adverse events reported during the study;
- Copy of notification to IRB/IEC indicating study completion.

15. SPONSOR DISCONTINUATION CRITERIA

Premature termination of this clinical trial may occur because of a regulatory authority decision, change in opinion of the IRB/IEC, drug safety problems, or at the discretion of VIVUS. In addition, VIVUS retains the right to discontinue development of VI-0521 at any time.

If a trial is prematurely terminated or discontinued, VIVUS will promptly notify the investigator. After notification, the investigator must contact all participating subjects within 15 days. As directed by VIVUS, all trial materials must be collected and all CRFs completed to the greatest extent possible.

16. PUBLICATION OF TRIAL RESULTS

All information and data, including the terms of this protocol, and all data, clinical results, and research conducted hereunder concerning VIVUS, Inc.'s products and operations including VIVUS, Inc. patent applications, formulas, manufacturing processes, basic scientific data, and formulation information that has been supplied by VIVUS, Inc. and not previously published are considered confidential by VIVUS, Inc. and will remain the sole property of VIVUS, Inc. The investigator understands and agrees that said proprietary and/or confidential information disclosed to or produced by him/her thereunder is highly valuable to VIVUS, Inc. and will be used exclusively by the investigator in accomplishing this study and will not use it for any other

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purposes without VIVUS, Inc's prior written consent. The investigator agrees that he/she will not use any such proprietary and/or confidential information for any other purpose. The investigator also understands and agrees that such disclosure will not be deemed to grant to the investigator a license for use of said proprietary and/or confidential information, except as expressly provided herein.

It is understood by the investigator that the information developed in the clinical study will be used by VIVUS, Inc. in connection with the development of this product. This information, therefore, may be disclosed and used solely by VIVUS, Inc. as required to such third parties and agencies as VIVUS, Inc., in its sole discretion, warrants. In order to allow for the use of the information derived from the clinical studies, it is understood that there is an obligation to provide to VIVUS, Inc. complete test results and all data developed in this study. The investigator agrees to promptly answer all inquires from VIVUS, Inc. regarding completion, legibility or accuracy of trial data in the case report.

VIVUS, Inc. recognizes the value of disseminating research results and expects that publication of all results from this study will be undertaken by a collaborative group of study investigators who made significant contributions to the study design, the treatment of study subjects, and evaluation of study data. However, after 1) submission of the multicenter results for publication, 2) notification ***.

Investigators shall furnish the *** with a written copy of any proposed publication or other disclosure of study results (including disclosures at research seminars, lectures and professional meetings) *** prior to submission for publication or disclosure so that *** may have a reasonable opportunity to protect its proprietary rights to information, inventions, or products developed under this study and to insure that reported data are factually correct. Upon the ***, the investigator shall not publish or disclose information related to this study. Further, if the *** believes that such publication or disclosure contains confidential information, the investigator agrees to remove such confidential information from the proposed publication or disclosure.

VIVUS, Inc. agrees that before it publishes any results of this study in a refereed journal, it will provide the investigator, for review, a prepublication manuscript *** prior to the submission of the manuscript to the publisher.

17. REFERENCES

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APPENDIX 1: SCHEDULE OF STUDY ACTIVITIES

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APPENDIX 2: *

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APPENDIX 3: *

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APPENDIX 4: PROTOCOL AMENDMENTS

Amendment Tracking

Protocol Title: **A Phase III, Randomized, Double-Blind, parallel-design study comparing multiple doses of VI-0521 to Placebo and their single-agent phentermine and topiramate constituents for the Treatment of Obesity in Adults**

Protocol Number: **OB-301**

Indicate any amendments to this protocol by writing the Amendment Number and the Date of the Amendment in the space below. This page will be used to track the original protocol and its amendments. This is the original protocol if no amendment number is listed below.

Amendment Number 3
Date of Amendment: ***
(19 items)

Rationale: This protocol amendment is being implemented at the request of the FDA to incorporate assessments of *** and *** using the ***, and assessments of *** using the *** in all study subjects at ***. Previously, follow-up *** evaluations were done only if other *** assessments revealed a ***. This change is not anticipated to have any impact on safety of study subjects.

Section and/or Item	Protocol Date	Amendment 3, *** Change Effected
Protocol Synopsis: Safety Endpoints	***	Change: "Adverse event assessments will include direct questions related to eye pain and *** at each visit. In addition, the presence of *** will be evaluated at baseline using the ***. Follow up assessments using the *** will be done if adverse events potentially related to ***, or ***." To: "**Adverse event assessments will include direct questions related to eye pain and *** will be assessed at each visit using the ***."**
Rationale	***	Change: "VI-0521 is an exploratory weight loss therapy that is a new combination of two currently approved drugs, phentermine and topiramate. As such, VI-0521 represents a potential advance in the medical treatment of obesity since the two agents comprising this combination product affect weight loss through different mechanisms." To: "VI-0521 is an **investigational** weight loss therapy that is **a combination** of two currently approved drugs, phentermine and topiramate. As such, VI-0521 represents a potential advance in the medical treatment of obesity since the two agents comprising this combination product **effect** weight loss through different mechanisms."
Trial Design	***	Change: "Safety evaluations will include summaries of adverse events, ***." To: "Safety evaluations will include summaries of adverse events, ***.**"**
Drug Storage and Drug Accountability	***	Change: "No investigational drug, used or unused, may be discarded. All used and unused drug must be returned to the sponsor upon completion of the study." To: "No investigational drug, used or unused, may be discarded. All used and unused drug must be returned to the sponsor **or designated representative** upon completion of the study."
Schedule of Visits: Visit 2	***	Change: "Assess adverse events (including eye pain and ***), and changes in concomitant medications;" To: "Assess adverse events (**including eye pain),** and changes in concomitant medications;"
Schedule of Visits: Visit 3	***	Added: "**Administer *** and ***;**" Change: "Assess adverse events (including eye pain and ***), and changes in concomitant medications;" To: "Assess adverse events (**including eye pain),** and changes in concomitant medications;"
Schedule of Visits: Visit 4	***	Added: "**Administer *** and ***;**" Change: "Assess adverse events (including eye pain and ***), and changes in concomitant medications;" To: "Assess adverse events (**including eye pain),** and changes in concomitant medications;"
Schedule of Visits: Visit 5	***	Added: "**Administer *** and ***;**" Change: "Assess adverse events (including eye pain and ***), and changes in concomitant medications;" To: "Assess adverse events (**including eye pain),** and changes in concomitant medications;"
Schedule of Visits: Visit 6	***	Added: "**Administer *** and ***;**" Change: "Assess adverse events (including eye pain and ***), and changes in concomitant medications;" To: "Assess adverse events (**including eye pain),** and changes in concomitant medications;"
Schedule of Visits:	***	Change: "Administer ***;"

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Visit 7		"Assess adverse events (including eye pain and ***), and changes in concomitant medications;" To: "Administer *** **and ***;**" "Assess adverse events (**including eye pain),** and changes in concomitant medications;"
Schedule of Visits: Visit 8	***	Added: "**Administer *** and ***;**"

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		Change: "Assess adverse events (including eye pain and ***), and changes in concomitant medications;" To: "Assess adverse events (**including eye pain),** and changes in concomitant medications;"
Schedule of Visits: Visit 9	***	Added: "**Administer *** and ***;**" Change: "Assess adverse events (including eye pain and ***), and changes in concomitant medications;" To: "Assess adverse events (**including eye pain),** and changes in concomitant medications;"
Schedule of Visits: Visit 10	***	Change: "Administer *** and ***;" "Assess adverse events (including eye pain and ***), and changes in concomitant medications;" To: "Administer ***, **and ***;**" "Assess adverse events (**including eye pain),** and changes in concomitant medications;"
***	***	Change: "The *** for the assessment of *** that will be completed ***.(22),(23)" To: "The *** for the assessment of *** that will be completed ***, **and at *** after the ***.**(22), (23)" Change: "The *** is being used ***. This questionnaire will be completed at ***, and ***." To: "**The *** is being used ***.**"
***	***	Change: "Subsequent *** evaluations will be done only in *** who demonstrate a ***." To: "Subsequent *** evaluations will be done **at *** after ***. All *** assessments must be administered by a trained staff member. If any test reveals ***, then test results must be confirmed by a physician investigator prior to ***."**
***	***	Change:" All subjects will be screened for the presence and *** at *** and subsequently at regular intervals throughout the study: *** and *** using a validated survey instrument *** designed for assessment of *** in a primary care setting." To: "All subjects will be screened for the presence and *** at *** and subsequently **monitored at *** after the ***** using a validated survey instrument *** designed for assessment of *** in a primary care setting." Change: "The *** is a *** module based directly on the diagnostic criteria for ***. At study visits where *** assessments are not included, subjects will be asked the following question to assess ***." To: "The *** is a *** module based directly on the diagnostic criteria for ***. ***** will also be assessed at *** and *** following the *** using the ***.**" Change: "Any *** must be ***. Investigators are encouraged to administer the *** on an ad-hoc basis as part of the clinical assessment of ***. These ad-hoc questionnaires will be maintained as source documentation, but will not be

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		analyzed as a separate ***." To: "**Any *** must be ***."**
Appendix 1: Schedule of Study Activities — ***	***	Add: ***
Appendix 1: Schedule of Study Activities — ***	***	Add: ***
Appendix 1: Schedule of Study Activities — ***	***	Change: "***" To: "***"

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Protocol Title: A Phase III, Randomized, Double-Blind, parallel-design study comparing multiple doses of VI-0521 to Placebo and their single-agent phentermine and topiramate constituents for the Treatment of Obesity in Adults

Protocol Number: OB-301

Indicate any amendments to this protocol by writing the Amendment Number and the Date of the Amendment in the space below. This page will be used to track the original protocol and its amendments. This is the original protocol if no amendment number is listed below.

Amendment Number 2
Date of Amendment: ***
(14 items)

Rationale: This protocol amendment is being implemented in response to comments from FDA and investigational sites to designate the percent weight loss from baseline to week 28 and the percentage of subjects achieving at least 5% weight loss as co-primary endpoints, to provide an additional *** at ***, and to specify that ***. Additionally miscellaneous inconsistencies and typographical errors have been addressed. Other than the potentially positive effects of ***, these changes are not anticipated to have any impact on subject safety.

Section and/or Item	Protocol Date	Amendment 2, *** Change Effected
Header	***	Changed: " Amendment 1: ***" To: "Amendment **2: *****"
Protocol Synopsis: Efficacy Endpoints	***	Change: "The primary study endpoints will be based on the percent weight loss at week 28, calculated as ***." To: "The primary study endpoints will be based on the percent weight loss at week 28, calculated as ***, **and the percentage of subjects achieving at least 5% weight loss at week 28**."
Protocol Synopsis: Efficacy Endpoints	***	Change: "Secondary efficacy endpoints will include the proportion of subjects achieving 5% and 10% weight loss," To: "Secondary efficacy endpoints will include the proportion of subjects **achieving 10%** weight loss,"
Protocol Synopsis: Statistical Methods	***	Change: "If each of these *** comparisons is significant at the ***, then this combination will be considered to have met requirements," To: "If each of these *** comparisons is significant at the *** **for both of the co-primary endpoints**, then this combination will be considered to have met requirements,"
Trial Design	***	Change: "The primary efficacy endpoints for this trial will be based on the

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		percent weight loss at week 28, calculated as ***. Secondary efficacy endpoints will include the percentage of subjects losing 5% and 10% of their body weight," To: " The primary efficacy endpoints for this trial will be based on the percent weight loss at week 28, calculated as ***, **and the percentage of subjects achieving at least 5% weight loss at week 28**. Secondary efficacy endpoints will include the percentage of subjects **losing 10%** of their body weight,"
Schedule of Visits: Visit 4	***	Change: "Administer *** for *** and ***;" To: "Administer *** for *** and ***, **and perform *** (see Section 7.4)**;"
Schedule of Visits: Visit 10	***	Change: "Collect blood sample for laboratory tests (all subjects)," To: "Collect blood **and urine samples** for laboratory tests (all subjects),"
Schedule of Visits: Visit 10	***	Add: "**Ask End of Treatment Questions (see Section 7.5);"** Change: "Discontinue subject's trial participation; if appropriate enroll subject into open label treatment protocol." To; "**Discontinue subject's trial participation**."
***	***	Change: "The *** measures ***" To: "The *** **will be assessed at ***, and ***, and** measures ***,"
***	***	Change: "*** assessments of *** and *** will be collected at selected visits at ***." To: "*** assessments of *** and *** will be **collected at ***.**"
Analysis of Primary Endpoint	***	Change: "The primary calculated endpoint for this trial is based on the percent weight loss at week 28. This outcome will be calculated as ***." To: "The primary calculated endpoints for this trial are based on the percent weight loss at week 28, **and the percentage of subjects with at least 5% weight loss at week 28. The percent weight loss at week 28** will be calculated as ***."
Analysis of Primary Endpoint	***	Change: "If any one of the *** does not reach the *** level, then the efficacy of that combination cannot be confirmed. A step-down multiple testing procedure will be used to control the overall type I error for this trial. The hypothesis that the *** is an effective combination therapy will be tested first. Once the efficacy of this *** is confirmed, then the efficacy of the *** will be tested using the same criteria. Comparisons between treatments will be assessed using a *** model with factors of ***." To: "If any one of the *** does not reach the *** **level for either of the co-primary endpoints**, then the efficacy of that combination cannot be confirmed. A step-down multiple testing procedure will be used to control the overall type I error for this trial. The hypothesis that the *** is an effective combination therapy will be tested first. Once the efficacy of this *** is confirmed, then the

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		efficacy of the *** will be tested using the same criteria. Comparisons between treatments **for the endpoint of percent weight loss** will be assessed using a *** model with factors of ***. **Comparisons between treatment of the percentage of subjects with at least 5% weight loss at week 28 will be evaluated by ***."**
Analysis of Secondary Endpoint	***	Change: "Categorical variables, including the proportion of subjects achieving 5% and 10% reductions in body weight at week 28 will be evaluated by ***." To: "Categorical variables, including the proportion of subjects **achieving 10%** reductions in body weight at week 28 will be evaluated by ***."
***	***	Change: "This trial will not involve a ***."

	To: “***.”

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Protocol Title: **A Phase III, Randomized, Double-Blind, parallel-design study comparing multiple doses of VI-0521 to Placebo and their single-agent phentermine and topiramate constituents for the Treatment of Obesity in Adults**

Protocol Number: **OB-301**

Indicate any amendments to this protocol by writing the Amendment Number and the Date of the Amendment in the space below. This page will be used to track the original protocol and its amendments. This is the original protocol if no amendment number is listed below.

Amendment Number 1
Date of Amendment: ***
(8 items)

Section and/or Item	Protocol Date	Amendment 1, *** Change Effected
Appendix 4	***	Added: Appendix 4: Protocol Amendment Section
List of Abbreviations	***	Add: “I-CAM: Intercellular Cell Adhesion Molecule”, “PAI-1: Platelet Activator Inhibitor 1”, “RBP-4: Retinol Binding Protein 4”, and “V-CAM: Vascular Cell Adhesion Molecule”
Inclusion Criteria	***	Change: “If females of child-bearing potential, be using adequate contraception, defined as double barrier methods, stable hormonal contraception plus single barrier, or tubal ligation. Females are considered to be of childbearing potential unless they are at least 55 years of age with spontaneous amenorrhea for at least 12 months, have a documented FSH value of 40 IU/L or greater, or have had a bilateral hysterectomy or oophorectomy; To: “If females of child-bearing potential, be using adequate contraception, defined as double barrier methods, stable hormonal contraception plus single barrier, or tubal ligation. Females are considered to be of childbearing potential unless they are at least 55 years of age with spontaneous amenorrhea for at least 12 months **o**r have a documented FSH value of 40 IU/L or greater, or have **had a hysterectomy or bilateral oophorectomy**;”
***	***	Change: “Should *** would cause subjects to consider ***, investigators may, at their discretion, ***. Such events may or may not be related to trial treatment. If dosing has been ***, a new titration kit should be ordered through *** to ***.” To: “Should *** would cause subjects to consider ***, investigators may, at their discretion, ***. ***** are possible with agreement from the medical monitor.** Such events may or may not be related to trial treatment.

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		All subjects undergoing * for *** may be *** based on discretion of the PI.** If dosing has been ***, a new titration kit should be ordered through *** to ***.”
Schedule of Visits: (Visit 2 through Visit 10)	***	Change: “Assess adverse events and changes in concomitant medications;” To: “Assess adverse events **(**including eye pain and ***), and changes in concomitant medications;
Laboratory Tests	***	Change: “Lipid panel including total cholesterol, LDL cholesterol (LDL-C), HDL cholesterol (HDL-C), triglycerides, apolipoprotein A, apolipoprotein B-100, and Lp (a) will be evaluated at screening and Visit 10 (end of treatment or early exit). · Blood biomarkers including HgbA1c, C-reactive protein, and adiponectin, will be evaluated at screening and at Visit 10 (end of treatment or early exit);”

		To: "Lipid panel including total cholesterol, LDL cholesterol (LDL-C), HDL cholesterol (HDL-C), triglycerides, apolipoprotein A, apolipoprotein B-100, and Lp (a) will be evaluated at screening and Visit 10 (end of treatment or early exit). **Visit 10 (end of treatment or early exit) results for apolipoprotein A, apolipoprotein B-100, and Lp (a) will be blinded to investigators and sponsor;** · Blood biomarkers including HgbA1c, C-reactive protein, **and** adiponectin**, retinol binding protein-4 (RBP-4), intercellular cell adhesion molecule (I-CAM), vascular cellular adhesion molecule (V-CAM), platelet activator inhibitor 1 (PAI-1) and fibrinogen**, will be evaluated at screening and at Visit 10 (end of treatment or early exit). **Visit 10 (end of treatment or early exit) results for all biomarkers with the exception of HgbA1c will be blinded to investigators and sponsor;"**
Appendix 1	***	Change: "***" To: "***"
Appendix 1	***	Change: "***" To: "***"

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Task Order #01
Appendix 2 — Scope of Work
VIVUS, Inc.
Qnexa OB-301

PROJECT OVERVIEW

OB-301

The OB-301 trial is a phase III, randomized, double-blind, parallel design study comparing multiple doses of VI-0521 to placebo and their single-agent phentermine and topiramate constituents for the treatment of obesity in adults.

PROJECT TEAM

Study Management

The overall management of the study will be the responsibility of the Senior Clinical Trial Manager (CTM). The Senior CTM will oversee and coordinate the management of the study as well as oversee the study specific CTM. This oversight will ensure consistency and allow VIVUS Study Management to have one primary contact for the Qnexa program. The Medpace CTM assigned to OB-301 will work closely with the VIVUS Study Manager, Medpace Medical Expert, and VIVUS Clinical Leader to address protocol questions and interpretations while maintaining close oversight of study-related processes and documents. The OB-301 CTM will supervise all Clinical Research Associates (CRAs) and Project Coordinator assigned to the project.

The Project Coordinator will be responsible for day-to-day study management functions, including the generation of status reports, organization of supplies, generation and compilation of newsletters, and input of all study information into the ClinTrak® Study Management System, a web-based, proprietary research management system designed by Medpace. The Project Coordinator will organize teleconferences and team meetings, including the compilation of agendas and meeting minutes.

The Study Start-Up Manager and Study Start-Up Coordinators will work closely with the CTM and Project Coordinator to ensure sites become active in the most time effective manner.

The Medpace Contracts Attorney will be responsible for the execution of Investigator contracts (upon VIVUS defined process). The Contracts Attorney will work closely with the Start-Up Manager and Medpace CTM to ensure contracts are executed in a timely manner.

The Medpace Medical Expert assigned to this project will work closely with the VIVUS Clinical Leader. The Medpace Medical Expert will assist with protocol design and medical interpretation of entry criteria and adverse events (AEs). The Medical Expert will also be involved in the training of CRAs and other staff members participating in the

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project. The Medical Expert will review and approve the coding of concomitant medications, medical histories, AEs, and will provide the medical context for the statistical analysis and medical writing.

The Medical Expert will assist in the review of the protocol, train Medpace personnel internally as to the background of the study compound and design of the study, participate in the project teleconferences and meetings, work hand-in-hand with the OB-301 CTM, and have heavy involvement in the clinical study report. The Medical Expert's role and decision making rights are dictated by VIVUS (e.g. inclusion/exclusion of patients, discussions with Investigators about withdrawing a patient, etc.). This decision making power often times reduces the oversight needed by the sponsor. For questions the OB-301 CTM is not comfortable answering, she will contact the Medical Expert for guidance. Obviously, VIVUS will be involved in study oversight based on pre-defined terms with the VIVUS Clinical Development Team. The Medpace Medical Expert is available 24 hours a day, 7 days a week via the Medpace Project Helpline.

Clinical Monitoring

Medpace operates in North America with a primarily centralized monitoring team of over 140 CRAs to promote greater standardization, cohesiveness, support, and stability. Each of the Medpace CRAs assigned to this project have monitoring experience and strong clinical backgrounds.

Clinical Safety

The Clinical Safety will be managed by VIVUS or its designee. VIVUS Clinical Leader to be involved with casualty assignment for all Serious Adverse Events (SAEs).

Data Management

A Data Manager will serve as the primary contact for the Data Management team. Data Coordinators will be involved in the day-to-day operations and report issues to the Data Manager. Data Entry Specialists and Database Programmers will also be utilized.

Biometrics

Key members of our Biometrics team include Biostatisticians and Statistical Analysts. The Biostatistician assigned to this project will develop the analysis plan and coordinate biometrics activities. The Lead Statistical Analyst will work closely with the Biostatistician to ensure a clear understanding of the analysis plan and communicate any programming issues that may arise.

Medical Writing

The Medical Writing team works in collaboration with the Medical Experts to prepare research reports meeting International Conference on Harmonisation (ICH) and Sponsor guidelines. All Medpace Medical Writers have extensive experience in regulatory

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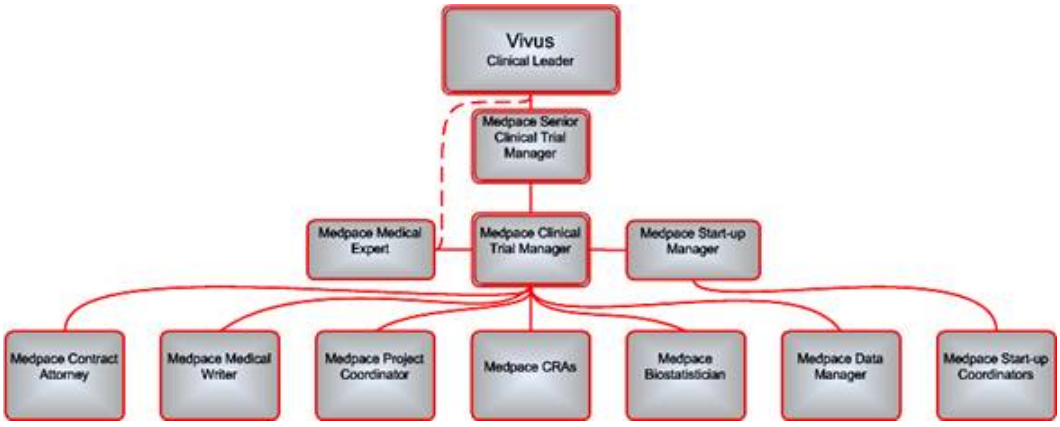
submission preparation. The Medical Writing team is actively involved throughout the conduct of the trial.

Team Organization Chart



PROJECT START-UP

Protocol

VIVUS will prepare the protocol. Medpace will review the protocol and provide comments before it is finalized.

Case Report Forms

Medpace will design the electronic case report forms (eCRFs) for the trial, including completion instructions, according to the final protocols and the Medpace template. VIVUS must review and approve the eCRFs before they are finalized.

Project Initiation

Prior to the study site initiation visits, a project kickoff meeting will be held at Medpace involving Medpace and VIVUS personnel to review the study protocol, eCRFs, and overall project coordination. Medpace project team members and VIVUS personnel will participate in this meeting.

Interactive Voice Response System

Medpace will provide a customized (study-specific) interactive voice response system (IVRS) to provide patient randomization, and drug management. The Medpace IVRS is a proprietary in-house developed system. The system provides both voice and web access and has been developed in conjunction with our web based Clintrak® system providing

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seamless functionality throughout the conduct of the study. The VIVUS Team (no limit applied to number of team members) will have access to review reports within the IVRS. Medpace will perform the User Acceptance Testing (UAT) for each site.

The IVRS will include:

- Subject Screens/Screen Failures;
- Subject randomization;
- Patient visit tracking;
- Inventory management (site supply set-up, initial bulk supply, and resupply of one additional shipment per patient);
- Notifications of site shipments;
- Confirmation of receipt of shipments; and
- Customized reports.

VIVUS will review IVRS and approve system prior to finalization.

Study Medication Supply and Storage

VIVUS will be responsible for the supply, packaging, labeling, storage, and destruction of study medication. Distribution of the study medication will be tracked and initiated via the Medpace IVRS. Study medication accountability procedures will follow Medpace standard operating procedures (SOPs) and utilize a study medication accountability log that has been approved by VIVUS.

Recruitment Oversight Plan

The Medpace CTM, in collaboration with VIVUS, will develop a recruitment oversight plan. Medpace understands the importance of rapid recruitment and the necessity to keep patients in the trial until completion. Medpace will develop processes prior to study initiation to ensure recruitment is efficient and retention of patients in the study is maximized. The plan will include details on:

- Initial collection of essential documents;
- Patient recruitment (including tools, site-specific plans, contingencies, etc.); and
- Patient recruitment tracking reports.

The tools noted above include:

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- Inclusion/exclusion cards;

- Patient emergency cards;
- Enrollment tracking forms;
- Laminated patient visit schedule;
- Pocket protocol; and
- Advertising tools (e.g., posters, table tents, language for newspaper/radio advertisements, etc.).

Medpace understands each site has a different experience and approach to patient recruitment. The Medpace CTM and Medpace CRAs will work with personnel from each site to help maximize their efforts. The project team maintains frequent contact during the active recruitment phase to assess each site's activity and offer assistance when needed. Medpace acknowledges the importance of site recognition and offers various incentives throughout the recruitment period. Examples of site incentives are "Site of the Month" awards and weekly faxes displaying each sites' activity (often included in the newsletter as well). The time associated with these types of incentives are inclusive of the budget. However, often times, monetary incentives are built into the Investigator's grant to encourage rapid essential document collection and/or timely recruitment.

Patient retention is vital to the success of a trial. The Medpace CTM and the Medpace CRAs will work with the sites to understand the needs and motivations for patients to remain in the study. They will help educate the sites on the importance of "customer service" and "patient satisfaction" as elements that ensure continued patient participation. Examples of patient retention methods include quarterly patient newsletters, ideas for site customer service, and tokens of appreciation for patients.

Site Selection and Pre-study Visits

VIVUS, in conjunction with Medpace, will identify qualified Investigators. VIVUS and Medpace will also work together to provide and negotiate Confidentiality Disclosure Agreements (CDAs) as well as create and evaluate site questionnaires. In not knowing the number of pre-study visits Medpace will be required to conduct, a unit price for a pre-study visit has been provided in the budget.

Pre-study visits will be conducted consistent with Medpace SOPs. Medpace will provide a pre-study visit report to VIVUS within 10 business days of each visit.

These visits will include, but are not limited to:

- Determining whether or not the site has clinical staff of appropriate education, training, and experience to manage the study and have sufficient capacity to perform the required tasks;
- Determining whether or not the site has appropriate facilities to conduct the study;
- Determining there are no competing studies that will conflict with patient enrollment and that the site has sufficient patients and processes to enroll patients in the time identified for patient recruitment; and
- Determining whether or not the site has appropriate resources and procedures to maintain appropriate records according to FDA requirements.

Study Start-up Team

The efficient start-up of the *** study sites for OB-301 will have a significant effect on patient recruitment time. Medpace will utilize its Study Start-up team for additional support during the initial phase of the trials to expedite the overall study start-up for each site.

The Study Start-up team works directly with the CTM and the Project Coordinators. The team is comprised of a Study Start-up Manager and several experienced Study Start-up Coordinators. The team is responsible for many of the key start-up activities, including:

- Submission to the central IRB;
- Coordination and tracking of essential documents packages for each site;
- Investigator meeting presentations and binders; and
- Site tools.

Central Laboratory Selection

Medpace Reference Laboratories (MRL) will be utilized for processing the clinical laboratory samples. MRL is committed to providing comprehensive laboratory services of the highest quality to the pharmaceutical and biotechnology industries.

Investigators' Meeting

An Investigators' Meeting will be held for the OB-301 study. VIVUS will arrange the meeting (including contracting with a third-party vendor) and Medpace will prepare the meeting materials, including preparation and distribution of binders. The Medpace OB-301 Team will attend the meeting. VIVUS will open the meeting and Medpace will present on the topics delegated by VIVUS. The meeting minutes will be prepared by Medpace, reviewed and approved by VIVUS, and distributed to the study sites by

Medpace. The preparation of the meeting minutes is optional; however, is included in the budget. Medpace assumes the Investigators' Meeting will serve as the initiation visit for the Investigators. Therefore, the budget reflects 20% of the sites will require an initiation visit (for those unable to attend the Investigators' Meeting).

Clinical Trial Agreements for Sites, Central Laboratory, and EDC Vendor

Medpace will prepare and provide sample clinical trial agreements (including budgets) for the study sites. VIVUS will review and approve the final draft versions of the clinical trial agreements. The agreements will be distributed and negotiated with each site by Medpace (with final approval by VIVUS). Medpace will make payments to the clinical sites according to the VIVUS-approved schedule. All payments for sites, Medpace Reference Laboratories, and Phase Forward will be made electronically to Medpace within seven days of invoice receipt. If electronic payment exceeds or falls below actual costs, VIVUS will adjust its payment based on the prior month's payment reconciliation. Investigator payment invoices will include the following detail:

- Clinical study number;
- PI or Site #;
- Patient ID;
- Amounts paid per visit;
- Total amount earned to date;
- Prior payments; and
- Current payment amount.

Institutional Review Board and Initial Essential Documents Packages

Medpace will select a central Institutional Review Board (IRB) and coordinate the initial submissions to the IRB. VIVUS must approve the central IRB selected. Medpace will be responsible for payments to the central IRB selected. Medpace will be responsible for payments to the central IRB utilizing funds provided in the same manner as described above.

A study-specific, prototype informed consent form (ICF) will be designed by Medpace. The ICFs will be reviewed and approved by VIVUS. Medpace will distribute the ICFs to the Central IRB. Medpace will be responsible for negotiating changes to the informed consents with the central IRB.

Deviations from the VIVUS template must be brought to the attention of the VIVUS Clinical Leader who will facilitate VIVUS legal review and approval, if required.

All components of the Initial Essential Documents Package will be collected, tracked, and maintained by Medpace according to Medpace SOPs. The Medpace Study Start-up team will review all documents, negotiate any changes with study site personnel, and correct any errors. The Initial Essential Document Package includes the following:

- Signed protocol signature pages;
- Financial disclosure questionnaires (FDQs) (template to be provided by VIVUS, Medpace to collect the forms);
- Clinical study agreement (includes study budget);
- FDA Form 1572;
- Laboratory certifications and reference values;

- Curricula vitae for all Investigators;
- IRB approval of the protocol (and any amendments), the informed consent and sponsor approved advertisements; and
- Qualification of IRB members.

The FDQs shall apply throughout the entire term of the study and for one year following last patient last visit (LPLV). If there is any change in the accuracy of a particular site's FDQ during that time period, that site will be responsible for notifying Medpace of the change. If a site notifies Medpace of a change in staff from LPLV to one year after LPLV, Medpace will collect an updated FDQ and forward on to VIVUS. Costs associated with this task are included in the budget. Once a study has ended, Medpace sends a fax to all sites notifying them of study end as well as reminding them of their responsibilities (one of which being to notify Medpace of any FDQ changes).

Site Initiation Visits

Site initiation visits will be conducted by the Medpace CRAs consistent with Medpace SOPs. For purposes of this proposal, it is assumed that the Investigators' Meeting will serve as the initiation visit and only 20% of the sites for each study will require separate initiation visits. Typically, if the Investigator Meeting is considered the initiation visit, the CRA will contact the site via phone to review study procedures and the CRA's first routine monitoring visit will occur shortly (can be defined as 1 or 2 weeks) after a patient is screened for the trial. During this visit, the CRA will review bullets 2-5 below. A site initiation visit report will be completed and forwarded to VIVUS within 7 business days of the visit. These visits will include, but are not limited to, the following tasks:

- Train site and applicable study personnel on the protocol and study procedures;

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- Ensure the site has received all study supplies required for the conduct of the study, including study medication and access to eCRFs;
- Provide and review the Trial Master File binder. Medpace CRAs will provide instruction to the site personnel on the organization and maintenance of the documents in the binder;
- Review study medication accountability procedures;
- Provide eCRF completion instructions; and
- Explain the serious adverse event (SAE) reporting procedures.

CLINICAL OPERATIONS

Monitoring Data Review Guidelines

The Medpace Lead CRA in collaboration with the project team members will develop a project-specific Monitoring Plan for the study. This plan will include detailed interpretations of study expectations for the CRAs assigned to the study. Issues are discussed and updated on an ongoing basis throughout the project. Medpace will request that VIVUS approve the initial document and then re-approve the document on a quarterly basis.

Routine Clinical Monitoring Visits

Medpace will conduct routine monitoring visits at each site consistent with Medpace SOPs. The frequency of the visits will be determined by the site's activity, but will be conducted on average every four to six weeks. Visits at the beginning and end of the study may be more frequent based on the needs of the study, including, but not limited to, recruitment, quality data and study close-out activities. Based on recruitment being very rapid, the first routine visit will be performed within 2 weeks after the first two patients are screened at the site. The CRA will perform 100% source documentation. In addition, data queries will be resolved during the visits, eCRF changes will be verified, and supporting documentation for SAEs will be obtained. The Medpace CRA will verify all laboratory samples have been obtained according to guidelines and the results are available in the patient's source documents. A monitoring visit report will be forwarded to VIVUS within 10 business days of the visit. VIVUS will be notified of any significant issues by phone within one business day.

The following tasks will also be performed:

- Train any new site personnel and review study issues with applicable site personnel;

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- Ensure the site has sufficient study supplies (including study medication);

- Ensure the site is entering eligible patients into the study in a timely manner, and notify the Medpace Study Manager immediately of any problems;
- Detect any significant compliance or other issues and notify the Medpace Study Manager by phone, within one business day of the monitoring visit;
- Confirm the Trial Master File is complete and current, and the site is complying with applicable regulations and the protocol. VIVUS will be notified immediately of any significant deviations;
- Ensure the site is completing eCRFs in a timely manner;
- Ensure all completed eCRFs are reviewed, verified, corrected, and transmitted to Medpace;
- Review eCRFs for accuracy and protocol adherence;
- Verify study medication dispensing, compliance, and accountability for each patient; and
- Ensure the Investigator reported all SAEs to Medpace and the applicable IRB.

Medpace will provide a follow-up letter to the study site after each visit. The letter will include, but will not be limited to, the following:

- Important findings during the visit;
- Recommendations of corrective actions to be taken by the site; and
- Follow-up information regarding questions asked during the visit.

The Monitoring Visit Reports with all attachments including follow-up letters, will be available for view through the Medpace web based Clintrak® Study Management system within 10 business days of the monitoring visit.

In-house Clinical Monitoring Activities

Investigators will be contacted on a regular basis (every week during the active recruitment period and between monitoring visits) to ensure progress at the study site. The CRA will take the opportunity to review enrollment, answer protocol-related questions, discuss eCRF completion issues, obtain information regarding AEs, and ensure the site continues to be committed to the completion of the study in a timely manner and according to the protocol.

Telephone contacts will be entered in the Medpace ClinTrak Study Management system. Contacts requiring urgent attention will be relayed to VIVUS immediately and will be resolved in collaboration with the Medpace CTM and the VIVUS Study Manager.

Withdrawals Due to Adverse Events

Withdrawals due to AEs will be tracked and reconciled with the eCRF database on an ongoing basis by Medpace. The CRA will be responsible for reporting withdrawals due to AEs to VIVUS using the monitoring visit report.

Medpace will write narratives for all withdrawals due to AEs, for use in the clinical trial study report.

Status Reporting

The Medpace Senior CTM will serve as the central channel for communication between Medpace and VIVUS. The OB-301 CTM will work in conjunction with the clinical monitoring group to track study progress and report to VIVUS on a weekly basis. In addition, the OB-301 CTM will be responsible for overall management of site information, overseeing the status of Investigator contracts, direct supervision of CRAs, tracking of enrollment information, and distribution of study supplies. The Medpace OB-301 CTM will be the primary contact for the sites to address protocol interpretations and inclusion/exclusion criteria. All protocol-related issues will be recorded in an ongoing document to ensure consistency. The CTM is available 24 hours a day, 7 days a week via the Medpace Project Helpline.

Medpace will develop a communication plan at the start-up of the study. The CTM will work with the VIVUS project team to define details regarding study communication, including status reporting and team conference calls. Medpace typically delivers status reports on a predetermined day (and time) of the week, which is established around the weekly team calls so that the information can be discussed. Utilization of IVRS will also allow the project team to review patient status on a real time basis.

The Medpace CTM will collaborate with the Medpace Medical Expert and the VIVUS Study Manager to address any questions that may arise. The ClinTrak Study Management databases will serve as the primary source of project status information and will allow the Medpace CTM to report on any aspect of the study. The databases are updated on a real-time basis, providing accurate and up-to-date information.

Elements of ClinTrak include:

- Phone contacts;

- Monitoring visit reports;

- Patient status including details on withdrawals during the treatment phase;
- Study supplies; and
- Protocol deviations.

Medpace will provide weekly status reports via a secure project website, to include the following status by site:

- Number of patients screened;
- Number of screen failures;
- Number of patients randomized;
- Number of patients dropped with drop rates; and
- Number of patients completed.

In addition, monthly reports will be provided, to include the following:

- Monitoring visits scheduled; and
- Monitoring visits completed.

Data Management status reports will be provided monthly via a secure website. These reports will include the following:

- Cumulative and interval eCRF status by site (including number of eCRFs transmitted and cleaned);
- Cumulative and interval patient status by site (including number of patients ongoing, completed, and early terminations) based on eCRF data in-house; and
- Cumulative and interval query status by site (including number of queries issued and days outstanding).

Project Website

Medpace will develop a secure OB-301 website that will be available to all project team members and site personnel. The website will include information and tools relevant to the study, such as status reports, meeting agendas and minutes, newsletters, monitor visit status, and the project timeline. Access is controlled by the type of user. Access to the tabs (sections) on the websites are controlled by the user type so that sites can have access to the section specifically designed for site access. Medpace can set up an automatic notification process of updates to the user email accounts. Clinical sites will have access only to parts of the website that pertain to their function. They will have the ability to receive study information and download study-related forms.

Team Meetings

VIVUS and Medpace

Medpace assumes that one face-to-face meeting, other than the Investigators' meeting and kickoff meeting will take place for the OB-301 study at VIVUS.

Weekly teleconferences will be held during the study. The teleconferences will be held to discuss study progress and review project documents (as necessary). The Medpace Project Coordinators will be responsible for preparing and distributing agendas and minutes for each meeting/teleconference.

Additional meetings/teleconferences will be scheduled throughout the project, as needed.

Internal Meetings

Medpace will develop a project-specific internal project development/training program for all project team members. Included in this program will be the following:

- Protocol/eCRF review meeting;
- Medical in-services;
- Periodic Monitoring Plan meetings; and
- Periodic project meetings.

Newsletter

Medpace will prepare a 2-4 page full color site monthly newsletter for OB-301 as an additional avenue of communication and training for all site personnel. VIVUS will provide input and approval of the newsletter prior to distribution. Medpace will be responsible for printing and distributing two copies of each newsletter to each site.

Closeout Visits

Medpace will conduct closeout visits at each site consistent with Medpace SOPs after all patients have completed or discontinued from the study at the respective site. This visit may be performed as part of a final routine site monitoring visit. Site closeout visit reports will be forwarded to VIVUS within 10 business days of the visit. The following tasks will be performed:

- Resolve outstanding data queries;
- Ensure all study medication supplies are accounted for and that medication records and unused supplies are returned to VIVUS;

- Ensure the Investigator's copies of data and source documents are properly stored;
- Ensure the Trial Master File is complete, correct, and properly stored;
- Ensure the Investigator is aware of record retention requirements and other obligations, and a final site status report is sent to the IRB and VIVUS; and
- Instruct the site to update the FDQs for one year after the study is completed.

Site Audits

Site audit visits will be conducted, as deemed necessary, by VIVUS.

Medpace will respond to any audit findings and ensure the proper actions are taken to resolve outstanding issues.

REGULATORY AFFAIRS AND SAFETY REPORTING

Serious Adverse Events

All SAEs will be reported immediately, within 24 hours of discovery or notification of the event, by the clinical study site to VIVUS, or its designee, according to SOPs specified by VIVUS.

VIVUS will be responsible for submitting all immediately reportable SAEs (serious, causally related and unexpected) to the Food and Drug Administration (FDA) in accordance with the current regulations.

If a SAE has occurred at a site, the Medpace CRA will always 100% source document verify the event during the monitoring visit to ensure it has been recorded, documented, and reported appropriately and accurately. In addition, data queries will be resolved during the visits, CRF changes will be verified, and supporting documentation for SAEs will be obtained.

Medpace will provide VIVUS listings of non-serious adverse events from all sites to support filing of the Annual Safety Reports. Medpace will reconcile SAE listings with the AE database.

DATA MANAGEMENT

Data Management activities performed by Medpace will include eCRF tracking, preparation of a data management manual, eCRF review, coding of adverse events and concomitant medications, medical histories, data cleaning/editing, querying, query

tracking, final database quality review, and delivery of the final SAS® database. The data cleaning process will be performed on an ongoing basis following Medpace Data Management SOPs. Two data transfers (SAS transport files) will be performed: a test transfer prior to FPFV and a final transfer. A unit price for additional data transfers has been provided in the budget.

Database Development and Data Management Manual

Medpace will design and validate the data entry systems prior to entry of data. A Data Management Manual will be prepared for each study using the Medpace template, and will include the following data management documents:

- Database specifications, based on VIVUS specifications;
- Guidelines for the tracking of eCRFs and data queries;
- Data Management Guidelines, which will include guidelines for reviewing the data, and description of the database edit check specifications to be performed for data cleaning; and
- Description of the database quality control (QC) plan.

The manuals will be reviewed and approved by VIVUS.

Data from the Central Laboratory

Medpace will arrange periodic data transfers from MRL. Medpace will track and reconcile discrepancies between the MRL demographic data and the eCRF database, which are generated during the data cleanup process throughout each project.

Data Entry and Data Querying

Medpace assumes no codable forms will be transmitted for screen failure patients. Data is entered by site personnel that have been trained on the eCRF system. Data will be reviewed according to Medpace Data Management Guidelines and edits. A data query will be generated electronically within the eCRF system. The resolutions/corrections are made by site personnel by changing the data. All changes are recorded in an audit trail. All answered queries are verified/closed by Medpace Data Management. All resolutions/corrections will be performed consistent with Medpace SOPs. The Data Coordinators will work directly with the site personnel in resolving queries.

Coding

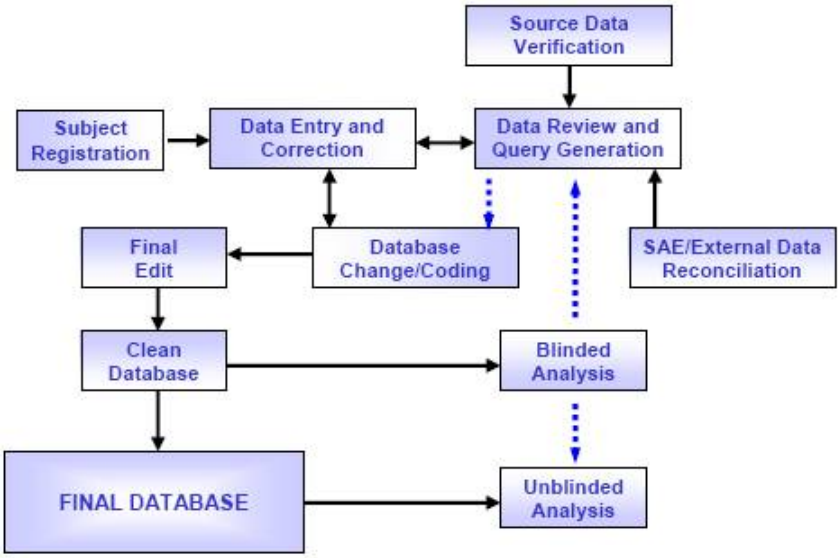
Medpace will be responsible for coding adverse events, medical histories, and concomitant medications.

- MedDRA will be used to code adverse events and medical histories. Adverse events and medical histories will be coded to the lowest level term, preferred term, and system organ class.

- WHO DRUG will be used to code concomitant medications. Concomitant medications will be coded to the generic name and anatomic therapeutic class 3. It is assumed by Medpace that VIVUS holds a valid agreement with the Uppsala Monitoring Centre (UMC) for the WHO DRUG dictionary.

All coding will be done on a single version of each coding system (versions to be agreed upon by VIVUS). Medpace will provide the coding dictionaries.

Data Flow Chart



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STATISTICAL ANALYSIS

Medpace will develop the data analysis plan (DAP) per the VIVUS/Medpace format and template. VIVUS will review and approve the DAP prior to initiation of programming. Included in the DAP is a detailed statistical methodology and programming specification for all statistical analyses, tables/figures/listings (TFLs), and derived datasets.

Medpace will be responsible for programming and generating all TFLs, according to the Medpace standard analysis validation and quality control procedures. All TFLs will be programmed using SAS (Version 8), according to the VIVUS Programming Standards document. Pre-final TFLs will be generated twice on clean data for format review. Final TFLs will be generated on final data for the clinical study report.

MEDICAL WRITING

The Medpace Medical Writing team works in collaboration with the Medpace Medical Expert to provide a clinical study report according to FDA/ICH guidelines. The preparation of the Integrated Clinical/Statistical Study Report involves three stages of development: (1) the Study Report Shell (SRS), (2) the Pre-Final Study Report (PFSR), and (3) the Final Study Report (FSR).

The SRS is prepared after sign-off of the Final DAP. The SRS is created using a template and/or style guide provided by VIVUS, or by utilizing the Medpace standard report template, which adheres to the ICH guideline, “Structure and Content of Clinical Study Reports,” and follows the *American Medical Association Manual of Style*. The SRS incorporates information from the protocol, amendments, and eCRFs into sections of the report, including but not limited to the study design, study population, treatments administered, and the evaluation schedule. The statistical methods and results sections encompass information derived from the Final DAP. The results sections include mock-up in-text tables and text. The SRS undergoes a complete team review, which includes the Medical Monitor, Statistician, CTM, Data Manager, and other team members, if applicable. After the Medical Writer incorporates all team changes into the SRS, the SRS undergoes Medpace’s comprehensive document QC process. Once all changes from the document QC process are implemented into the SRS, the SRS is forwarded to the VIVUS for review.

Preparation of the PFSR occurs after receipt and implementation of VIVUS comments on the SRS, declaration of a clean database, and completion of Pre-Final Analyses. If necessary, a results review meeting is conducted with key members of the Medpace and VIVUS project team as the Medical Writer begins preparing the PFSR. The PFSR is a complete version of the report without the appendices. The PFSR undergoes a complete

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team review, which includes the Medical Monitor, Statistician, CTM, Data Manager, and other team members, if applicable. After the Medical Writer incorporates all team changes into the PFSR, the PFSR undergoes Medpace’s comprehensive document QC process. Once all changes from the document QC process are implemented into the PFSR, the PFSR is forwarded to VIVUS for review.

The FSR is prepared once VIVUS’ comments on the PFSR are returned and all requested changes are agreed upon (including the acceptance of final text for all complicated or sensitive sections, which may require sending non-QC’d drafts of the report to VIVUS), and the Final Analyses are completed. The FSR is a complete version of the report including paginated appendices and/or supplements. The FSR undergoes a complete internal QC review and is forwarded to VIVUS for sign-off. The signed cover sheet is returned by VIVUS to verify their acceptance of the FSR.

STUDY CLOSEOUT

At the conclusion of each study, once all deliverables have been met, Medpace will return the original study files to VIVUS. These will include:

- General project administration files (this file includes items such as: Outside Vendor Correspondence, Multiple Site Correspondence (e.g. faxes to all sites), Central IRB Correspondence, Project Specific SOPs and Procedures, Monitoring Plan, Trial Master File, Project Timelines, Newsletters, and Meeting Minutes)

- Site files (this file includes site items such as: Essential Documents, Budget, Site Correspondence, Monitoring Visit Reports, Drug shipment documents, Study Supply forms, and Protocol Deviations);

- Final statistical tables and listings with results;

- Data management documentation (this file includes items such as: Database Definition Document, Final eCRFs, External Database Import Specs., Data Management Plan, Coding Reports, Analysis Plan, and Randomization Code); and

- Final clinical study report.

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Assumptions

OB-301	Description
Number of Investigators	***
Number of Screened Patients	***
Number of Randomized Patients	***
Number of Randomized Patients/Site	***
Duration of Enrollment Period	***
Duration of Treatment Period	***
Number of Investigators' Meetings	***
Number of Kickoff Meetings (at Medpace)	***
Number of Sponsor Meetings (at VIVUS)	***
Number of Conference Calls	***
Frequency of Calls	***
Number of Clinical Monitors	***
Number of Pre-study Visits	***
Number of Initiation Visits	***
Number of Routine Monitoring Visits	***
Number of Closeout Visits	***
Monitoring Frequency	***
Number of Newsletters per Site (monthly)	***
Estimated Number of eCRFs per Completed Patient	***
Estimated Number of Unique eCRFs per Completed Patient	***
Total Number of eCRFs	***
Estimated Number of AE Codes Per Patient	***
Estimated Number of Medical History Codes Per Patient	***

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Estimated Number of Concomitant Medications Codes Per Patient	***
Estimated Number of Queries Per Patient	***
External Data Sources	***
Data Transfers from Medpace to VIVUS	***
Number of Raw Listings	***
Number of Unique TFs	***
Number of Version TFs	***

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Task Order #01
Appendix 5 — Project Schedule
VIVUS, Inc.
Qnexa OB-301

Milestones

OB-301	Date
Medpace Begins Work	***
Protocol Finalized	***
First Patient First Visit	***
Last Patient First Visit	***
Last Patient Last Visit	***
Final Database Lock	***
Final TFLs Available	***
Delivery of Final Clinical Study Report	***

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Task Order #01
Appendix 4 — Budget
VIVUS, Inc.
Qnexa OB-301

Medpace Fee Estimate

***

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CONFIDENTIAL *September 11, 2007*

***

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Task Order #01
Appendix 3 — Payment Schedule
VIVUS, Inc.
Qnexa OB-301

Payment Schedule

As set forth in this Agreement, professional service fees totalling $*** will be paid by VIVUS for professional services rendered by Medpace according to the following schedule.

***

Pass-through expenses will be billed to VIVUS on a monthly basis as incurred. The first Wire-Transfer payment will be invoiced prior to any site becoming active to ensure funds are available for site payments. Medpace will pay sites immediately following receipt of Wire-Transfers. Medpace will invoice VIVUS on a monthly basis and payments will be made by VIVUS within seven days of invoice receipt.

Payment Information and General Conditions

***

Inflation

The fees stipulated in the fee estimate *include* inflation for the duration of the study as specified in this proposal. Any significant shift in timelines will require a revision to the fees.

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Appendix 6 **Transfer of Obligations Form**
CONFIDENTIAL

Directions: Complete a form for each clinical study where Sponsor obligations have been transferred in accordance with 21 CFR Part 312, Subpart D (Responsibilities of Sponsors). Forward the completed form to Sponsor's Regulatory Affairs Department for submission to the applicable regulatory agencies.

Drug: VI-0521 Study ID: OB 301
Study Title: A phase III, randomized, double-blind, parallel design study comparing multiple doses of VI-0521 to placebo and their single-agent phentermine and topiramate constituents for the treatment of obesity in adults.
CRO Name: Medpace, Inc.
CRO Address: ***

OBLIGATIONS TRANSFERRED TO MEDPACE: R THE APPROPRIATE BOX(ES).

o All obligations in 21 CFR 312, Subpart D (Responsibilities of Sponsors) have been transferred to Medpace.
x The following obligations have been transferred to Medpace:

Sec. 312.32: IND Safety Reports
x Promptly review safety information. *Sponsor will be notified within one (1) business day of discovery of significant new or serious adverse events or risks, or any unusual frequency of reactions with respect to the drug.
o Notify all participating investigators in a written IND safety report of any AE associated with the drug that is both serious and unexpected.
o Notify the FDA in a written IND safety report of any AE associated with the drug that is both serious and unexpected.

Sec. 312.53: Selecting investigators and monitors
x (a) Select qualified investigators
x (b) Control investigational drug shipment
x (c) Obtain information from investigators
  x (1) Signed Form FDA-1572
  x (2) CV or other qualification statement
  x (3) Clinical protocol outline
  x (4) Financial disclosure information
x (d) Select qualified monitors

Sec. 312.54: Emergency research
o (a) Monitor the progress of all studies involving an exception from informed consent.
o (b) Monitor such studies to identify when an IRB determines that it can't approve the research.

Sec. 312.55: Informing investigators
x (a) Provide sites with the current Inv. Brochure.
x (b) Inform investigators of new observations on the drug, particularly with respect to AEs and safe use.

Sec. 312.56: Review of ongoing investigations
o (a) Monitor the progress of all IND studies.
x (b) Secure compliance from noncompliant investigators or discontinue drug shipments and end the investigator's participation in the study.
o (c) Review and evaluate the safety and efficacy results as it is obtained from the investigator.
o (d) Discontinue use of the investigational drug if it is determined to present an unreasonable and significant risk to subjects, notify all IRBs and investigators, and assure the return or alternate disposition of the drug from the investigators.

Sec. 312.57: Record keeping and record retention
x (a) Maintain adequate records showing investigational drug receipt, shipment, or other disposition. *Master Drug Logs will include the name of the Investigator to whom the drug is shipped, the date, and the quantity and batch of each such shipment.
x (b) Maintain complete and accurate records showing any financial interests of the investigator subject to 21 CFR 54.
x (c) Retain the records and reports required by the regulations for 2 years after the marketing application is approved, or if not approved, until 2 years after investigational drug shipment is discontinued and FDA has been notified.

o (d) Retain reserve samples of any test article and reference standard identified and used in bioequivalence or bioavailability studies.

Sec. 312.58: Inspection of sponsor's records and reports

x (a) Permit FDA personnel to have access to and copy and verify any records and reports related to the clinical investigation.

x (b) Permit DEA personnel to have access to and copy records related to the shipment, delivery, receipt and disposition of any investigational controlled substance. Assure adequate storage precautions are taken for investigational new drug substances listed in any schedule of the Controlled Substances Act.

Sec. 312.59: Disposition of unused supply of investigational drug

x Assure the return (or alternate disposition) of all unused supplies of the investigational drug from each discontinued/terminated investigator; maintain written records of any disposition of the investigational drug.

Other

o Please describe any other applicable transfers below:

September 7, 2007

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MEDPACE
VIVUS Task Order #02

EXHIBIT A

Qnexa OB-302 TASK ORDER

MEDPACE Task Order Number: 02

MEDPACE Project Number: VOB302

This Task Order, dated September 12, 2007, is between Medpace, Inc. (**"MEDPACE"**), and VIVUS, Inc. (**"VIVUS"**).

RECITALS:

WHEREAS, MEDPACE and VIVUS have entered into that certain Master Services Agreement dated September 12, 2007 (the "Master Services Agreement"); and

WHEREAS, pursuant to the Master Services Agreement, MEDPACE has agreed to perform certain Services in accordance with Task Orders from time to time entered into by the Parties and VIVUS and MEDPACE now desire to enter into such a Task Order; and

WHEREAS, MEDPACE and VIVUS desire that MEDPACE provide certain services with respect to a phase III randomized, double blind, placebo controlled multicenter study to determine the safety and efficacy of VI-0521 in the treatment of obesity in otherwise healthy adults (the **"**Study") for the study of the product VI-0521 (**"**Study Product") as set out in the Protocol Number: OB-302, which is attached hereto as Appendix 1;

NOW, THEREFORE, in consideration of the mutual covenants contained herein, the Parties hereby agree as follows:

1. Scope of Work: MEDPACE shall perform the services described in the Scope of Work, attached hereto as Appendix 2, in accordance with the Project Schedule, attached hereto as Appendix 3 and any other documents attached to and specifically referenced in this Task Order ("Services")

2. Compensation: For performance of these Services, VIVUS shall pay to MEDPACE an amount equal to the Project Budget set forth in Appendix 4, which amount shall be payable pursuant to the Payment Schedule set forth in Appendix 5.

3. Transfer of Obligations: Sponsor Obligations transferred to MEDPACE by VIVUS (consistent with the regulations set forth in 21 C.F.R. Section 312, Subpart D) are identified in Appendix 6.

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4. MSA. The provisions of the Master Services Agreement are hereby expressly incorporated by reference into and made a part of this Task Order.

IN WITNESS WHEREOF, the Parties have hereunto signed this Task Order effective as of the day and year first written above.

MEDPACE, INC.

Signature: /s/ August J. Troendle

By: August J. Troendle
(Print Name)
Title: President

Date: September 12, 2007

SPONSOR

Signature: /s/ Wesley W. Day

By: Wesley W. Day
(Print Name)
Title: Vice President, Clinical Development

Date: September 10, 2007

List of Appendices:

Appendix 1: Protocol
Appendix 2: Scope of Work
Appendix 3: Project Schedule
Appendix 4: Project Budget
Appendix 5: Payment Schedule
Appendix 6: Transfer of Obligations

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VI-0521
Protocol No. OB-302
***

CLINICAL PROTOCOL

A PHASE III RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED MULTICENTER STUDY TO DETERMINE THE SAFETY AND EFFICACY OF VI-0521 IN THE TREATMENT OF OBESITY IN AN ADULT POPULATION WITH BMI ≥ ***

Compound:	VI-0521
Compound Name (if applicable):	Phentermine plus Topiramate
US IND Number (if applicable):	***
Protocol Number:	OB 302
Phase:	3
Medical Monitor:	***
Sponsor:	VIVUS, Inc. 1172 Castro St. Mountain View, CA 94040 Tel: (650) 934-5200 Fax: (650) 934-5209
Version and Date:	***

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INTERNAL PROTOCOL APPROVAL

Protocol Number: OB-302

Title: A Phase III Randomized, Double-Blind, Placebo-Controlled Multicenter Study to Determine the Safety and Efficacy of VI-0521 in the Treatment of Obesity in an Adult Population with BMI ≥ *

The signature below documents that the reviewer has read and approved the attached protocol.

	Signature	Date
Author **Charlene Wisdom, PhD, MPH** **Clinical Consultant**		
Wesley W. Day, PhD **VP, Clinical Development**		
Jacqueline Dombroski, PhD **Sr. Director, Regulatory Affairs**		
Ted Broman **Sr. Director, Pharmaceutical Development**		

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PRINCIPAL INVESTIGATOR SIGNATURE

Protocol Number: OB-302

Title: A Phase III Randomized, Double Blind, Placebo-Controlled Multicenter Study to Determine the Safety and Efficacy of VI-0521 in the Treatment of Obesity in an Adult Population with BMI ≥ *

The signature below indicates that the principal investigator has read and understands the protocol and agrees to conduct the study in accordance with the protocol, applicable guidelines for Good Clinical Practices, the Declaration of Helsinki and all applicable regulatory guidelines and requirements. Please return one copy of this executed page to VIVUS, Inc.

Printed Name: _____

Signature: _____ Date: _____

Facility Name: _____

Address: _____

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PROTOCOL SYNOPSIS

Rationale:

Obesity leads to the development of co-morbidities such as hypertension, type 2 diabetes, dyslipidemia, coronary artery disease (CAD) and stroke. Weight reduction in obese individuals has been shown to delay or prevent the onset of these co-morbidities, or even reverse the damage caused by these co-morbidities. Diet, exercise and behavior modification therapy can be effective short-term treatments; however, many people experience difficulty in achieving and maintaining weight reduction without pharmacotherapy. VI-0521 is an investigational weight loss therapy that is a new combination of two

currently approved drugs, phentermine and topiramate. This novel combination treatment may provide a safe and effective option for the achievement and maintenance of weight loss in obese adults.

Objectives:

The objectives of this study are to evaluate the safety and efficacy of two doses of VI-0521 for the treatment of obesity in obese adults with body mass index (BMI) $\geq$ ***.

Trial Design:

The study is a randomized, double-blind placebo-controlled trial with subjects randomized to receive daily treatment with VI-0521 *** or *** or ***, with the total duration of treatment being 56 weeks. Randomization will be stratified by *** of subjects will be ***. Approximately 1250 subjects will be treated under the protocol with *** subjects randomized to *** and ***. Up to *** study sites in the USA will be employed.

Subjects will be instructed to follow a mild hypocaloric diet representing a 500-calorie/day deficit and to implement a lifestyle modification program, as tolerated, throughout the study period. During the first 4 weeks of treatment (weeks 1-4), study medication will be titrated to the assigned dose level, with the dosage increased each week as determined by randomization group. During treatment weeks 5-56, the dose will be maintained at the final dose level. Subjects who are unable to tolerate the assigned dosage may be treated at a reduced dose level or may take a drug holiday as defined in the protocol.

All subjects will return at approximately 4-week intervals for measurement and evaluation. Female subjects of child bearing potential will undergo a urine pregnancy test at each visit. Subjects who discontinue the treatment during the study will be encouraged to remain on study for all study-related procedures. Additionally, those who choose to discontinue the study will be encouraged to return at the 56-week time point for measurements and evaluation.

Study Subjects

The study population will consist of adult males and females up to 70 years of age with BMI ^{3}***, fasting blood glucose ***. Female subjects of childbearing potential must agree to use adequate contraception (a double barrier method, stable hormonal contraception plus single barrier method or tubal ligation) for the duration of treatment.

Major exclusion criteria include: type 2 diabetes; known or suspected clinically significant valvular heart disease; clinically significant ECG abnormality; clinically significant hepatic or renal disease; clinically significant thyroid dysfunction, as evidenced by signs, symptoms, or TSH > 1.5 x ULN; obesity of known genetic or endocrine origin; history of bipolar disorder or psychosis, depression of moderate or greater severity, or presence or history of suicidal behavior or active suicidal ideation; recent weight instability; history of glaucoma or increased intraocular pressure; prior bariatric surgery; or smoking cessation within 3 months prior to enrollment.

Efficacy Endpoints:

The primary endpoints are the differences between *** and *** groups in mean percent loss of baseline body weight, determined by weight at randomization (baseline) and weight at end of treatment (week 56), and percent of subjects with weight loss of 5% or more at end of treatment (week 56). Percent weight loss will be calculated as ***.

Secondary efficacy endpoints are:

- The difference in absolute weight loss between randomization (baseline) and end of treatment (week 56) between *** and *** groups;
- The difference in percent of subjects who achieve a reduction in total body weight of at least 10% between randomization (baseline) and end of treatment (week 56) between *** and *** groups; and
- The difference in change in waist circumference (randomization to week 56) between *** and *** groups.

Additional efficacy endpoints include:

- Effect on ***;
- Effect on body composition, as evaluated by ***. *** assessments will be performed at only at a ***.
- Effect on *** for *** and ***;
- The change in obesity-associated risk factors (total cholesterol, triglycerides, LDL-C, HDL-C, fasting glucose, blood pressure);
- Change from baseline to week 28 and week 56 in BMI;

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· Difference between *** and *** groups in the rate of progression to type 2 diabetes; and

· Baseline adjusted change in Framingham 10-year risk score at weeks 28 and 56.

The change in weight loss (percent, absolute, percent of subjects achieving weight loss of ≥ 5% and ≥ 10% of starting weight), waist circumference and obesity associated risk factors will also be assessed over time. Subgroup analyses, including but not limited to analysis by gender, age and race, may be performed.

*****:**

*** will also be evaluated. Data will be obtained using a multiple trough sampling scheme with samples collected at *** and ***. Effects of various cofactors including (but not limited to) ***, gender, race, ***, and age will be evaluated.

Safety Endpoints:

Safety will be assessed by an evaluation of adverse events, including eye symptoms (collected each study visit); ***. All subjects will be screened for the *** using a validated survey instrument ***, and for *** using the ***. Follow-up assessments will be done at *** after ***.

Statistical Methods:

All subjects who are randomized, take one or more doses of test material and have at least one post treatment measurement will be included in the analysis. Comparisons between treatments will be assessed using a *** with factors of *** and *** and with *** for percent weight loss, and by *** for percent of subjects achieving at least 5% weight loss. A step-down multiple comparison procedure will be used to compare each dose group with ***. That is, comparison with *** will start at the ***. If the statistical test is significant at *** for both co-primary endpoints, then the test will proceed to the *** also at the ***. If the statistical comparison is not significant at the ***, then the statistical test will be stopped and the *** will not be tested. If both dose groups are significantly better than ***, then the two active dose groups will be compared. A *** of difference in response rate between treatment groups will be derived. The *** for subjects who discontinue treatment prior to completion of the study, ***.

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LIST OF ABBREVIATIONS

ACE	angiotensin converting enzyme
***	***
***	***
***	***
***	***
***	***
Cl	apparent clearance
cm	centimeters
CRFs	case report forms
***	***
***	***
***	***
DSM-IV	Diagnostic and Statistical Manual IV
ECG	electrocardiogram
FDA	Food and Drug Administration
***	***
GCP	Good Clinical Practices
***	***
HBsAg	hepatitis B surface antigen
HCV	hepatitis C virus
HDL-C	high density lipoprotein cholesterol
HIV	human immunodeficiency virus
ICH	International Conference on Harmonization
IEC	Independent Ethics Committee
IND	Investigational New Drug
IRB	Institutional Review Board
ITT	intent to treat
IVRS	Interactive Voice Response System
***	***
kcal/day	kilocalories per day
kg	kilogram
kg/m^2	kilogram per square meter
***	***
LDL-C	low density lipoprotein cholesterol
µU/mL	microunits per milliliter
mg	milligram
mg/day	milligram per day
mg/dL	milligram per deciliter
mmHg	millimeters of mercury
MedDRA	Medical Dictionary for Regulatory Activities
NYHA	New York Heart Association

***	***
***	***
QOD	every other day
RBC	red blood cell
SAE	serious adverse event
***	***
***	***
TSH	thyroid stimulating hormone
ULN	upper limit of normal
***	***
WBC	white blood cells
WHO	World Health Organization
WNL	within normal limits

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1 INTRODUCTION

VI-0521 is an investigational weight loss therapy that is a combination of two approved drugs, phentermine and topiramate. Phentermine hydrochloride (phentermine), an anorectic agent, has sympathomimetic actions and stimulates the central nervous system.(1),(2) It is postulated that ***, and there is a ***.(3), (4) Topiramate, an anticonvulsant agent that has been shown to induce weight loss, is known to ***.(5) However, the specific mechanism mediating the weight loss is not known. The present study is being conducted to evaluate the combined use of phentermine and topiramate at doses of 3.75 mg phentermine/23 mg topiramate and 15 mg phentermine/92 mg topiramate in the treatment of obesity in adult subjects with body mass index (BMI) greater than or equal to ***.

1.1 Background

Recent studies have shown that about 129 million adults in the United States are clinically overweight or obese.(6) In recent years, there has been a dramatic increase in obesity in both children and adults.(7), (8) Results from the National Health and Nutrition Examination Survey showed an overall 32.2% prevalence of obesity during 2003-2004, with obesity increasing from 27.5% in 1999-2000 to 31.1% in 2003-2004 in men but remaining relatively unchanged in women (1999-2000, 33.4%; 2003-2004, 33.2%).(8)

Obesity is associated with numerous co-morbidities including dyslipidemia, coronary artery disease, hypertension, stroke and type 2 diabetes.(7), (9) Epidemiological data indicate that obesity is associated with increased mortality,(10) and a recent study of over 500,000 individuals concluded that excess body weight during midlife was associated with an increased risk of death.(11) A modest weight loss (5-10%) can result in a marked reduction in obesity-related metabolic and cardiovascular risk factors.(12), (13), (14) Diet, exercise and behavior modification are standard treatments for obesity although most obese individuals do not achieve prolonged weight reduction without supplemental pharmacotherapy. However, the medications currently approved by the Food and Drug Administration (FDA) for weight loss are often poorly tolerated due to side effects and often fail to maintain long-term efficacy.(15)

Phentermine hydrochloride, a synthetic sympathomimetic amine, is an anorectic agent approved by the FDA as a short-term adjunct to a weight loss regimen based on exercise, behavior modification and caloric restriction. The usual adult dosage is *** administered either once daily or in divided doses.(1) The mechanism of action of phentermine for weight loss is similar to that of other anorectic agents; it decreases appetite and stimulates the central nervous system. (1) It is postulated that ***, and there is a ***.(3), (4) Additionally, increased *** levels may result in a decrease in *** that may result in increased satiety and decreased appetite.

Topiramate, a sulfamate-substituted monosaccharide, is an anticonvulsant agent indicated as adjunctive therapy for partial onset seizures, primary generalized tonic-clonic seizures, seizures

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associated with Lennox-Gastaut syndrome and for migraine headache prophylaxis.(5) The recommended total daily dose of topiramate for treatment of seizures in adults is *** administered in two divided doses; ***. Topiramate is known to ***.(5) Recent clinical studies have shown that topiramate can promote weight loss in ***.(16), (17), (18) However, the exact mechanism by which topiramate exerts its anorectic effect is unknown although it is postulated to ***. A detailed summary of the clinical and nonclinical toxicology, pharmacokinetics and metabolism of phentermine and topiramate is provided in the Investigator Brochure.

VI-0521 has been studied in a Phase 2, randomized, double-blind clinical trial of 200 otherwise healthy obese adults under an investigator-initiated investigational new drug application (IND).(19) In this study, subjects were randomized into 1 of 4 treatment groups: ***. Treatment was continued for *** (including ***). Weight loss (percent of total body weight) among subjects treated with VI-0521 ***, compared to *** among *** among ***, and *** among ***. Subjects treated with VI-0521 *** than subjects in the other treatment groups. Significant decreases vs. *** and *** were observed in subjects receiving VI-0521. Of the 200 subjects randomized, *** completed treatment to ***; a *** completion rate was reported for subjects in the *** group. No

deaths or serious adverse events were reported during the study and no significant changes in heart valve morphology were observed. The most commonly reported adverse events in subjects treated with VI-0521 were ***.

1.2 Rationale

VI-0521 is an investigational weight loss therapy that is a combination of two currently approved drugs, phentermine and topiramate. As such, VI-0521 represents a potential advance in the medical treatment of obesity since the two agents comprising this combination product effect weight loss through different mechanisms. Additionally, some of the expected side effects of the two drugs may be mitigated by complementary effects of the other. Thus, combining phentermine with topiramate may produce a similar or better adverse event profile compared to either of these agents individually. Topiramate therapy has been associated with ***. Due to the ***, it is mechanistically possible that ***. Thus, the dual mechanisms and low drug doses employed in VI-0521 may provide a safe and effective pharmacotherapy for the achievement and maintenance of weight loss in obese adults.

2 TRIAL OBJECTIVES

The objectives of this study are to evaluate the safety and efficacy of two doses of VI-0521 for the treatment of obesity in adults with body mass index (BMI) $\geq$ ***.

3 TRIAL DESIGN

In this prospective, randomized, double blind, placebo-controlled trial, subjects meeting the eligibility criteria will be randomly assigned in a ratio of *** among the *** treatment groups described in Figure 1.

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***

Figure 1. Schematic Representation of Study Design.

Approximately 1250 subjects will be randomized *** at up to *** study sites. The randomization schedule will be stratified by *** to ***; at least *** of subjects enrolled into the study will be ***.

Subjects will initiate treatment with a dose titration during weeks 1-4 with doses gradually increased at *** intervals, as determined by randomization assignment, until the specified dose is reached and will be treated for 52 weeks (weeks 5-56) at the assigned dose level. Subjects will return to the site at the end of weeks 2 and 4 (Visits 3 and 4) during titration and at 4-week intervals thereafter. A schedule of events is provided in Appendix 1.

The primary endpoints are differences between *** and *** groups in mean percent loss of baseline body weight, determined by weight at randomization (baseline) and weight at end of treatment (week 56), and percent of subjects with weight loss of 5% or more at end of treatment (week 56). Percent weight loss will be calculated as ***.

Secondary efficacy endpoints are:

- The difference in absolute weight loss between randomization (baseline) and end of treatment (week 56) for *** and *** groups.
- The difference in percent of subjects who achieve a reduction in total body weight of at least 10% between randomization (baseline) and end of treatment (week 56) for *** and *** groups.
- The difference in change in waist circumference (randomization to week 56) for *** and *** groups.

Additional efficacy endpoints will include the effect of treatment on obesity-associated cardiovascular risk factors (total cholesterol, triglycerides, LDL-C, HDL-C, fasting glucose, blood pressure), ***, *** of *** and *** and ***, *** and ***. The difference between *** and *** groups in the rate of progression to type 2 diabetes will be calculated. Baseline adjusted Framingham 10-year risk scores will be calculated and compared between groups at weeks 28 and 56. Change in BMI between baseline and week 28 and end of treatment (Visit 17, week 56) will be evaluated. Additionally, body composition will be assessed by *** at ***. These evaluations will be made at ***, and at *** and ***.

The change in weight loss (percent, absolute, percent of subjects achieving weight loss of $\geq$ 5% and $\geq$ 10% of starting weight), waist circumference and obesity associated risk factors will also be assessed over time. Subgroup analyses, including but not limited to analysis by gender, age and race, may be performed.

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Safety evaluations will include assessment of adverse events, including eye symptoms, ***.

*** will also be obtained, and effects of various cofactors including (but not limited to) ***, gender, race, ***, and age will be evaluated. ***.

4 SUBJECT SELECTION

This clinical trial can fulfill its objectives only if appropriate subjects are enrolled. The following eligibility criteria are designed to select subjects for whom protocol treatment is considered appropriate. All relevant medical and non-medical conditions should be taken into consideration when deciding whether this protocol is suitable for a particular subject.

4.1 Inclusion Criteria

This study is designed to treat obese adult subjects with BMI $\geq$ *** who have *** or whose *** using reasonable measures. To be eligible for enrollment into this trial, subjects must meet all of the following criteria. Specifically, subjects must:

1. Be adults 70 years of age or less;
2. Have a BMI $\geq$ ***;
3. If females of child-bearing potential, be using adequate contraception, defined as double barrier methods, stable hormonal contraception plus single barrier method, or tubal ligation. Females are considered to be of child-bearing potential unless they have undergone a hysterectomy or bilateral oophorectomy, are 55 years of age or greater and have experienced spontaneous cessation of menses for at least 1 year, or have a documented follicle stimulating hormone level $\geq$40 IU/L;
4. Have a ***;
5. Have blood pressure of ***;
6. Have a fasting blood glucose level of ***;
7. Provide written informed consent; and
8. Be willing and able to comply with scheduled study visits, treatment plan, laboratory tests and other study procedures.

4.2 Exclusion Criteria

Subjects presenting with any of the following will not be included in the trial:

1. Known allergy or hypersensitivity to phentermine or topiramate, any prior use of a combination of phentermine and topiramate for weight loss or use of phentermine or topiramate for any indication within the past 3 months;
2. Weight gain or loss of greater than 5 kg, use of a very low-calorie diet, or participation in a formal weight loss program (investigational or otherwise) within the past 3 months (this includes: Weight Watchers and related dietary/lifestyle intervention programs; prepared food programs; prescribed or over-the-counter weight loss medications; dietary supplement or herbal preparations, teas, or tinctures intended for weight loss; or any supervised fast or very low calorie diet);
3. Obesity that is of a known genetic or endocrine origin;
4. History of any eating disorders (e.g. bulimia, binge eating disorder) within the past year;
5. History of drug abuse within the past year;
6. History of alcohol abuse (defined as >14 drinks per week) within the past year;
7. Previous bariatric surgery;
8. Diagnosis of type 2 diabetes by history, or as confirmed by a fasting blood glucose of 126 mg/dL or greater, or history of any antidiabetic medication use;
9. Smoking cessation within the previous 3 months or plans to quit smoking during study participation;
10. History of glaucoma, history of increased intraocular pressure or any past or present use of medications to treat increased intraocular pressure;
11. Clinically significant thyroid dysfunction as evidenced by signs or symptoms of hypothyroidism, a TSH > 1.5 x ULN, or use of thyroid hormone treatment that has not been stable for at least 3 months;
12. Use of chronic systemic glucocorticoid therapy, or any other steroid hormone therapy that has not been stable for at least 3 months;

13. Any history of bipolar disorder or psychosis, greater than one lifetime episode of major depression, current depression of moderate or greater severity (PHQ-9 score of 10 or more), presence or history of suicidal behavior or ideation with some intent to act on it, or antidepressant use that has not been stable for at least 3 months;

14. Stroke, myocardial infarction, life-threatening arrhythmia or coronary re-vascularization within the past 6 months;

15. Unstable angina, congestive heart failure (NYHA Class II, III or IV), or known or suspected clinically significant cardiac valvulopathy;

16. Blood pressure medication that has not been stable for at least 1 month;

17. Any history of malignancy within the past 5 years other than basal or squamous cell carcinoma of the skin that has been completely excised or cervical cancer that has been surgically excised.

18. Cholelithiasis within the past 6 months;

19. Any history of nephrolithiasis;

20. For female subjects of childbearing potential, pregnancy, breastfeeding, or plans for pregnancy during the study period;

21. Use of any investigational medication or device for any indication within the last month;

22. Evidence of any clinically significant renal, pulmonary, hepatic, psychiatric or other condition by history, physical examination or laboratory studies that, in the opinion of the investigator, would contraindicate the administration of study medications, affect compliance, interfere with study evaluations or confound the interpretation of study results.

4.3 Randomization Criteria

The following criteria must be met prior to randomization and dispensing of study medication to subjects:

1. Baseline physical examination, ECG and laboratory findings with no abnormalities that are considered clinically significant by the principal investigator;

2. Laboratory values that are within the ranges specified below:

   ***

4.4 Life Style Guidelines

Subjects randomized into the study will receive counseling on how to reduce their caloric intake by 500 kcal/day, will be advised to increase their daily water intake and will be advised to implement a simple exercise program, as tolerated. Subjects will be advised to initiate a lifestyle change program utilizing the LEARN® Program for Weight Management.(20) The LEARN® program is a 16-week program designed to aid in weight management by providing tools to facilitate lifestyle, attitude, relationship, nutrition and exercise changes. Each subject will be

provided with a LEARN® manual and advised to read and implement the material as appropriate to their individual situation. Site personnel will be encouraged to discuss these materials with subjects at their regularly scheduled visits. However, no data will be collected to document the level of compliance with the program's dietary, lifestyle and/or exercise recommendations.

To facilitate discussions between study subjects and research staff, subjects will complete a 24-hour dietary recall at their randomization visit (Visit 2); however, information provided as part of this exercise will be used only for discussions related to recommended dietary modification and will not be retained as documentation. No data will be collected during the study to document the level of compliance with dietary recommendations.

5 TRIAL TREATMENTS

5.1 Allocation to Treatment

Subjects meeting the randomization requirements specified in Section 4.3 will be randomized to study treatment at Visit 2 using a centralized computer-generated randomization system. Eligible subjects will be randomly assigned to *** or *** at a ratio of ***. Randomization will be stratified by ***, and at

least *** of subjects will be ***. Both the subject and the study site will be blinded as to subject randomization.

To implement subject randomization among treatment groups, each participating site will be pre-stocked with titration kits corresponding to each treatment group. When a subject qualifies for randomization, study site personnel will contact an Interactive Voice Response System (IVRS), either by telephone or through a designated web site, and provide the information required regarding the study subject. The randomization assignment will then be made, and the site will be instructed to dispense a specific kit number to the study subject. Additional kits will be shipped to the site to replace those dispensed according to the randomization schedule. When subjects return for subsequent study visits, the IVRS system will be used to dispense replacement study medication kits, as appropriate.

5.2 Breaking the Blind

Study medication must not be unblinded during the study unless it is considered absolutely necessary by the investigator for the management of an adverse event or other medical emergency. Under such conditions, the identity of the study treatment will be obtained by contacting the IVRS. Any subject who is unblinded during the study will be discontinued from participation in the trial.

VIVUS, Inc. will be notified of any unblinding of subject treatment group ***. The investigators are also required to ensure that any potential serious adverse events are reported according to the requirements outlined in Sections 8.2 and 8.5 and to provide a written report to document the reason for unblinding within ***.

5.3 Drug Supplies

5.3.1 Formulation and Packaging

Medications for this trial will consist of ***. Doses specified for each treatment group will be achieved by varying the *** added to each capsule. Regardless of the dosage assignment, all study treatments will be administered as a ***.

Clinical supplies will be manufactured for VIVUS, Inc. by *** in accordance with current Good Manufacturing Practices. All clinical supplies will be labeled with information required by national and/or international regulations. Study drug will be packaged into 2 types of kits; titration kits for use during the first 4 weeks of study therapy when doses are being increased gradually to the final assigned dose, and treatment kits, for use once subjects have been titrated to their assigned dosage of medication. Each titration kit contains *** for use during weeks 1 through 4 of titration, with each ***. Each *** on the *** will be labeled with the *** and will contain capsules with the dose specified for that week of treatment, as outlined in Table 1.

Table 1: VI-0521 Dosage Strengths by Titration Week for Each Treatment Group

	***	***				
***	***	***	***	***	***	***
***	***	***	***	***	***	***
***	***	***	***	***	***	***
***	***	***	***	***	***	***

Titration kits will consist of *** labeled with the ***. Each *** will be labeled with the ***.

Treatment kits will consist of bottles, *** of study medication at the treatment dosages (week 4) shown in Table 1. Each kit will contain a single bottle, will be labeled with the ***.

5.3.2 Preparation and Dispensing

Clinical supplies provided by the sponsor are to be dispensed only by or under the direct supervision of qualified investigators to subjects meeting the criteria for study entry and in accordance with this protocol. Assignment of specific titration and treatment drug kits to study subjects will require the use of the IVRS system; however, no other preparation of clinical supplies is required of the investigational staff.

5.3.3 Administration

Investigators will instruct subjects to take 1 capsule of study medication every morning. When dispensing titration kits, investigators should ensure that subjects understand that each card contains a 4-week supply of medication, and that the capsules must be taken ***. Investigators will also instruct subjects to return the study medication kit to the site at each site visit. For the

week 2 visit, the site will perform drug accountability and return the *** to the subject for use during titration weeks 3 and 4.

5.3.4 *

*** is an option for subjects who experience ***. *** is implemented through the ***, and will be done without ***. *** is not an option for subjects who experience ***.

When *** is not appropriate or when *** may be required due to events unrelated to subject treatment, subjects may ***. *** are possible with agreement from the medical monitor. All subjects undergoing *** for *** may be *** based on discretion of the PI. If dosing has been ***, a new titration kit should be ordered through *** to ***. Subjects who have a ***. For subjects having a ***. For ***, subjects may ***.

If ***, subjects may be ***. Subjects *** will be encouraged to *** and to continue to make site visits at the regularly scheduled intervals. The last date on which the subject ***. If the subject ***. If the subject elects to withdraw completely from the trial (Section 6.4), the end of treatment (Visit 17) testing should be completed.

5.3.5 Compliance

Subject compliance with study medication will be assessed by ***, and *** should implement any corrective action necessary. Subjects who remain noncompliant with study dosing despite corrective actions by site personnel may be discontinued from the trial.

5.4 Drug Storage and Drug Accountability

All unused study drug must be stored in its packaging at room temperature in a dry, secure area. Access to drug storage areas should be limited to the investigator and designated staff involved with the study. All used and unused drug must be maintained at the study site and made available for audits by VIVUS, Inc. personnel or their designee. It should be noted that one component of the study drug combination is a Schedule IV controlled substance. The investigator should take all appropriate measures to control access to and dispensing of study drug.

The investigator must maintain records documenting the amount, condition and date of delivery of all study drug received from the sponsor. In addition, all drug dispensed to study subjects during the course of the study must be ***. Subjects must be instructed to *** by each subject. No investigational drug or packaging, used or unused, may be discarded. All packaging and used and unused drug must be returned to the sponsor or designated representative upon completion of the study.

5.5 Concomitant Medication(s)

5.5.1 Excluded Medications

Subjects must not take the following medications during their participation in this trial:

- ***;
- ***;
- ***;
- ***;
- ***.

Although the need for any antidiabetic medications at screening would exclude subjects from trial participation, subjects who develop a need for these medications during the course of the trial need not be discontinued for this reason alone. Refer to Section 5.6 for treatment and monitoring recommendations.

5.5.2 Other Restricted Medications

Subjects using *** or allowed *** must be on doses that have been stable for at least 3 months prior to screening. For subjects who develop symptoms consistent with *** during the study, *** replacement may be initiated following appropriate diagnostic work-up (Section 5.8). In the event that subjects require any other changes in these medications, the sponsor should be contacted regarding their continued eligibility.

*** and *** are permitted, provided that the dosage has been stable for at least 1 month prior to screening, and the frequency of use does not exceed twice a week.

All other medications used for the treatment of *** associated with *** must be stable for at least 1 month prior to screening. However, adjustment of these medications during the trial is permitted if the subject's requirements for treatment change.

5.5.3 Documentation of Concomitant Medication Use

All concomitant medications, including both prescription and over-the-counter products, vitamins and nutritional/herbal supplements, must be listed on the appropriate case report form at trial entry. Any change in concomitant medication during the course of the trial must be noted on the appropriate CRF.

5.6 Treatment of Diabetes

Subjects who become diabetic during the course of the study will be provided with ***. They will be instructed to ***. Diabetic subjects will ***.

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Subjects who develop elevated fasting blood glucose values during the study should ***. *** is suggested as the initial therapy for *** type 2 diabetes ***. ***, including ***, should be reserved for subjects who cannot achieve adequate control with other modes of treatment. *** are prohibited, and subjects requiring treatment with these medications must be discontinued from the trial. Subjects whose blood glucose cannot be adequately controlled with the concomitant treatments allowed in this trial should be maintained in the study but discontinued from treatment, and referred back to their primary health care provider for more intensive treatment (see Section 6.4).

During treatment, subjects whose fasting blood glucose is ***.

5.7 Treatment of *

For subjects whose ***. If these medications are already present, ***.

Subjects whose ***, should be discontinued from study treatment and referred back to their primary healthcare provider for more intensive management. Subjects may continue attending study visits ***.

Subjects whose ***.

5.8 Treatment of *

Individuals who experience rapid weight loss sometimes ***. Subjects who develop symptoms of *** need not be discontinued from therapy. These subjects should be assessed clinically and with appropriate laboratory testing ***. Subjects found to be *** may be ***, as appropriate.

6 TRIAL PROCEDURES

This trial is being conducted in conjunction with a companion study (OB-303: A Phase III Randomized, Double-Blind, Placebo Controlled Multicenter Study to Determine the Safety and Efficacy of VI-0521 in the Treatment of Obesity in Adults with Obesity-Related Co-Morbid Conditions) that is of similar design. The distinguishing factors between the two trials are related to the subject populations, specifically, the subjects enrolled into this trial will have a *** associated with obesity than the subjects enrolled into study OB-303. Because there is little overlap between the populations for these two trials, the majority of sites participating in this trial will also be conducting study OB-303. Because results of the screening evaluations may be required to determine which trial a particular subject qualifies for, the initial screening procedures for both of these trials are identical, and will be done under a generic screening informed consent. Once the determination of trial placement has been made a specific informed consent document for that study will be obtained and specific trial evaluations will continue. A schedule of study activities by visit is presented in Appendix 1. A detailed list of these activities is provided in the following sections.

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6.1 Screening (Visit 1)

Activities at screening (Visit 1) are:

- Obtain written informed consent for screening evaluations;
- Obtain demographics (including age, gender, race, ethnicity, education, history of smoking) and medical history (including history of hypertension, vascular disease and dyslipidemia) and family history of hypertension, smoking and premature cardiovascular disease
- Assess weight (kg), height (cm), waist circumference (cm) and BMI (note: the BMI calculation must be obtained from the IVRS following informed consent and should be obtained prior to initiating the testing described below);
- Assess vital signs;
- Record baseline concomitant medications;
- Administer *** and ***;

- Administer ***;
- Assess Inclusion/Exclusion criteria;
- Obtain blood and urine samples for laboratory testing (including TSH);
- Collect urine sample for pregnancy test (females of childbearing potential only) and perform pregnancy test;
- Schedule the randomization visit in 2 weeks (± 7 days).

6.2 Treatment Period

6.2.1 Randomization (Visit 2)

Subjects eligible for treatment will be randomized and study drug dispensed at Visit 2. Activities at randomization are:

- Obtain study-specific written informed consent;
- Collect urine sample for pregnancy test (females of childbearing potential only) and perform pregnancy test;
- Obtain blood sample for laboratory testing (biomarkers);
- Perform complete physical examination, including neurological examination and auscultation for heart sounds (may be performed between Visits 1 and 2 after results from Visit 1 indicate subject may be eligible to participate);

- Obtain written informed consent for *** procedures and perform *** scan ***. *** scans may be performed between Visit 1 and Visit 2, after results from Visit 1 indicate subject may be eligible to participate;
- Perform 12-lead electrocardiogram (may be performed between Visits 1 and 2 after results from Visit 1 indicate subject may be eligible to participate);
- Assess adverse events (including eye symptoms), if any;
- Obtain vital signs;
- Obtain weight and waist circumference measurements;
- Assess changes in concomitant medications;
- Administer *** for *** and ***;
- Evaluate randomization criteria (Section 4.3);
- If subject is eligible, contact IVRS and obtain subject study medication identification;
- Obtain 5 mL serum sample to be retained for possible use for scientific exploratory testing;
- Complete 24 hour dietary recall, distribute LEARN® materials and perform lifestyle counseling;
- Dispense study medication *** from the assigned titration kit and provide instructions for proper use;
- Schedule the next study visit in 2 weeks (± 2 days).

6.2.2 Titration (Visit 3)

Subjects will visit the study site at the end of the second week of titration (Visit 3). Activities at Visit 3 are:

- Obtain weight and waist circumference measurements;
- Obtain vital signs;
- Assess adverse events (including eye symptoms), if any;
- Assess concomitant medications;
- Administer *** and ***;

- Collect urine sample for pregnancy test (females of childbearing potential only) and perform pregnancy test;

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- Review the study medication used during weeks 1 and 2; assess treatment compliance and perform drug accountability. Return the titration card to the subject for use during weeks 3 and 4;
- Perform brief review of lifestyle counseling and answer questions, if any;
- Schedule the next study visit in 2 weeks (± 2 days).

6.2.3 Treatment (Visits 4 through 16)

Subject titration will be completed on Visit 4; subsequently, subjects will return to the site at 4-week intervals for evaluation and to obtain additional study medication. Activities will be as follows:

- Obtain weight and waist circumference measurements;
- Obtain vital signs;
- Assess adverse events (including eye symptoms), if any;
- Assess concomitant medications;
- Administer *** and ***;
- Collect urine sample for pregnancy test (females of childbearing potential only) and perform pregnancy test;
- Collect study medication from previous visit; assess for treatment compliance and perform drug accountability;
- Perform brief review of lifestyle counseling and answer questions, if any;
- Obtain blood samples for blood chemistry testing *(Visits 4, 5, 7 and 10 only);*
- Administer *** for *** and *** *(Visits 4, 7 and 10 only);*
- Ensure that the previous dose of trial medications was taken between 20 and 28 hours ago, and obtain a *** blood sample for *** evaluations (if the previous dose of trial medications is outside this window, *** should be postponed for 1 day) *(Visits 7 and 10 only)*;
- Obtain blood samples for hematology testing *(Visit 10 only);*
- Administer *** *(Visit 10 only);*
- Perform *** scan *** (*Visit 10 only)*;
- Dispense study medication for the upcoming study interval and provide the proper instructions for use;
- Schedule the next study visit in 4 weeks (± 1 week).

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6.2.4 End of Treatment (Visit 17 or withdrawal from study)

The end of treatment for subjects completing the study is Visit 17 (week 56). End of treatment testing will also be performed for subjects who are withdrawn from the study prior to completion of the study at the time of their treatment termination. For subjects who withdraw from the study prior to completion, the site will also attempt to contact the subject at or about the 56 week time point to obtain end of study assessments (except ***).

Activities at the end of treatment visit include:

- Obtain weight and waist circumference measurements;

- Obtain vital signs;
- Assess adverse events (including eye symptoms), if any;
- Assess concomitant medications;
- Administer ***;
- Administer ***;
- Administer *** for *** and ***;
- Administer ***;
- Complete End of Treatment Questions: ***;
- Perform *** scan ***;
- Collect urine sample for pregnancy test (females of childbearing potential only) and perform pregnancy test;
- Obtain blood and urine samples for laboratory testing;
- Perform complete physical examination, including neurological examination and auscultation for heart sounds;
- Perform 12-lead electrocardiogram;
- Collect study medications dispensed at previous visit, assess treatment compliance and perform drug accountability.

6.3 Study Period

The study period for each subject will begin when written informed consent is provided and will continue until Visit 17 (week 56 or early termination) is completed. Sites should link the scheduling of visits to the randomization visit (Visit 2). Visit windows are provided to allow subject and site scheduling convenience. However, every effort should be made to ensure that visits occur within these windows so that the overall treatment duration is 56 weeks, including

titration period, for subjects who complete all visits. In certain instances, adverse event information may be required for events occurring after the study period (Section 8.4).

6.4 Subject Withdrawal

Subjects may withdraw from the trial at any time and for any reason. Additionally, the subject may be withdrawn because of:

- Adverse event;
- Subject lost to follow-up;
- Requirement for other medical treatment excluded by the protocol;
- Lack of compliance with the provisions of the protocol;
- Treatment unblinded by investigator;
- Pregnancy;
- Lack of efficacy;
- Termination of trial.

Withdrawn subjects will not be replaced.

Subjects discontinued from treatment should be encouraged to remain in the trial off-treatment and to continue site visits at the scheduled intervals (Section 5.3.4). Subjects who withdraw completely from the trial at any point should complete the end of treatment (Visit 17, week 56) testing. The date of last dose should be recorded.

Every effort should be made to document subject outcome. For subjects who elect to withdraw from the trial without continuing site visits, the investigator should ***.

At about the 56 week time point, withdrawn subjects who have not continued site visits should be asked to return to the site to obtain weight and waist circumference measurements at a minimum and, if possible, the following additional information: adverse events, vital signs, laboratory tests (chemistry, hematology, urinalysis), concomitant medications, questionnaires ***.

If a subject withdraws from the trial and also withdraws consent for disclosure of future information, ***. ***.

Investigators must discontinue trial participation for all subjects if the sponsor terminates the trial, and evaluations that would normally be performed upon trial completion should be made at that time. For subjects who have received ***, this includes obtaining information requested for the Visit 17 (week 56) end of treatment visit.

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7 ASSESSMENTS

7.1 Weight, Waist Circumference, Height and BMI Assessment

Subjects will be weighed (kg) and a waist circumference (cm) measurement obtained at each study visit (Visits 1-17). Height (cm) and BMI will be determined at the screening visit (Visit 1) only.

7.1.1 Weight Assessment

Subjects should be weighed in kilograms using a calibrated digital scale. The same scale should be used for each measurement and measurements should be evaluated by the same site personnel at each visit, whenever possible. Subject weights should be obtained, whenever possible, under the same conditions (no shoes, clothing of similar weight) that were employed at the first (screening) weighing. Subjects should be encouraged to complete their weigh-in visits in the morning and should be fasting prior to weigh-in.

7.1.2 Waist Circumference Measurement

Waist circumference measurements (cm) will be performed using a measuring tape provided by VIVUS, Inc., and should be obtained by the same individual at each visit, when possible. To measure the waist circumference, locate the top of the right iliac crest. Place the measuring tape in a horizontal plane (parallel to the floor) around the abdomen at the level of the top of the iliac crest as shown in Figure 2.

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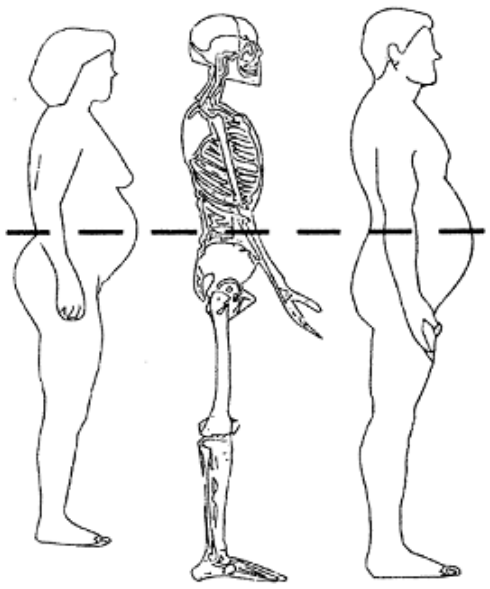

Figure 2. Measuring Tape Position for Waist Circumference Assessments

Ensure that the subject is relaxed. Ensure that the tape is snug but does not indent or compress the skin, and make the measurement at the end of a normal expiration.(21)

7.1.3 Height and BMI

Height measurements (cm) and BMI (kg/m^2) will be determined by the site at screening only. Height measurements should be made without shoes.

BMI will be calculated for purposes of screening using the IVRS. A printed copy of the BMI obtained from the IVRS should be retained as part of the subject's source documentation. Manual BMI calculations should not be performed. If a subject does not meet the BMI criterion for inclusion into the study, no further screening procedures should be undertaken.

7.2 Vital Signs

Vital signs (systolic blood pressure, diastolic blood pressure, heart rate, respiration rate, temperature) will be assessed at each study visit. Subjects should be seated comfortably for at least *** prior to assessing vital signs. Pulse rate and respiratory rate measurements should be made by counting events (heartbeats or breaths) for a period of 30 seconds and multiplying these values by 2 to obtain the rates per minute. A calibrated cuff should be employed for blood pressure measurements. Whenever possible, the same person should perform all assessments for a given subject.

7.3 Questionnaires

7.3.1 *

The *** for the assessment of ***.(22)-(24)

Because this instrument is intended to be completed ***, it is important that *** on this questionnaire in any way. Should subjects ***. Because this questionnaire assesses the ***. Site personnel, therefore, must carefully review questionnaires for completeness before ***, and assure that questionnaires are properly completed.

The *** is being used ***. This questionnaire will be completed at ***, and at *** after the ***. Answers to the questionnaire may reveal evidence of ***, including the ***. It is the responsibility of the investigator to evaluate ***. The evaluation by the Investigator will be guided by the ***. Investigators should document any such problems ***. It is expected that any randomized ***.

7.3.2 *

The ***(25) is an ***. Each of the ***, and is answered on a yes/no basis. This assessment will be administered to all *** at *** in order to confirm the *** included in the treatment program. Subsequent *** evaluations will be done at *** after ***. All *** assessments must be administered by a trained interviewer. If any assessments reveal ***, then the results must be reviewed by a physician investigator prior to ***.

7.3.3 *

The *** that will be completed at *** and ***.

This questionnaire is designed to evaluate the ***.(26), (27) This instrument is intended to be completed ***.

Site personnel must ***. It is critical, therefore, that site personnel review questionnaires for completeness at the time they are initially filled out, and that any missing answers are completed before the ***.

7.4 * and End of Treatment Questions**

7.4.1 *

*** for *** and *** will be assessed at *** and at the ***. For the *** assessment, subjects will *** For the *** assessment, a ***

7.4.2 End of Treatment Questions

At the end of treatment, subjects will be asked to respond to *** questions assessing ***. These questions are:

- ***.
- ***.

. ***

7.5 Laboratory Tests

Laboratory tests will be performed at a licensed, certified central testing laboratory identified by the sponsor. Urine pregnancy tests will be performed at the site using kits supplied by VIVUS, Inc. Testing will be conducted according to the schedule provided below. For blood chemistry tests, the subject must have fasted for a minimum of 8 hours before the sample can be drawn.

Testing for phentermine and topiramate will be conducted in a sponsor-approved central laboratory using validated laboratory assays.

7.5.1 Blood Chemistry

Fasting blood chemistries will be evaluated at screening (Visit 1), Visit 4 (week 4), Visit 5 (week 8), Visit 7 (week 16), Visit 10 (week 28) and end of treatment (Visit 17 or study withdrawal). Tests will be made for the following: albumin, alkaline phosphatase, alanine transaminase (ALT), aspartate amino transferase (AST), blood urea nitrogen (BUN), serum calcium, serum chloride, serum sodium, bicarbonate, creatinine, creatinine clearance, direct bilirubin, gamma-glutamyl transferase (GGT), glucose, lactate dehydrogenase (LDH), serum phosphorus, serum potassium, total bilirubin, total cholesterol, total protein, uric acid, triglycerides, HDL cholesterol (HDL-C) and LDL cholesterol (LDL-C).

7.5.2 Hematology

Hematology studies will be evaluated at screening (Visit 1), Visit 10 (week 28) and end of treatment (Visit 17 or study withdrawal) for hemoglobin, hematocrit, red blood cell count (RBC), total white blood cell count (WBC), WBC differential (neutrophils, lymphocytes, monocytes, eosinophils, basophils) and platelet count.

7.5.3 Urinalysis

A routine midstream urinalysis with reflex microscopic evaluation will be obtained at screening (Visit 1) and end of treatment (Visit 17 or study withdrawal).

7.5.4 Biomarkers

Blood biomarkers including C-reactive protein, adiponectin, and fibrinogen will be evaluated at baseline (Visit 2) and end of treatment (Visit 17 or study withdrawal). All post-screening biomarker results will be blinded to investigators and sponsor.

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7.5.5 Urine Pregnancy Test

A urine pregnancy test will be obtained for females of childbearing potential at each study visit (Visits 1-17). Urine pregnancy testing will be performed at the site and results reported on the appropriate CRF.

Female subjects who have undergone a hysterectomy or bilateral oophorectomy, who have a follicle stimulating hormone level > 40 IU/L or who are 55 years of age or greater and have experienced cessation of menses for at least 1 year are considered to not be of childbearing potential. Urine pregnancy testing is not required in these subjects.

Management of any subject who becomes pregnant during this study is described in Section 8.5.3.

7.5.6 Thyroid Stimulating Hormone (TSH)

A test for thyroid stimulating hormone (TSH) will be conducted at screening (Visit 1).

7.5.7 Antibody to HIV, HCV, HBsAg

Testing for hepatitis B surface antigen (HBsAg) and antibodies to human immunodeficiency virus (HIV) and hepatitis C virus (HCV) will be conducted at screening.

7.5.8 Urine Drug Screen

A urine drug screen will be conducted at screening. Subjects will be tested for cannabinoids, cocaine, amphetamines, opiates and phencyclidine.

7.5.9 Screening Serum Sample (Retain)

A 5.0 mL serum sample will be obtained at Visit 2 to be retained at the central laboratory for possible use in scientific experimental studies.

7.6 *** Evaluation

Samples for the evaluation of *** will be obtained at ***.

Subjects should be advised at the previous visit to refrain from dosing with study medication until after the clinic visit on *** and should be reminded about 1 week prior to the visit to delay dosing on the days of *** until after testing at the site. If the subject has taken study medication < 20 hours prior to the clinic visit, *** should be postponed until the next day.

7.7 Physical Examination

A complete physical examination will be performed prior to randomization (between Visits 1 and 2 or at visit 2) and at Visit 17 (week 56) or early withdrawal. The screening physical

examination should not be completed until results of testing at Visit 1 indicate that the subject may be eligible for entry into the trial.

The physical examination will consist of the following: general appearance, skin, head, eyes, ears, nose, throat, neck (including thyroid), lymph nodes, chest, heart (including auscultation for heart sounds and murmurs), abdomen, extremities, and neurological examination. Subjects will be evaluated for clinically significant abnormalities that would prevent entry into the study and for clinically significant differences between screening and end of treatment.

7.8 Electrocardiogram (ECG)

Twelve-lead electrocardiographic studies will be obtained prior to randomization (between Visits 1 and 2 or at Visit 2) and the end of treatment (Visit 17 or early withdrawal). Screening ECG studies should not be performed until results of testing at Visit 1 have been reviewed to confirm that the subject may be eligible for treatment. Whenever possible, ECGs should be obtained in the morning with the timing of the studies matched as closely as possible.

Studies will be evaluated for clinically significant abnormalities that would prevent entry into the study and for clinically relevant changes between screening and end of treatment. Parameters including R-R, QRS, QT, and QTc intervals will also be recorded.

7.9 Framingham Risk Score

The Framingham risk assessment evaluates the 10-year risk for development of coronary heart disease.(28) In order to calculate the Framingham risk, the following information will be recorded at screening: demographics (age, gender, race, and ethnicity), medical history (including histories of smoking, diabetes, congestive heart failure, myocardial infarction, hypertension, and dyslipidemia) and family history of premature cardiovascular disease. The Framingham risk assessment will be calculated by VIVUS, Inc. or its designee based on data provided on the CRF.

7.10 Body Composition

At a selected subset of study sites, body composition assessments will be made at baseline (Visit 2), week 28 (Visit 10) and week 56 (Visit 17) using ***. Scans will be collected at a sufficient number of study sites to provide body composition data on approximately *** subjects from this study combined with protocol OB-303. Equipment and procedures used to obtain *** data will be standardized as described in a separate document. All sites will be trained on these procedures prior to performing scans on study subjects. Scans will be read at a central facility and the reader will be blinded.

8 ADVERSE EVENTS

8.1 Adverse Events

Adverse events (AEs) are defined as any untoward medical occurrences in subjects administered the trial treatment, whether or not they have a causal relationship to the treatment. All observed or volunteered adverse events regardless of suspected causal relationship to the investigational product must be reported as described in the following sections.

The investigator must pursue and obtain information adequate to describe adverse events, their severity and relationship to study treatment, and their outcomes. Descriptions of neurological or psychological adverse events should be consistent with standard diagnostic criteria and terminology (such as DSM-IV) rather than general reports of symptoms. For adverse events with a causal relationship to the investigational product, follow-up by the investigator is required until the events or their sequelae resolve or stabilize at a level acceptable to the investigator, and VIVUS, Inc. concurs with that assessment. Investigators must also assess whether adverse events meet the criteria for classification as serious adverse events (see Section 8.2) requiring immediate notification to VIVUS, Inc. or its designated representative.

8.1.1 Severity Assessment

The investigator will assess the severity of all adverse events using the ***, ***, or *** to describe the maximum intensity of each adverse event. For purposes of consistency, these intensity grades are defined as follows:

- ***;
- ***;
- ***.

Note the distinction between the severity and the seriousness of an adverse event. A *** is not necessarily a ***. For example, a headache may be *** but would not be classified as serious unless it met one of the criteria for ***.

8.1.2 Causality Assessment

Trial investigators are required to provide an assessment of causality for all adverse events (serious and non-serious) observed during this trial. This assessment will provide a determination of whether, in the investigator's judgment, there exists a reasonable possibility that the investigational product caused or contributed to an adverse event. For this assessment, investigators must categorize the causality as either "related" or "not related." For an adverse event to be considered "related" to the trial treatment, there should be evidence that the event follows a reasonable temporal sequence from the administration of trial treatment or that the event follows a known response pattern to the drug. Causality would be further confirmed by

improvement in the adverse event upon stopping the trial treatment and reappearance of the event upon rechallenge.

8.1.3 Abnormal Test Findings

The criteria for determining whether an abnormal objective test finding should be reported as an adverse event are as follows:

- Test result is associated with accompanying symptoms, and/or
- Test result requires additional diagnostic testing or medical/surgical intervention, and/or
- Test result leads to a change in trial dosing or discontinuation from the trial, significant additional concomitant drug treatment, or other therapy, and/or
- Test result is considered by the investigator or sponsor to represent a clinically significant finding.

Merely repeating an abnormal test, in the absence of any of the above conditions, does not constitute an adverse event. Any abnormal test result that is determined to be an error does not require reporting as an adverse event.

8.2 Serious Adverse Events

As defined in the Code of Federal Regulations (21 CFR 312.32), a serious adverse event (SAE) or serious adverse drug reaction is any untoward medical occurrence at any dose that:

- Results in death;
- Is life-threatening (immediate risk of death);
- Requires inpatient hospitalization or prolongation of existing hospitalization;
- Results in persistent or significant disability/incapacity;
- Results in congenital anomaly/birth defect.

Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious adverse drug experiences when, based on appropriate medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed above. Adverse events that, in the investigator's judgment, significantly jeopardize trial subjects or require medical or surgical intervention in order to prevent any of the outcomes listed above should therefore be reported as serious adverse events.

8.2.1 Definition of Hospitalization

Adverse events reported from clinical trials that result in hospitalization or prolong an existing hospitalization are considered serious. Any initial admission (even if less than 24 hours) to a healthcare facility meets these criteria.

Outpatient ambulatory surgical procedures (same day surgeries) and routine emergency room treatment do not qualify as hospitalizations. Additionally, hospitalization in the absence of a precipitating, clinical adverse event is not in itself a serious adverse event. Examples include, but are not limited to:

- Admission for treatment of a preexisting condition not associated with the development of a new adverse event or with a worsening of the preexisting condition (e.g., for work-up of persistent pre-treatment lab abnormality);
- Administrative admission (e.g., for yearly physical exam);
- Optional admission not associated with a precipitating clinical adverse event (e.g., for elective cosmetic surgery);
- Pre-planned treatments or surgical procedures should be noted in the baseline documentation for the entire protocol and/or for the individual subject.

Diagnostic and therapeutic non-invasive and invasive procedures, such as surgery, should not be reported as adverse events. However, the medical condition for which the procedure was performed should be reported if it meets the definition of an adverse event. For example, an acute appendicitis that begins during the adverse event reporting period should be reported as the adverse event, and the resulting appendectomy should be recorded as treatment of the adverse event.

8.3 Eliciting Adverse Event Information

The investigator is to report all directly observed adverse events and all adverse events spontaneously reported by the trial subject. In addition, trial subjects should be ***

Certain adverse events require prompt and specific action by the investigator in any clinical trial. The following sections describe additional requirements to ensure ***.

8.3.1 Eye Pain

At each visit, subjects will be queried regarding eye symptoms, *** Subject responses will be recorded as adverse events, where appropriate. If any subject reports eye pain and/or ***, the subject should be referred to *** or ***. Treatment with study drug should be discontinued until the ***.

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8.3.2 ***

All subjects will be screened for the presence and *** at *** and subsequently at *** after the *** using a validated survey instrument *** designed for assessment of *** in a primary care setting. The *** is a *** module based directly on the diagnostic criteria for ***. *** will also be assessed at ***and at *** following the *** using the ***.

Should this additional assessment indicate the presence ***. Any such event must be ***. Subjects must be ***.

Any *** must be ***.

8.4 Reporting Period

The reporting period for adverse events begins when the subject provides written informed consent and extends until *** after the last dose of the investigational product is administered. All adverse events that occur during this period and are known to the investigator must be reported according to the requirements outlined in Section 8.5.

8.5 Reporting Requirements

All adverse events will be reported on the adverse event page(s) of the CRF. In addition, serious adverse events must also be reported on a separate serious adverse event form. Where the same data are collected on both AE and SAE forms, the forms must be completed in a consistent manner. For example, the same adverse event term should be used on both forms. Adverse events should be reported using concise medical terminology on the CRFs as well as on the form for collection of serious adverse event information.

8.5.1 Serious Adverse Event Reporting Requirements

If a serious adverse event occurs, VIVUS, Inc., or designee, is to be notified within 1 business day of awareness of the event by the investigator. In particular, if the serious adverse event is fatal or life-threatening, notification to VIVUS, Inc., or designee, must be made immediately, irrespective of the extent of available adverse event information. This timeframe also applies to additional new information (follow-up) on previously forwarded serious adverse event reports.

***

For all serious adverse events, the investigator is obligated to pursue and provide information to VIVUS, Inc. in accordance with the timeframes for reporting specified above. In addition, an investigator may be requested by VIVUS, Inc. or designee to obtain specific additional follow-up information in an expedited fashion. This information may be more detailed than that captured on the AE or SAE CRFs. In general, this will include a description of the adverse event in sufficient detail to allow for a complete medical assessment of the case and independent determination of possible causality. Information on other possible causes of the event, such as

concomitant medications and illnesses, must be provided. In the case of a subject death, a summary of available autopsy findings must be submitted as soon as possible to VIVUS, Inc. or its designated representative.

8.5.2 Non-Serious Adverse Event Reporting Requirements

Non-serious adverse events are to be reported on the adverse event CRFs, which are to be submitted to VIVUS, Inc. or its designee.

8.5.3 ***

If any trial subject becomes or is found to be *** while receiving the investigational product, the investigator must submit this information to VIVUS, Inc. on an ***.

The investigator will follow the *** and then notify VIVUS, Inc. or its designee of the outcome. The investigator will provide this information as a follow up to the ***.

For reported ***. The status of an ***.

If *** meet the criteria for immediate classification as a serious adverse event ***, the investigator should follow the procedures for reporting serious adverse events. Similarly, any *** that are considered to be adverse events should be reported as such on the appropriate CRF. However, *** need not be reported as an adverse event if there is no associated adverse outcome.

For reporting purposes, *** should be reported as serious adverse events, but because the ***.

9 DATA ANALYSIS/STATISTICAL METHODS

9.1 Sample Size Determination

In a previous *** study evaluating the effects of VI-0521, subjects treated with a *** had a mean (SD) weight loss of *** for subjects receiving *** treated subjects. If similar standard deviations are achieved in the present trial, the planned sample size of at least 250 subjects per treatment group should provide *** power to detect these differences.

9.2 Efficacy Analysis

9.2.1 Analysis of Primary Endpoint

The primary hypotheses are:

***

The primary calculated endpoints for the trial are the percent weight loss at week 56 calculated as *** and the percentage of subjects achieving at least 5% weight loss at week 56.

The intent to treat (ITT) population (Section 9.4) is the primary analysis population. For subjects who discontinue treatment prior to trial completion, every attempt will be made to have them return to the clinic at week 56 for a final weight assessment, regardless of when they discontinued treatment. For subjects who ***.

Comparisons between treatments of percent weight loss will be assessed using a *** with factors of *** and ***and with ***. Comparisons between treatments of the percentage of subjects with at least 5% weight loss will be assessed by ***, with *** and *** and ***. A step-down multiple comparison procedure will be used to compare each dose group with ***. That is, comparison with *** will start at the ***. If the statistical test is significant for each of

the co-primary end points at ***, then the testing will proceed to the *** also at ***. If the statistical comparison is not significant at the *** for the *** when compared with ***, then the statistical test will be stopped and the *** will not be tested.

If both dose groups are significantly better than ***, then the *** and *** dose groups will be compared. The *** for the difference in the mean percent body weight reduction between treatment groups will be derived.

The cumulative probability distribution as a function of percentage change in body weight for each treatment group will be plotted.

9.2.2 Analysis of Secondary Endpoints

Secondary efficacy endpoints are:

- The difference in absolute weight loss between randomization and end of treatment (week 56) for *** and *** groups.
- The difference in percent of subjects who achieve a reduction in total body weight of at least 10% between randomization (baseline) and end of treatment (week 56) for *** and *** groups.
- The difference in change in waist circumference (randomization to week 56) for *** and *** groups.

The ITT population will be employed to evaluate all secondary efficacy endpoints, and a step down strategy analogous to that used for the primary endpoint will be implemented to protect the overall alpha levels for these analyses.

The difference in absolute weight reduction and the difference in change in waist circumference at week 56 from baseline will also be compared using the same *** as the primary end point. ***, with ***and *** and ***, will be used to compare the probability of reaching 10% body weight reduction from randomization (baseline) to week 56 between treatment groups.

9.3 Analysis of Other Endpoints

9.3.1 Other Efficacy Endpoints

The changes in primary and secondary outcomes over monthly intervals during the study will be evaluated. The methodology for these comparisons will be similar to that used for primary and secondary endpoints. Details of these analyses will be provided in the Statistical Analysis Plan.

The *** data will consist of ***, each of which will be analyzed separately. Changes from baseline will be summarized using *** and ***. Effect sizes (change divided by baseline standard deviation) will also be summarized. Changes from baseline will be compared between treatment groups using *** as appropriate for *** assessments of ***. Results of the *** questions will be calculated for each study group and compared.

Changes in BMI between baseline and Visits 10 and 17 (weeks 28 and 56) and change in Framingham 10-year risk assessments between baseline and Visits 10 and 17 (weeks 28 and 56) will be evaluated. For these analyses, BMI and Framingham risk scores will be calculated by the central analysis group.

The change from baseline to Visit 17 (week 56) in the number and dosage of medications used to treat cardiovascular or metabolic risk factors will be calculated.

In the *** of subjects treated at ***, changes from *** to *** and *** in percent lean body mass and percent *** will be evaluated. Differences between treatment groups will be evaluated using methods similar to those used to evaluate other continuous variables. For these evaluations, data will be pooled from protocols OB-302 and OB-303.

9.3.2 * Analysis**

*** will be obtained during this trial using a multiple trough sampling scheme, where samples are obtained from each subject at ***. These data will be combined for analyses with data from other Phase 3 trials that will utilize similar sampling schemes. *** analyses will characterize the *** for both drugs. The effects of various covariates including (but not limited to) ***, gender, race, *** and age will be evaluated.

9.4 Analysis Populations

Intent-to-treat (ITT) and safety populations: All subjects who are randomized, take one or more doses of study medication and have at least one post dosing assessment will be included in the ITT (efficacy assessment) and safety (safety assessment) populations.

9.5 *

For those subjects who ***. If a subject ***.

9.6 *

***

9.7 Safety Analysis

Safety analyses will be performed on the safety population and will include all data on all doses reported during the study.

9.7.1 Adverse Events

Adverse events will be coded using a MedDRA coding dictionary. The number and percentage of subjects who reported at least one adverse event in each system organ class and preferred term category, and the total number and percentage of subjects with any AE over all system organ classes will be summarized by treatment group.

Subsets of AEs that are considered serious or required discontinuation of the study medication will be listed by subject and presented separately.

9.7.2 Clinical Laboratory Tests

A summary of observed values and change from baseline will be presented for all laboratory parameters with numerical measures. For selected laboratory parameters, scatter plots of baseline versus week 56 results, will be produced by treatment group.

A laboratory value that is above or below normal range will be considered an abnormal value. For selected laboratory parameters, threshold limits of clinical concern will be defined as multiplicative factors of the normal ranges. The list of multiplicative factors for each laboratory parameter will be included in the Statistical Analysis Plan. The frequency and percentage of subjects with laboratory results above or below the normal range and threshold limits at each scheduled assessment or any time during the treatment will be summarized by treatment group.

9.7.3 Vital Signs and Other Safety Evaluations

Mean blood pressures, heart rate, respiration rate and temperature, obtained at each visit, will be summarized and plotted by treatment group. Medications, other than study medication, taken during the study will be considered as concomitant medications. Variables will be summarized by treatment group according to preferred terms using the World Health Organization (WHO) Drug Dictionary.

9.7.4 Questionnaire Assessments

Changes in total *** will be summarized by treatment group *** and ***. Since the proposed indication for the study medication is weight loss, ***. Descriptive summaries of individual questionnaire items will also be presented.

9.8 Interim Analysis

An interim analysis may be conducted once approximately half of the study subjects have completed the intended course of treatment to provide information for the planning of future clinical trials that may be designed or commenced prior to the completion of this trial. No changes will be made to the conduct of the present study, including premature termination or increased sample size, based on the results of this interim analysis and no statistical adjustments for this interim analysis, if conducted.

9.9 *

***

10 Quality control and quality assurance

During trial conduct, VIVUS, Inc. or its agent will conduct periodic monitoring visits to ensure that the protocol and good clinical practices (GCP) are being followed. The monitors may review source documents to confirm that the data recorded on CRFs are accurate. The investigator and institution will allow VIVUS, Inc. monitors or its agents and appropriate regulatory authorities direct access to all appropriate source documents to perform this verification.

The trial site and trial-related documents may be subject to review by the institutional review board (IRB)/independent ethics committee (IEC), and/or to quality assurance audits performed by VIVUS, Inc. or its agents and/or to inspection by appropriate regulatory authorities. Refer to Section 13.

It is important that the investigator(s) and their relevant personnel are available during monitoring visits and possible audits or inspections and that sufficient time is devoted to the process by the investigator and site personnel.

11 DATA HANDLING AND RECORD KEEPING

11.1 Case Report Forms / Electronic Data Record

As used in this protocol, the term case report form (CRF) should be understood to refer to either a paper form or an electronic data record or both, depending on the data collection method used in this trial.

A CRF is required and should be completed for each included subject. The completed original CRFs are the sole property of VIVUS, Inc. and should not be made available in any form to third parties, except for authorized representatives of VIVUS, Inc. or appropriate regulatory authorities, without written permission from VIVUS, Inc.

It is the investigator's responsibility to ensure CRF completion and to review and approve all CRFs. CRFs must be signed by the investigator or by an authorized staff member. These signatures serve to attest that the information contained on the CRFs is complete and accurate. At all times, the investigator has final personal responsibility for the accuracy and authenticity of all clinical and laboratory data entered on the CRFs. Subject source documents are the physician's subject records maintained at the trial site. In most cases, the source documents will be the hospital's or the physician's chart. In cases where the source documents are the hospital or the physician's chart, the information collected on the CRFs must match those charts.

11.2 Record Retention

To enable evaluations and/or audits from regulatory authorities or VIVUS, Inc. the investigator will keep records, including the identity of all participating subjects (sufficient information to link records, e.g., CRFs and hospital records), all original signed informed consent forms, copies of all CRFs, serious adverse event forms, source documents, and detailed records of treatment disposition. The records should be retained by the investigator according to specifications in the ICH guidelines, local regulations, or as specified in the Clinical Study Agreement, whichever is longer. The investigator must obtain written permission from VIVUS, Inc. before disposing of any records, even if retention requirements have been met.

If the investigator relocates, retires, or for any reason withdraws from the trial, VIVUS, Inc. should be prospectively notified. The trial records must be transferred to an acceptable designee, such as another investigator, another institution, or to VIVUS, Inc.

12 ETHICS

12.1 Institutional Review Board (IRB)/Independent Ethics Committee (IEC)

Regulations require that an IRB/IEC oversee all investigational drug studies. This board or committee, the makeup of which must conform to local, regional and national regulations, will approve all aspects of the study, including the protocol, advertising and written informed consent form to be used prior to initiation of the study. It is the responsibility of the investigator to have prospective approval of the trial protocol, protocol amendments, informed consent forms and other relevant documents, e.g., advertisements, if applicable, from the IRB/IEC. All correspondence with the IRB/IEC should be retained in the Investigator File. Copies of IRB/IEC approvals should be forwarded to VIVUS, Inc. or designee. All correspondence with the IRB/IEC should be retained in the Investigator file and copies forwarded to VIVUS, Inc. or designee.

All amendments to the protocol must be reviewed and approved by VIVUS, Inc. and the IRB/IEC prior to implementation. The only circumstance in which an amendment may be initiated prior to IRB/IEC approval is where the change is necessary to eliminate apparent immediate hazards to the subjects. In that event, the investigator must notify the IRB/IEC and VIVUS, Inc. in writing within 5 working days after the implementation.

The investigator is responsible for obtaining annual (at a minimum) IRB/IEC renewal for the duration of the study. The investigator is also responsible for keeping the IRB/IEC advised of the progress of the study, of any changes made to the protocol as deemed appropriate, but at least once a year. Copies of the investigator's report and of the IRB/IEC extension approval must be forwarded to VIVUS, Inc. or designee.

12.2 Ethical Conduct of the Trial

The trial will be performed in accordance with the protocol, International Conference on Harmonization Good Clinical Practice (ICH-GCP) guidelines and applicable local regulatory requirements and laws.

12.3 Subject Information and Consent

The informed consent form and any changes to the informed consent form made during the course of the trial must be agreed to by VIVUS, Inc. or designee and the IRB/IEC prior to its use and must be in compliance with all ICH-GCP, local regulatory requirements and legal requirements.

The investigator must ensure that each trial subject is fully informed about the nature and objectives of the trial and possible risks associated with participation and must ensure that the subject has been informed of his/her rights to privacy. The investigator will obtain written informed consent from each

subject before any trial-specific activity is performed and should document in the source documentation that consent was obtained prior to enrollment in the trial. The original signed copy of the informed consent form must be maintained by the investigator and is subject to inspection by a representative of VIVUS, Inc., their representatives, auditors, the IRB/IEC and/or regulatory agencies. A copy of the signed informed consent form will be given to the subject.

12.4 Disclosure of Data

Data generated by this trial must be available for inspection by the U.S. Food and Drug Administration (FDA), by the sponsor or a designate acting on behalf of the sponsor, by applicable foreign health authorities, and by the IRB or IEC as appropriate. At a subject's request, medical information may be given to their personal physician or other appropriate medical personnel responsible for their welfare.

Subject medical information obtained during the course of this trial is confidential and disclosure to third parties other than those noted above is prohibited.

13 REGULATORY CORRESPONDENCE

The trial site and trial-related documents may be subject to review by the IRB/IEC and/or to quality assurance audits performed by VIVUS, Inc. or its designee and/or to inspection by the FDA and/or applicable foreign health authorities. The investigator will notify VIVUS, Inc. or designee within *** working days following any FDA or other regulatory agency contact with the investigative site regarding this study. The investigator will provide VIVUS, Inc. with copies of all correspondence with the FDA or other regulatory agency which may affect the review of the current study (e.g., Form 483, Inspection Observations) or their qualification as an investigator in studies conducted by VIVUS, Inc. (e.g., warning letters).

14 DEFINITION OF END OF TRIAL

The end of trial is defined as the date when the last subject completes the last trial visit.

Additionally, data and materials that are required by the Sponsor before any trial site's activity can be considered complete include:

- All completed Case Report Forms, appropriately signed by the investigator;
- All laboratory findings, clinical data and special test results collected during the trial period;
- Completed drug accountability and investigational materials return records;
- Statement of outcome for any serious adverse events reported during the study;
- Copy of notification to IRB or IEC indicating study completion.

15 SPONSOR DISCONTINUATION CRITERIA

Premature termination of this clinical trial may occur because of a regulatory authority decision, change in opinion of the IRB/IEC, drug safety problems, or at the discretion of VIVUS, Inc. In addition, VIVUS, Inc. retains the right to discontinue development of VI-0521 at any time.

If a trial is prematurely terminated or discontinued, VIVUS, Inc. will promptly notify the investigator. After notification, the investigator must contact all participating subjects within 15 days. As directed by VIVUS, Inc. or its designee, all trial materials must be collected and all CRFs completed to the greatest extent possible.

16 PUBLICATION OF TRIAL RESULTS

All information and data, including the terms of this protocol, and all data, clinical results, and research conducted hereunder concerning VIVUS, Inc's products and operations including VIVUS, Inc. patent applications, formulas, manufacturing processes, basic scientific data, and formulation information that has been supplied by VIVUS, Inc. and not previously published are considered confidential by VIVUS, Inc. and will remain the sole property of VIVUS, Inc. The investigator understands and agrees that said proprietary and/or confidential information disclosed to or produced by him/her thereunder is highly valuable to VIVUS, Inc. and will be used exclusively by the investigator in accomplishing this study and will not be used for any other purposes without VIVUS. Inc's prior written consent. The investigator agrees that he/she will not use any such proprietary and/or confidential information for any other purpose. The investigator also understands and agrees that such disclosure will not be deemed to grant to the investigator a license for use of said proprietary and/or confidential information, except as expressly provided herein.

It is understood by the investigator that the information developed in the clinical study will be used by VIVUS, Inc. in connection with the development of this product. This information, therefore, may be disclosed and used solely by VIVUS, Inc. as required to such third parties and agencies as VIVUS, Inc, in its sole discretion, warrants. In order to allow for the use of the information derived from the clinical studies, it is understood that there is an obligation to provide to VIVUS, Inc. complete test results and all data developed in this study. The investigator agrees to promptly answer all inquires from VIVUS, Inc. regarding completion, legibility or accuracy of trial data in the case report.

VIVUS, Inc. recognizes the value of disseminating research results and expects that publication of all results from this study will be undertaken by a collaborative group of study investigators who made significant contributions to the study design, the treatment of study subjects, and evaluation of study data. However, after 1) submission of the multicenter results for publication, 2) notification ***.

Investigators shall furnish the *** with a written copy of any proposed publication or other disclosure of study results (including disclosures at research seminars, lectures and professional meetings) *** prior to submission for publication or disclosure so that *** may have a reasonable opportunity to protect its proprietary rights to information, inventions, or products developed under this study and to insure that reported data are factually correct. Upon the ***, the investigator shall not publish or disclose information related to this study. Further, if the *** believes that such publication or disclosure contains confidential information, the investigator agrees to remove such confidential information from the proposed publication or disclosure.

VIVUS, Inc. agrees that before it publishes any results of this study in a refereed journal, it will provide the investigator, for review, a prepublication manuscript *** prior to the submission of the manuscript to the publisher.

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APPENDIX 1: SCHEDULE OF STUDY ACTIVITIES

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APPENDIX 2: ***

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APPENDIX 3: ***

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APPENDIX 4: PROTOCOL AMENDMENTS

Amendment Tracking

Protocol Title: **A Phase III Randomized, Double-Blind, Placebo-Controlled Multicenter Study to Determine the Safety and Efficacy of VI-0521 in the Treatment of Obesity in an Adult Population with BMI ≥ *****

Protocol Number: **OB-302**

Indicate any amendments to this protocol by writing the Amendment Number and the Date of the Amendment in the space below. This page will be used to track the original protocol and its amendments. This is the original protocol if no amendment number is listed below.

Amendment Number 3
Date of Amendment: ***
(19 items)

Rationale: This protocol amendment is being implemented at the request of the FDA to incorporate assessments of *** and *** using the ***, and assessments of *** using the *** in all study subjects at ***. Previously, follow-up *** evaluations were done only if other *** assessments revealed a ***. This amendment also provides for body composition assessments at selected sites using ***. These changes are not anticipated to have any impact on the safety of study subjects.

Section and/or Item	Protocol Date	Amendment 3, *** Change Effected
Protocol Synopsis: Efficacy Endpoints - Additional efficacy endpoints include:	***	Added: "**Effect on body composition, as evaluated by ***. *** assessments will be performed at only at a ***."**
Protocol Synopsis: Safety Endpoints	***	Change: "Follow-up *** assessments will be done at ***, and a single question assessment of *** and *** will be asked at ***." To: "**Follow-up assessments will be done at *** after *****."
List of Abbreviations	***	Added: "*******"
Rationale	***	Change: "VI-0521 is an exploratory weight loss therapy that is a new combination of two currently approved drugs, phentermine and topiramate." To: "VI-0521 is an **investigational** weight loss therapy that is **a combination** of two currently approved drugs, phentermine and topiramate."
Trial Design: Secondary	***	Change: "Change in BMI between baseline and week 28 and end of treatment

efficacy endpoints are:		(Visit 17, week 56) will be evaluated. ." To: "Change in BMI between baseline and week 28 and end of treatment (Visit 17, week 56) will be evaluated. **Additionally, body composition will be assessed by *** at ***. These evaluations will be made at ***, and at *** and ***.**" Change: "Safety evaluations will include assessment of adverse events, including eye symptoms, ***." To: "Safety evaluations will include assessment of adverse events, including eye symptoms, ***."
Trial Period: Randomization (Visit 2)	***	Added: "**Obtain written informed consent for *** procedures and perform *** scan ***. *** scans may be performed between Visits 1 and 2, after results from Visit 1 indicate subject may be eligible to participate;**"

		Change: “Assess adverse events (including eye symptoms and ***), if any;” To: “Assess adverse events (including **eye symptoms**), if any;”
Trial Period: Titration (Visit 3)	***	Added: “**Administer *** and ***;**” Change: “Assess adverse events (including eye symptoms and ***), if any;” To: “Assess adverse events (including **eye symptoms**), if any;”
Trial Period: Treatment (Visits 4 through 16)	***	Added: “**Administer *** and ***;**” Delete: “Administer *** *(Visits 7, 10, and 13 only);”* Change: “Assess adverse events (including eye symptoms and ***), if any;” To: “Assess adverse events (including **eye symptoms**), if any;” Added: **“Perform *** scan *** *(Visit 10 only);”**
End of Treatment (Visit 17 or Withdrawal from Study)	***	Added: “**Administer ***;**” Change: “Assess adverse events (including eye symptoms and ***), if any;” To: “Assess adverse events (including **eye symptoms**), if any;” Added: “**Perform *** scan ***;”**
Subject Withdrawal	***	Change: “At about the 56 week time point, withdrawn subjects who have not continued site visits should be asked to return to the site to obtain weight and waist circumference measurements at a minimum and, if possible, the following additional information: adverse events, vital signs, laboratory tests (chemistry, hematology, urinalysis), concomitant medications, questionnaires ***.” To: “At about the 56 week time point, withdrawn subjects who have not continued site visits should be asked to return to the site to obtain weight and

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		waist circumference measurements at a minimum and, if possible, the following additional information: adverse events, vital signs, laboratory tests (chemistry, hematology, urinalysis), concomitant medications, questionnaires ***.”
***	***	Change: “The *** is being used ***. This questionnaire will be completed at *** and at ***.” To: “The *** is being used ***. This questionnaire will be completed at ***, **and at *** after the ***.**”
***	***	Change: “Subsequent *** evaluations will be done only in *** who demonstrate a ***.” To: “Subsequent *** evaluations will be done **at *** after ***. All *** assessments must be administered by a trained interviewer. If any assessments reveal ***, then the results must be reviewed by a physician investigator prior to ***.”**
Body Composition	***	Added new section: “**At a selected subset of study sites, body composition assessments will be made at baseline (Visit 2), week 28 (Visit 10) and week 56 (Visit 17) using ***. Scans will be collected at a sufficient number of study sites to provide body composition data on approximately *** subjects from this study combined with protocol OB-303. Equipment and procedures used to obtain *** data will be standardized as described in a separate document. All sites will be trained on these procedures prior to performing scans on study subjects. Scans will be read at a central facility and the reader will be blinded to the identity of the subjects, the treatment assignment, and the visit number**.”
***	***	Change: “All subjects will be screened for the presence and *** at *** and subsequently at regular intervals throughout the study: ***, and *** using a validated survey instrument *** designed for assessment of *** in a primary care setting.”

		To: "All subjects will be screened for the presence and *** at *** and subsequently at ***** after the *** using a validated survey instrument *** designed for assessment of *** in a primary care setting**." Change: "The *** is a *** module based directly on the diagnostic criteria for ***. At study visits where *** assessments are not included, subjects will be asked the following question to assess ***." To: "The *** is a *** module based directly on the diagnostic criteria for ***. ***** will also be assessed at *** and at *** following the *** using the ***."** Change: **"**Any ***. Investigators are encouraged to administer the *** on an ad-hoc basis as part of the clinical assessment of ***. These ad-hoc questionnaires will be maintained as source documentation, but will not be analyzed as a separate ***." To: "**Any *** must be ***."**
Other Efficacy Endpoints	***	Added: "**In the *** of subjects treated at ***, changes from *** to *** and *** in percent lean body mass and percent *** will be evaluated.**

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		Differences between treatment groups will be evaluated using methods similar to those used to evaluate other continuous variables. For these evaluations, data will be pooled from protocols OB-302 and OB-303."
Appendix 1: Schedule of Study Activities	***	Added: "*******" and only marked at ***
Appendix 1: Schedule of Study Activities — ***	***	Added at ***
Appendix 1: Schedule of Study Activities — ***	***	Added at ***
Appendix 1: Schedule of Study Activities — ***	***	Change: "***" To: "***"

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Protocol Title: **A Phase III Randomized, Double-Blind, Placebo-Controlled Multicenter Study to Determine the Safety and Efficacy of VI-0521 in the Treatment of Obesity in an Adult Population with BMI ≥ *****

Protocol Number: **OB-302**

Indicate any amendments to this protocol by writing the Amendment Number and the Date of the Amendment in the space below. This page will be used to track the original protocol and its amendments. This is the original protocol if no amendment number is listed below.

Amendment Number 2
Date of Amendment: ***
(10 items)

Rationale: This amendment is being implemented to address inconsistencies in the description of various study exclusions and analyses, and to specify that an ***. Various typographical errors in the previous version of the protocol have also been corrected. None of the changes implemented with this amendment are anticipated to have any impact on safety risks to the study subjects.

Section and/or Item	Protocol Date	Amendment 2, *** Change Effected
Protocol Synopsis: Study Subjects	***	Change: "Major exclusion criteria include: type 2 diabetes; known or suspected valvular heart

		disease;" To: "Major exclusion criteria include: type 2 diabetes; known or suspected **clinically significant** valvular heart disease;"
Protocol Synopsis: Statistical Methods	***	Change: "Comparisons between treatments will be assessed using a *** with factors of *** and ***and with ***. A step-down multiple comparison procedure will be used to compare each dose group with ***. That is, comparison with *** will start at the ***. If the statistical test is significant at ***, then the test will proceed to the *** also at the ***." To: "Comparisons between treatments will be assessed using a *** with factors of *** and *** and with *** **for percent weight loss, and by *** for percent of subjects achieving at least 5% weight loss.** A step-down multiple comparison procedure will be used to compare each dose group with ***. That is, comparison with *** will start at the ***. If the statistical test is significant at *** **for both co-primary endpoints**, then the test will proceed to the *** also at the ***."
Background	***	Change: "Obesity is associated with numerous co-morbidities including dyslipidemia, coronary artery disease, hypertension, stroke and type 2 diabetes.(7), (9) Epidemiological data indicate that obesity is associated with increased mortality,(10) and a recent study of over 500,000 individuals concluded that excess body weight during midlife, including overweight, was associated with an increased risk of death.(11)" To: "Obesity is associated with numerous co-morbidities including dyslipidemia,

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		coronary artery disease, hypertension, stroke and type 2 diabetes.(7), (9) Epidemiological data indicate that obesity is associated with increased mortality,(10) and a recent study of over 500,000 individuals concluded that excess body weight **during midlife was associated with an** increased risk of death.(11) "
Trial Design	***	Change: "In this prospective, randomized, double blind, placebo-controlled prospective trial, subjects meeting the eligibility criteria will be randomly assigned (with equal probability) among the *** treatment groups described in Figure 1." To: "In this prospective, randomized, double blind, placebo-**controlled trial**, subjects meeting the eligibility criteria will be randomly assigned **in a ratio of ***** among the *** treatment groups described in Figure 1."
Exclusion Criteria #15	***	Change: "Unstable angina, congestive heart failure (NYHA Class II, III or IV), or suspected or known cardiac valvulopathy;" To: "Unstable angina, congestive heart failure (NYHA Class II, III or IV), **or known** or suspected **clinically significant** cardiac valvulopathy;"
Titration: (Visit 3)	***	Change: "Review the study medication used during weeks 1 and 2; assess treatment compliance and perform drug accountability. Return the card to the subject for use during weeks 3 and 4;" To: "Review the study medication used during weeks 1 and 2; assess treatment compliance and perform drug accountability. Return the **titration** card to the subject for use during weeks 3 and 4;"
Analysis of Primary Endpoint	***	Change: "The primary calculated endpoints for the trial are based on the percent weight loss at week 56 calculated as *** and the percentage of subjects achieving at least 5% weight loss at week 56. The intent to treat (ITT) population (Section 9.4) is the primary subject population. For subjects who discontinue treatment prior to trial completion, every attempt will be made to have them return to the clinic at week 56 for a final weight assessment, regardless of when they discontinued treatment. For subjects who ***. Comparisons between treatments will be assessed using a *** with factors of *** and *** and with ***. A step-down multiple comparison procedure will be used to compare each dose group with ***. That is, comparison with *** will start at the ***. If the statistical test is significant for the primary end points at ***, then the test will proceed to the *** also at ***."

		To: “The primary calculated endpoints for the trial **are the percent** weight loss at week 56 calculated as *** and the percentage of subjects achieving at least 5% weight loss at week 56. The intent to treat (ITT) population (Section 9.4) is the primary **analysis** population. For subjects who discontinue treatment prior to trial completion, every attempt will be made to have them return to the clinic at week 56 for a final weight assessment, regardless of when they discontinued treatment. For subjects who ***. Comparisons between treatments **of percent weight loss** will be assessed using a *** with factors of *** and *** and with ***. **Comparisons between treatments of the percentage of subjects with at least 5% weight loss will be assessed by ***, with *** and *** and ***.** A step-down multiple comparison procedure will be used to compare each dose group with ***. That is, comparison with *** will start at the ***. If the statistical test is significant for

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		each of the **co**-primary end points at ***, then the test**ing** will proceed to the *** also at ***.”
Analysis of Secondary Endpoint	***	Change: “The difference in absolute weight reduction and the difference in change in waist circumference at week 56 from baseline will also be compared using the same *** as the primary end point. ***, with *** and *** and ***, will be used to compare the probability to reach 5% and 10% body weight reduction between randomization (baseline) and week 56 between treatment groups.” To: “The difference in absolute weight reduction and the difference in change in waist circumference at week 56 from baseline will also be compared using the same *** as the primary end point. ***, with *** and *** and ***, will be used to compare the probability of **reaching 10%** body weight reduction **from** randomization (baseline) **to** week 56 between treatment groups.”
Adverse Events	***	Change: “Adverse events will be coded using a MedDRA coding dictionary. The number and percentage of subjects who reported at least one adverse event in each organ class and preferred term category, and the total number and percentage of subjects with any AE over all organ system will be summarized by treatment group.” To: “Adverse events will be coded using a MedDRA coding dictionary. The number and percentage of subjects who reported at least one adverse event in each **system** organ class and preferred term category, and the total number and percentage of subjects with any AE overall **system organ classes** will be summarized by treatment group.”
***	***	Change: “No *** will be employed for this study.” To: “*******”

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Protocol Title: **A Phase III Randomized, Double-Blind, Placebo-Controlled Multicenter Study to Determine the Safety and Efficacy of VI-0521 in the Treatment of Obesity in an Adult Population with BMI ≥ ***

Protocol Number: **OB-302**

Indicate any amendments to this protocol by writing the Amendment Number and the Date of the Amendment in the space below. This page will be used to track the original protocol and its amendments. This is the original protocol if no amendment number is listed below.

Amendment Number 1
Date of Amendment: ***
(14 items)

This protocol amendment is being implemented to add a co-primary endpoint to the study analysis section and to add additional laboratory tests to the schedule of evaluations. The definition of child-bearing potential has also been clarified, and miscellaneous typographical errors have been corrected. These

changes are being made at the request of the FDA, and are not anticipated to significantly affect the risk to study subjects.

Section and/or Item	Protocol Date	Amendment 1, *** Change Effected
Protocol Synopsis: Efficacy Endpoints	***	Change: "The primary endpoint is the differences between *** and *** groups in mean percent loss of baseline body weight, determined by weight at randomization (baseline) and weight at end of treatment (week 56), and percent of subjects with weight loss of 5% or more at end of treatment (week 56). Percent weight loss will be calculated as ***. Secondary efficacy endpoints are: · The difference in absolute weight loss between randomization (baseline) and end of treatment (week 56) between *** and *** groups; · The difference in percent of subjects who achieve a reduction in total body weight of at least 5% and at least 10% between randomization (baseline) and end of treatment (week 56) between *** and *** groups; and" To: "The primary **endpoints are** the differences between *** and *** groups in mean percent loss of baseline body weight, determined by weight at randomization (baseline) and weight at end of treatment (week 56), and percent of subjects with weight loss of 5% or more at end of treatment (week 56). Percent weight loss will be calculated as ***. Secondary efficacy endpoints are: · The difference in absolute weight loss between randomization (baseline) and end of treatment (week 56) between *** and *** groups;

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		· The difference in percent of subjects who achieve a reduction in total body weight of **at least 10%** between randomization (baseline) and end of treatment (week 56) between *** and *** groups; and"
Trial Design	***	Change: "The primary endpoint is the difference between *** and *** groups in mean percent loss of baseline body weight, determined by weight at randomization (baseline) and weight at end of treatment (week 56), Percent weight loss will be calculated as ***. Secondary efficacy endpoints are: · The difference in absolute weight loss between randomization (baseline) and end of treatment (week 56) between *** and *** groups; · The difference in percent of subjects who achieve a reduction in total body weight of at least 5% and at least 10% between randomization (baseline) and end of treatment (week 56) between *** and *** groups; and" To: **"**The primary **endpoints are** the differences between *** and *** groups in mean percent loss of baseline body weight, determined by weight at randomization (baseline) and weight at end of treatment (week 56), **and percent of subjects with weight loss of 5% or more at end of treatment (week 56).** Percent weight loss will be calculated as ***. Secondary efficacy endpoints are: · The difference in absolute weight loss between randomization (baseline) and end of treatment (week 56) between *** and *** groups; · The difference in percent of subjects who achieve a reduction in total body weight of **at least 10%** between randomization (baseline) and end of treatment (week 56) between *** and *** groups; and"
Inclusion Criteria	***	Change: "Females are considered to be of child-bearing potential unless they have undergone a hysterectomy or bilateral oophorectomy, have a documented follicle stimulating hormone level ≥40 IU/L or are 55 years of age or greater and have experienced cessation of menses for at least 1 year." To: "Females are considered to be of child-bearing potential unless they have undergone a hysterectomy or bilateral oophorectomy, **are 55 years of age or greater and have experienced spontaneous cessation of menses for at least 1 year, or have a documented follicle stimulating hormone level ≥40 IU/L."**

***	***	Change: “When *** is not appropriate or when *** may be required due to events unrelated to subject treatment, subjects may ***. If dosing has been ***, a new titration kit should be ordered through *** to ***.” To: “When *** is not appropriate or when *** may be required due to events unrelated to subject treatment, subjects may ***. ***** are possible with agreement from the medical monitor. All subjects undergoing *** for *** may be *** based on discretion of the PI**. If dosing has been ***, a new titration kit should be ordered through ***to ***.”
Randomization (Visit 2)	***	Add: “Obtain blood sample for laboratory testing (biomarkers);” Change: “Assess adverse events (including eye symptoms), if any; To: “Assess adverse events (including eye symptoms **and *****), if any;”
Titration (Visit 3)	***	Change: “Assess adverse events (including eye symptoms), if any;

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		To: “Assess adverse events (including eye symptoms **and *****), if any;”
Treatment (Visit 4-16)	***	Change: “Assess adverse events (including eye symptoms), if any; To: “Assess adverse events (including eye symptoms **and *****), if any;”
End of Treatment (Visit 17 or withdrawal from study)	***	Change: “Assess adverse events (including eye symptoms), if any; To: “Assess adverse events (including eye symptoms **and *****), if any;”
Biomarkers	***	Added new section: “Blood biomarkers including C-reactive protein, adiponectin, and fibrinogen will be evaluated at basline (Visit 2) and end of treatment (Visit 17 or study withdrawal). All post-screening biomarker results will be blinded to investigators and sponsor.”
Analysis Primary Endpoint	***	Change: “*** The primary calculated endpoints for the trial are based on the percent weight loss at week 56 calculated as ***.” To: “*** The primary calculated endpoints for the trial are based on the percent weight loss at week 56 calculated as *** **and the percentage of subjects achieving at least 5% weight loss at week 56**. “
Analysis of Secondary Endpoint	***	Change: “The difference in percent of subjects who achieve a reduction in total body weight of at least 5% and at least 10% between randomization (baseline) and end of treatment (week 56) for *** and *** groups. “ To: “ The difference in percent of subjects who achieve a reduction in total body **weight of at least 10% between randomization** (baseline) and end of treatment (week 56) for *** and *** groups. “
Interim Analysis	***	Change: “No changes will be made to the conduct of the present study, including premature termination or increased sample size, based on the results of this interim analysis and no statistical adjustments for this interim analysis, if conducted, will be made. To: “No changes will be made to the conduct of the present study, including premature termination or increased sample size, based on the results of this interim analysis and no statistical adjustments **for this interim analysis, if conducted**.”
Appendix 1	***	Added: “***”
Appendix 1	***	Change: “***” To: “***”

Task Order #02
Appendix 2 – Scope of Work
VIVUS, Inc.
Qnexa OB-302

PROJECT OVERVIEW

OB-302

The OB-302 trial is a phase III randomized, double blind, placebo controlled multicenter study to determine the safety and efficacy of VI-0521 in the treatment of obesity in otherwise healthy adults.

PROJECT TEAM

Study Management

The overall management of the study will be the responsibility of the Senior Clinical Trial Manager (CTM). The Senior CTM will oversee and coordinate the management of the study as well as oversee the study specific CTM. This oversight will ensure consistency and allow VIVUS Study Management to have one primary contact for the Qnexa program. The Medpace CTM assigned to OB-302 will work closely with the VIVUS Study Manager, Medpace Medical Expert, and VIVUS Clinical Leader to address protocol questions and interpretations while maintaining close oversight of study-related processes and documents. The OB-302 CTM will supervise all Clinical Research Associates (CRAs) and Project Coordinators assigned to the project.

The Project Coordinators will be responsible for day-to-day study management functions, including the generation of status reports, organization of supplies, generation and compilation of newsletters, and input of all study information into the ClinTrak® Study Management System, a web-based, proprietary research management system designed by Medpace. The Project Coordinators will organize teleconferences and team meetings, including the compilation of agendas and meeting minutes.

The Study Start-Up Manager and Study Start-Up Coordinators will work closely with the CTM and Project Coordinators to ensure sites become active in the most time effective manner.

The Medpace Contracts Attorney will be responsible for the execution of Investigator contracts (upon VIVUS defined process). The Contracts Attorney will work closely with the Start-Up Manager and Medpace CTM to ensure contracts are executed in a timely manner.

The Medpace Medical Expert assigned to this project will work closely with the VIVUS Clinical Leader. The Medpace Medical Expert will assist with protocol design and medical interpretation of entry criteria and adverse events (AEs). The Medical Expert will also be involved in the training of CRAs and other staff members participating in the project. The Medical Expert will review and approve the coding of concomitant medications, medical histories, AEs, and will provide the medical context for the statistical analysis and medical writing.

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The Medical Expert will assist in the review of the protocol, train Medpace personnel internally as to the background of the study compound and design of the study, participate in the project teleconferences and meetings, work hand-in-hand with the OB-302 CTM, and have heavy involvement in the clinical study report. The Medical Expert's role and decision making rights are dictated by VIVUS (e.g. inclusion/exclusion of patients, discussions with Investigators about withdrawing a patient, etc.). This decision making power often times reduces the oversight needed by the sponsor. For questions the OB-302 CTM is not comfortable answering, she will contact the Medical Expert for guidance. Obviously, VIVUS will be involved in study oversight based on pre-defined terms with the VIVUS Clinical Development Team. The Medpace Medical Expert is available 24 hours a day, 7 days a week via the Medpace Project Helpline.

Clinical Monitoring

Medpace operates in North America with a primarily centralized monitoring team of over 140 CRAs to promote greater standardization, cohesiveness, support, and stability. Each of the Medpace CRAs assigned to this project have monitoring experience and strong clinical backgrounds.

Clinical Safety

The Clinical Safety will be managed by VIVUS or its designee. VIVUS Clinical Leader to be involved with casualty assignment for all Serious Adverse Events (SAEs).

Data Management

A Data Manager will serve as the primary contact for the Data Management team. Data Coordinators will be involved in the day-to-day operations and report issues to the Data Manager. Data Entry Specialists and Database Programmers will also be utilized.

Biometrics

Key members of our Biometrics team include Biostatisticians and Statistical Analysts. The Biostatistician assigned to this project will develop the analysis plan and coordinate biometrics activities. The Lead Statistical Analyst will work closely with the Biostatistician to ensure a clear understanding of the analysis plan and communicate any programming issues that may arise.

Medical Writing

The Medical Writing team works in collaboration with the Medical Experts to prepare research reports meeting International Conference on Harmonisation (ICH) and Sponsor guidelines. All Medpace Medical Writers have extensive experience in regulatory submission preparation. The Medical Writing team is actively involved throughout the conduct of the trial.

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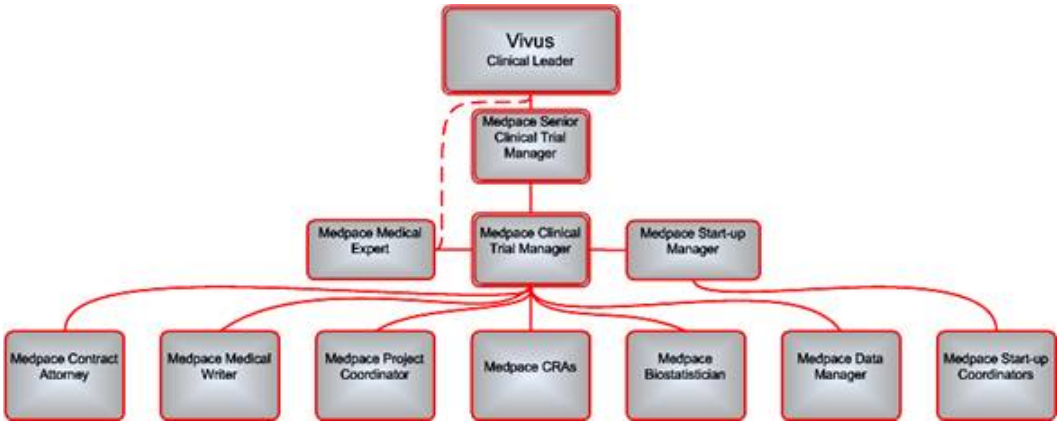
Team Organization Chart



PROJECT START-UP

Protocol

VIVUS will prepare the protocol. Medpace will review the protocol and provide comments before it is finalized.

Case Report Forms

Medpace will design the electronic case report forms (eCRFs) for the trial, including completion instructions, according to the final protocols and the Medpace template. VIVUS must review and approve the eCRFs before they are finalized.

Project Initiation

Prior to the study site initiation visits, a project kickoff meeting will be held at Medpace involving Medpace and VIVUS personnel to review the study protocol, eCRFs, and overall project coordination. Medpace project team members and VIVUS personnel will participate in this meeting.

Interactive Voice Response System

Medpace will provide a customized (study-specific) interactive voice response system (IVRS) to provide patient randomization, and drug management. The Medpace IVRS is a proprietary in-house developed system. The system provides both voice and web access and has been developed in conjunction with our web based Clintrak® system providing seamless functionality throughout the conduct of the study. The VIVUS Team (no limit applied to number of team members) will have access to review reports within the IVRS. Medpace will perform the User Acceptance Testing (UAT) for each site.

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The IVRS will include:

- Subject Screens/Screen Failures;
- Subject randomization;
- Patient visit tracking;
- Inventory management (site supply set-up, initial bulk supply, and resupply of one additional shipment per patient);
- Notifications of site shipments;
- Confirmation of receipt of shipments; and
- Customized reports.

VIVUS will review IVRS and approve system prior to finalization.

Study Medication Supply and Storage

VIVUS will be responsible for the supply, packaging, labeling, storage, and destruction of study medication. Distribution of the study medication will be tracked and initiated via the Medpace IVRS. Study medication accountability procedures will follow Medpace standard operating procedures (SOPs) and utilize a study medication accountability log that has been approved by VIVUS.

Recruitment Oversight Plan

The Medpace CTM, in collaboration with VIVUS, will develop a recruitment oversight plan. Medpace understands the importance of rapid recruitment and the necessity to keep patients in the trial until completion. Medpace will develop processes prior to study initiation to ensure recruitment is efficient and retention of patients in the study is maximized. The plan will include details on:

- Initial collection of essential documents;
- Patient recruitment (including tools, site-specific plans, contingencies, etc.); and
- Patient recruitment tracking reports.

The tools noted above include:

- Inclusion/exclusion cards;
- Patient emergency cards;
- Enrollment tracking forms;
- Laminated patient visit schedule;

- Pocket protocol; and
- Advertising tools (e.g., posters, table tents, language for newspaper/radio advertisements, etc.).

Medpace understands each site has a different experience and approach to patient recruitment. The Medpace CTM and Medpace CRAs will work with personnel from each site to help maximize their efforts. The project team maintains frequent contact during the active recruitment phase to assess each site's activity and offer assistance when needed. Medpace acknowledges the importance of site recognition and offers various incentives throughout the recruitment period. Examples of site incentives are "Site of the Month" awards and weekly faxes displaying each site's activity (often included in the newsletter as well). The time associated with these types of incentives are inclusive of the budget. However, often times, monetary incentives are built into the Investigator's grant to encourage rapid essential document collection and/or timely recruitment.

Patient retention is vital to the success of a trial. The Medpace CTM and the Medpace CRAs will work with the sites to understand the needs and motivations for patients to remain in the study. They will help educate the sites on the importance of "customer service" and "patient satisfaction" as elements that ensure continued patient participation. Examples of patient retention methods include quarterly patient newsletters, ideas for site customer service, and tokens of appreciation for patients.

Site Selection and Pre-study Visits

VIVUS, in conjunction with Medpace, will identify qualified Investigators. VIVUS and Medpace will also work together to provide and negotiate Confidentiality Disclosure Agreements (CDAs) as well as create and evaluate site questionnaires. In not knowing the number of pre-study visits Medpace will be required to conduct, a unit price for a pre-study visit has been provided in the budget.

Pre-study visits will be conducted consistent with Medpace SOPs. Medpace will provide a pre-study visit report to VIVUS within 10 business days of each visit.

These visits will include, but are not limited to:

- Determining whether or not the site has clinical staff of appropriate education, training, and experience to manage the study and have sufficient capacity to perform the required tasks;
- Determining whether or not the site has appropriate facilities to conduct the study;
- Determining there are no competing studies that will conflict with patient enrollment and that the site has sufficient patients and processes to enroll patients in the time identified for patient recruitment; and

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- Determining whether or not the site has appropriate resources and procedures to maintain appropriate records according to FDA requirements.

Study Start-up Team

The efficient start-up of the *** study sites for OB-302 will have a significant effect on patient recruitment time. Medpace will utilize its Study Start-up team for additional support during the initial phase of the trials to expedite the overall study start-up for each site.

The Study Start-up team works directly with the CTM and the Project Coordinators. The team is comprised of a Study Start-up Manager and several experienced Study Start-up Coordinators. The team is responsible for many of the key start-up activities, including:

- Submission to the central IRB;
- Coordination and tracking of essential documents packages for each site;
- Investigator meeting presentations and binders; and
- Site tools.

Central Laboratory Selection

Medpace Reference Laboratories (MRL) will be utilized for processing the clinical laboratory samples. MRL is committed to providing comprehensive laboratory services of the highest quality to the pharmaceutical and biotechnology industries.

Investigators' Meeting

An Investigators' Meeting will be held for the OB-302 study. VIVUS will arrange the meeting (including contracting with a third-party vendor) and Medpace will prepare the meeting materials, including preparation and distribution of binders. The Medpace OB-302 Team will attend the meeting. VIVUS will open the meeting and Medpace will present on the topics delegated by VIVUS. The meeting minutes will be prepared by Medpace, reviewed and approved by VIVUS, and distributed to the study sites by Medpace. The preparation of the meeting minutes is optional; however, is included in the budget. Medpace assumes the Investigators' Meeting will serve as the initiation visit for the Investigators. Therefore, the budget reflects 20% of the sites will require an initiation visit (for those unable to attend the Investigators' Meeting).

Clinical Trial Agreements for Sites, Central Laboratory, and EDC Vendor

Medpace will prepare and provide sample clinical trial agreements (including budgets) for the study sites. VIVUS will review and approve the final draft versions of the clinical trial agreements. The agreements will be distributed and negotiated with each site by Medpace (with final approval by VIVUS). Medpace will make payments to the clinical sites according to the VIVUS-approved schedule. All payments for sites, Medpace Reference Laboratories, and Phase

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Forward will be made electronically to Medpace within seven days of invoice receipt. If electronic payment exceeds or falls below actual costs, VIVUS will adjust based on the prior month's payment reconciliation. Investigator payment invoices will include the following detail:

- Clinical study number;
- PI or Site #;

- Patient ID;
- Amounts paid per visit;
- Total amount earned to date;
- Prior payments; and
- Current payment amount.

Institutional Review Board and Initial Essential Documents Packages

Medpace will select a central Institutional Review Board (IRB) and coordinate the initial submissions to the IRB. VIVUS must approve the central IRB selected. Medpace will be responsible for payments to the central IRB utilizing funds provided in the same manner as described above.

A study-specific, prototype informed consent form (ICF) will be designed by Medpace. The ICFs will be reviewed and approved by VIVUS. Medpace will distribute the ICFs to the Central IRB. Medpace will be responsible for negotiating changes to the informed consents with the central IRB.

Deviations from the VIVUS template must be brought to the attention of the VIVUS Clinical Leader who will facilitate VIVUS legal review and approval, if required.

All components of the Initial Essential Documents Package will be collected, tracked, and maintained by Medpace according to Medpace SOPs. The Medpace Study Start-up team will review all documents, negotiate any changes with study site personnel, and correct any errors. The Initial Essential Document Package includes the following:

- Signed protocol signature pages;
- Financial disclosure questionnaires (FDQs) (template to be provided by VIVUS, Medpace to collect the forms);
- Clinical study agreement (includes study budget);
- FDA Form 1572;
- Laboratory certifications and reference values;
- Curricula vitae for all Investigators;

- IRB approval of the protocol (and any amendments), the informed consent and sponsor approved advertisements; and
- Qualification of IRB members.

The FDQs shall apply throughout the entire term of the study and for one year following last patient last visit (LPLV). If there is any change in the accuracy of a particular site's FDQ during that time period, that site will be responsible for notifying Medpace of the change. Medpace will send a fax to all sites once the study has ended reminding them of their responsibilities (one of which includes notifying Medpace of any FDQ changes). If a site notifies Medpace of a change in staff from LPLV to one year after LPLV, Medpace will collect an updated FDQ and forward on to VIVUS. Costs associated with this task are included in the budget.

Site Initiation Visits

Site initiation visits will be conducted by the Medpace CRAs consistent with Medpace SOPs. For purposes of this proposal, it is assumed that the Investigators' Meeting will serve as the initiation visit and only 20% of the sites for each study will require separate initiation visits. Typically, if the Investigator Meeting is considered the initiation visit, the CRA will contact the site via phone to review study procedures and the CRA's first routine monitoring visit will occur shortly (can be defined as 1 or 2 weeks) after a patient is screened for the trial. During this visit, the CRA will review bullets 2-5 below. A site initiation visit report will be completed and forwarded to VIVUS within 10 business days of the visit. These visits will include, but are not limited to, the following tasks:

- Train site and applicable study personnel on the protocol and study procedures;
- Ensure the site has received all study supplies required for the conduct of the study, including study medication and access to eCRFs;
- Provide and review the Trial Master File binder. Medpace CRAs will provide instruction to the site personnel on the organization and maintenance of the documents in the binder;
- Review study medication accountability procedures;
- Provide eCRF completion instructions; and
- Explain the serious adverse event (SAE) reporting procedures.

CLINICAL OPERATIONS

Monitoring Data Review Guidelines

The Medpace Lead CRA in collaboration with the project team members will develop a project-specific Monitoring Plan for the study. This plan will include detailed interpretations of study expectations for the CRAs assigned to the study. Issues are discussed and updated on an ongoing basis throughout the project. Medpace will request that VIVUS approve the initial document and then re-approve the document on a quarterly basis.

Routine Clinical Monitoring Visits

Medpace will conduct routine monitoring visits at each site consistent with Medpace SOPs. The frequency of the visits will be determined by the site's activity, but will be conducted on average every four to six weeks. Visits at the beginning and end of the study may be more frequent based on the needs of the study, including, but not limited to, recruitment, quality data and study close-out activities. Based on recruitment being very rapid, the first routine visit will be performed within 2 weeks after the first two patients are screened at the site. The CRA will perform 100% source documentation. In addition, data queries will be resolved during the visits, eCRF changes will be verified, and supporting documentation for SAEs will be obtained. The Medpace CRA will verify all laboratory samples have been obtained according to guidelines and the results are available in the patient's source documents. A monitoring visit report will be forwarded to VIVUS within 10 business days of the visit. VIVUS will be notified of any significant issues by phone within one business day.

The following tasks will also be performed:

- Train any new site personnel and review study issues with applicable site personnel;
- Ensure the site has sufficient study supplies (including study medication);
- Ensure the site is entering eligible patients into the study in a timely manner, and notify the Medpace Study Manager immediately of any problems;
- Detect any significant compliance or other issues and notify the Medpace Study Manager by phone, within one business day of the monitoring visit;
- Confirm the Trial Master File is complete and current, and the site is complying with applicable regulations and the protocol. VIVUS will be notified immediately of any significant deviations;
- Ensure the site is completing eCRFs in a timely manner;
- Ensure all completed eCRFs are reviewed, verified, corrected, and transmitted to Medpace;
- Review eCRFs for accuracy and protocol adherence;
- Verify study medication dispensing, compliance, and accountability for each patient; and

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- Ensure the Investigator reported all SAEs to Medpace and the applicable IRB.

Medpace will provide a follow-up letter to the study site after each visit. The letter will include, but will not be limited to, the following:

- Important findings during the visit;
- Recommendations of corrective actions to be taken by the site; and
- Follow-up information regarding questions asked during the visit.

The Monitoring Visit Reports with all attachments including follow-up letters, will be available for view through the Medpace web based Clintrak® Study Management system within 10 days of the monitoring visit.

In-house Clinical Monitoring Activities

Investigators will be contacted on a regular basis (every week during the active recruitment period and between monitoring visits) to ensure progress at the study site. The CRA will take the opportunity to review enrollment, answer protocol-related questions, discuss eCRF completion issues, obtain information regarding AEs, and ensure the site continues to be committed to the completion of the study in a timely manner and according to the protocol.

Telephone contacts will be entered in the Medpace ClinTrak Study Management system. Contacts requiring urgent attention will be relayed to VIVUS immediately and will be resolved in collaboration with the Medpace CTM and the VIVUS Study Manager.

Withdrawals Due to Adverse Events

Withdrawals due to AEs will be tracked and reconciled with the eCRF database on an ongoing basis by Medpace. The CRA will be responsible for reporting withdrawals due to AEs to VIVUS using the monitoring visit report.

Medpace will write narratives for all withdrawals due to AEs, for use in the clinical trial study report.

Status Reporting

The Medpace Senior CTM will serve as the central channel for communication between Medpace and VIVUS. The OB-302 CTM will work in conjunction with the clinical monitoring group to track study progress and report to VIVUS on a weekly basis. In addition, the OB-302 CTM will be responsible for overall management of site information, overseeing the status of Investigator contracts, direct supervision of CRAs, tracking of enrollment information, and distribution of study supplies. The Medpace OB-302 CTM will be the primary contact for the sites to address protocol interpretations and inclusion/exclusion criteria. All protocol-related issues will be recorded in an ongoing document to ensure consistency. The CTM is available 24 hours a day, 7 days a week via the Medpace Project Helpline.

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Medpace will develop a communication plan at the start-up of the study. The CTM will work with the VIVUS project team to define details regarding study communication, including status reporting and team conference calls. Medpace typically deliver status reports on a predetermined day (and time) of the week, which is established around the weekly team calls so that the information can be discussed. Utilization of IVRS will also allow the project team to review patient status on a real time basis.

The Medpace CTM will collaborate with the Medpace Medical Expert and the VIVUS Study Manager to address any questions that may arise. The ClinTrak Study Management databases will serve as the primary source of project status information and will allow the Medpace CTM to report on any aspect of the study. The databases are updated on a real-time basis, providing accurate and up-to-date information.

Elements of ClinTrak include:

- Phone contacts;
- Monitoring visit reports;
- Patient status including details on withdrawals during the treatment phase;
- Study supplies; and
- Protocol deviations.

Medpace will provide weekly status reports via a secure project website, to include the following status by site:

- Number of patients screened;
- Number of screen failures;
- Number of patients randomized;
- Number of patients dropped with drop rates; and
- Number of patients completed.

In addition, monthly reports will be provided, to include the following:

- Monitoring visits scheduled; and
- Monitoring visits completed.

Data Management status reports will be provided monthly via a secure website. These reports will include the following:

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- Cumulative and interval eCRF status by site (including number of eCRFs transmitted and cleaned);
- Cumulative and interval patient status by site (including number of patients ongoing, completed, and early terminations) based on eCRF data in-house; and
- Cumulative and interval query status by site (including number of queries issued and days outstanding).

Project Website

Medpace will develop a secure OB-302 website that will be available to all project team members and site personnel. The website will include information and tools relevant to the study, such as status reports, meeting agendas and minutes, newsletters, monitor visit status, and the project timeline. Access is controlled by the type of user. Access to the tabs (sections) on the websites are controlled by the user type so that sites can have access to the section specifically designed for site access. Medpace can set up an automatic notification process of updates to the user email accounts. Clinical sites will have access only to parts of the website that pertain to their function. They will have the ability to receive study information and download study-related forms.

Team Meetings

VIVUS and Medpace

Medpace assumes that one face-to-face meeting, other than the Investigators' meeting and kickoff meeting will take place for the OB-302 study at VIVUS.

Weekly teleconferences will be held during the study. The teleconferences will be held to discuss study progress and review project documents (as necessary). The Medpace Project Coordinators will be responsible for preparing and distributing agendas and minutes for each meeting/teleconference.

Additional meetings/teleconferences will be scheduled throughout the project, as needed.

Internal Meetings

Medpace will develop a project-specific internal project development/training program for all project team members. Included in this program will be the following:

- Protocol/eCRF review meeting;
- Medical in-services;
- Periodic Monitoring Plan meetings; and

- Periodic project meetings.

Newsletter

Medpace will prepare a 2-4 page full color site monthly newsletter for OB-302 as an additional avenue of communication and training for all site personnel. VIVUS will provide input and approval of the newsletter prior to distribution. Medpace will be responsible for printing and distributing two copies of each newsletter to each site.

Closeout Visits

Medpace will conduct closeout visits at each site consistent with Medpace SOPs after all patients have completed or discontinued from the study at the respective site. This visit may be performed as part of a final routine site monitoring visit. Site closeout visit reports will be forwarded to VIVUS within 10 business days of the visit. The following tasks will be performed:

- Resolve outstanding data queries;
- Ensure all study medication supplies are accounted for and that medication records and unused supplies are returned to VIVUS;
- Ensure the Investigator's copies of data and source documents are properly stored;
- Ensure the Trial Master File is complete, correct, and properly stored;
- Ensure the Investigator is aware of record retention requirements and other obligations, and a final site status report is sent to the IRB and VIVUS; and
- Instruct the site to update the FDQs for one year after the study is completed.

Site Audits

Site audit visits will be conducted, as deemed necessary, by VIVUS.

Medpace will respond to any audit findings and ensure the proper actions are taken to resolve outstanding issues.

REGULATORY AFFAIRS AND SAFETY REPORTING

Serious Adverse Events

All SAEs will be reported immediately, within 24 hours of discovery or notification of the event, by the clinical study site to VIVUS, or its designee, according to SOPs specified by VIVUS.

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VIVUS will be responsible for submitting all immediately reportable SAEs (serious, causally related and unexpected) to the Food and Drug Administration (FDA) in accordance with the current regulations.

If a SAE has occurred at a site, the Medpace CRA will always 100% source document verify the event during the monitoring visit to ensure it has been recorded, documented, and reported appropriately and accurately. In addition, data queries will be resolved during the visits, CRF changes will be verified, and supporting documentation for SAEs will be obtained.

Medpace will provide VIVUS listings of non-serious adverse events from all sites to support filing of the Annual Safety Reports. Medpace will reconcile SAE listings with the AE database.

DATA MANAGEMENT

Data Management activities performed by Medpace will include eCRF tracking, preparation of a data management manual, eCRF review, coding of adverse events and concomitant medications, medical histories, data cleaning/editing, querying, query tracking, final database quality review, and delivery of the final SAS® database. The data cleaning process will be performed on an ongoing basis following Medpace Data Management SOPs. Two data transfers (SAS transport files) will be performed: a test transfer prior to FPFV and a final transfer. A unit price for additional data transfers has been provided in the budget.

Database Development and Data Management Manual

Medpace will design and validate the data entry systems prior to entry of data. A Data Management Manual will be prepared for each study using the Medpace template, and will include the following data management documents:

- Database specifications, based on VIVUS specifications;
- Guidelines for the tracking of eCRFs and data queries;
- Data Management Guidelines, which will include guidelines for reviewing the data, and description of the database edit check specifications to be performed for data cleaning; and
- Description of the database quality control (QC) plan.

The manuals will be reviewed and approved by VIVUS.

Data from the Central Laboratory

Medpace will arrange periodic data transfers from MRL. Medpace will track and reconcile discrepancies between the MRL demographic data and the eCRF database, which are generated during the data cleanup process throughout each project.

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Data Entry and Data Querying

Medpace assumes no codable forms will be transmitted for screen failure patients. Data is entered by site personnel that have been trained on the eCRF system. Data will be reviewed according to Medpace Data Management Guidelines and edits. A data query will be generated electronically within the eCRF system. The resolutions/corrections are made by site personnel by changing the data. All changes are recorded in an audit trail. All answered queries are verified/closed by Medpace Data Management. All resolutions/corrections will be performed consistent with Medpace SOPs. The Data Coordinators will work directly with the site personnel in resolving queries.

Coding

Medpace will be responsible for coding adverse events, medical histories, and concomitant medications.

- MedDRA will be used to code adverse events and medical histories. Adverse events and medical histories will be coded to the lowest level term, preferred term, and system organ class.

- WHO DRUG will be used to code concomitant medications. Concomitant medications will be coded to the generic name and anatomic therapeutic class 3. It is assumed by Medpace that VIVUS holds a valid agreement with the Uppsala Monitoring Centre (UMC) for the WHO DRUG dictionary.

All coding will be done on a single version of each coding system (versions to be agreed upon by VIVUS). Medpace will provide the coding dictionaries.

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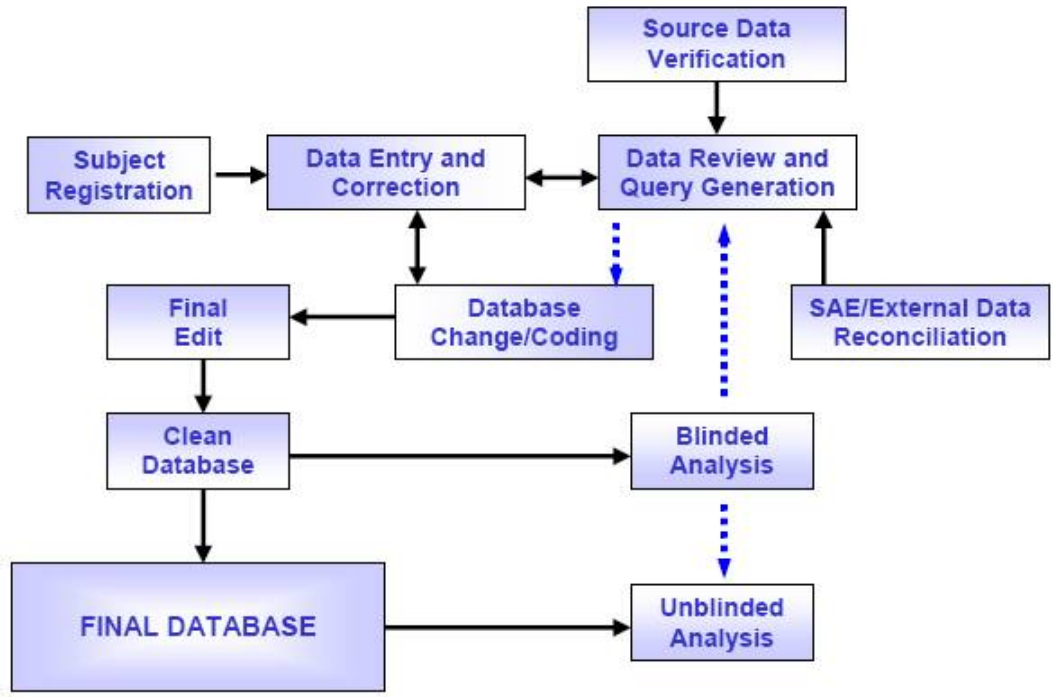
Data Flow Chart



STATISTICAL ANALYSIS

Medpace will develop the data analysis plan (DAP) per the VIVUS/Medpace format and template. VIVUS will review and approve the DAP prior to initiation of programming. Included in the DAP is a detailed statistical methodology and programming specification for all statistical analyses, tables/figures/listings (TFLs), and derived datasets.

Medpace will be responsible for programming and generating all TFLs, according to the Medpace standard analysis validation and quality control procedures. All TFLs will be programmed using SAS (Version 8), according to the VIVUS Programming Standards document. Pre-final TFLs will be generated twice on clean data for format review. Final TFLs will be generated on final data for the clinical study report.

MEDICAL WRITING

The Medpace Medical Writing team works in collaboration with the Medpace Medical Expert to provide a clinical study report according to FDA/ICH guidelines. The preparation of the Integrated Clinical/Statistical Study Report involves three stages of development: (1) the Study Report Shell (SRS), (2) the Pre-Final Study Report (PFSR), and (3) the Final Study Report (FSR).

The SRS is prepared after sign-off of the Final DAP. The SRS is created using a template and/or style guide provided by VIVUS, or by utilizing the Medpace standard report template, which

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adheres to the ICH guideline, "Structure and Content of Clinical Study Reports," and follows the *American Medical Association Manual of Style*. The SRS incorporates information from the protocol, amendments, and eCRFs into sections of the report, including but not limited to the study design, study population, treatments administered, and the evaluation schedule. The statistical methods and results sections encompass information derived from the Final DAP. The results sections include mock-up in-text tables and text. The SRS undergoes a complete team review, which includes the Medical Monitor, Statistician, CTM, Data Manager, and other team members, if applicable. After the Medical Writer incorporates all team changes into the SRS, the SRS undergoes Medpace's comprehensive document QC process. Once all changes from the document QC process are implemented into the SRS, the SRS is forwarded to the VIVUS for review.

Preparation of the PFSR occurs after receipt and implementation of VIVUS comments on the SRS, declaration of a clean database, and completion of Pre-Final Analyses. If necessary, a results review meeting is conducted with key members of the Medpace and VIVUS project team as the Medical Writer begins preparing the PFSR. The PFSR is a complete version of the report without the appendices. The PFSR undergoes a complete team review, which includes the Medical Monitor, Statistician, CTM, Data Manager, and other team members, if applicable. After the Medical Writer incorporates all team changes into the PFSR, the PFSR undergoes Medpace's comprehensive document QC process. Once all changes from the document QC process are implemented into the PFSR, the PFSR is forwarded to VIVUS for review.

The FSR is prepared once VIVUS' comments on the PFSR are returned and all requested changes are agreed upon (including the acceptance of final text for all complicated or sensitive sections, which may require sending non-QC'd drafts of the report to VIVUS), and the Final Analyses are completed. The FSR is a complete version of the report including paginated appendices and/or supplements. The FSR undergoes a complete internal QC review and is forwarded to VIVUS for sign-off. The signed cover sheet is returned by VIVUS to verify their acceptance of the FSR.

STUDY CLOSEOUT

At the conclusion of each study, once all deliverables have been met, Medpace will return the original study files to VIVUS. These will include:

- General project administration files (this file includes items such as: Outside Vendor Correspondence, Multiple Site Correspondence (e.g. faxes to all sites), Central IRB Correspondence, Project Specific SOPs and Procedures, Monitoring Plan, Trial Master File, Project Timelines, Newsletters, and Meeting Minutes)

- Site files (this file includes site items such as: Essential Documents, Budget, Site Correspondence, Monitoring Visit Reports, Drug shipment documents, Study Supply forms, and Protocol Deviations);

- Final statistical tables and listings with results;

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- Data management documentation (this file includes items such as: Database Definition Document, Final eCRFs, External Database Import Specs., Data Management Plan, Coding Reports, Analysis Plan, and Randomization Code); and

- Final clinical study report.

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Assumptions

OB-302	Description
Number of Investigators	***
Number of Back-up Investigators	***
Number of Screened Patients	***
Number of Randomized Patients	***
Number of Randomized Patients/Site	***
Duration of Enrollment Period	***
Duration of Treatment Period	***
Number of Investigators' Meetings	***
Number of Kickoff Meetings (at Medpace)	***
Number of Sponsor Meetings (at VIVUS)	***
Number of Conference Calls	***
Frequency of Conference Calls	***
Number of Clinical Monitors	***
Number of Pre-study Visits	***
Number of Initiation Visits	***

Number of Routine Monitoring Visits	***
Number of Closeout Visits	***
Monitoring Frequency	***
Number of Newsletters per Site (monthly)	***
Estimated Number of eCRFs per Completed Patient	***
Estimated Number of Unique eCRFs per Completed Patient	***
Total Number of eCRFs	***
Estimated Number of AE Codes Per Patient	***

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Estimated Number of Medical History Codes Per Patient	***
Estimated Number of Concomitant Medications Codes Per Patient	***
Estimated Number of Queries Per Patient	***
External Data Sources	***
Data Transfers from Medpace to VIVUS	***
Number of Raw Listings	***
Number of Unique TFs	***
Number of Version TFs	***

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Task Order #02
Appendix 3 — Project Schedule
VIVUS, Inc.
Qnexa OB-302

Milestones

OB-302	Date
Medpace Begins Work	***
Protocol Finalized	***
First Patient First Visit	***
Last Patient First Visit	***
Last Patient Last Visit	***
Final Database Lock	***
Final TFLs Available	***
Delivery of Final Clinical Study Report	***

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Task Order #02
Appendix 4 — Budget
VIVUS, Inc.
Qnexa OB-302

Medpace Fee Estimate

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***

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Task Order #02
Appendix 5 — Payment Schedule
VIVUS, Inc.
Qnexa OB-302

Payment Schedule

As set forth in this Agreement, professional service fees totalling $*** will be paid by VIVUS for professional services rendered by Medpace according to the following schedule.

***

Pass-through expenses will be billed to VIVUS on a monthly basis as incurred. The first Wire-Transfer payment will be invoiced prior to any site becoming active to ensure funds are available for site payments. Medpace will pay sites immediately following receipt of Wire-Transfers. Medpace will invoice VIVUS on a monthly basis and payments will be made by VIVUS within seven days of invoice receipt.

Payment Information and General Conditions

***

Inflation

The fees stipulated in the fee estimate *include* inflation for the duration of the study as specified in this proposal. Any significant shift in timelines will require a revision to the fees.

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Appendix 6 **Transfer of Obligations Form**
CONFIDENTIAL

Directions: Complete a form for each clinical study where Sponsor obligations have been transferred in accordance with 21 CFR Part 312, Subpart D (Responsibilities of Sponsors). Forward the completed form to Sponsor's Regulatory Affairs Department for submission to the applicable regulatory agencies.

Drug: VI-0521 Study ID: OB 302

Study Title: A phase III randomized, double blind, placebo controlled multicenter study to determine the safety and efficacy of VI-0521 in the treatment of obesity in otherwise healthy adults.

CRO Name: Medpace, Inc.

CRO Address: ***

OBLIGATIONS TRANSFERRED TO MEDPACE: x THE APPROPRIATE BOX(ES).

o All obligations in 21 CFR 312, Subpart D (Responsibilities of Sponsors) have been transferred to Medpace.

x The following obligations have been transferred to Medpace:

Sec. 312.32: IND Safety Reports

x Promptly review safety information. *Sponsor will be notified within one (1) business day of discovery of significant new or serious adverse events or risks, or any unusual frequency of reactions with respect to the drug.

o Notify all participating investigators in a written IND safety report of any AE associated with the drug that is both serious and unexpected.

o Notify the FDA in a written IND safety report of any AE associated with the drug that is both serious and unexpected.

Sec. 312.53: Selecting investigators and monitors

x (a) Select qualified investigators

x (b) Control investigational drug shipment

x (c) Obtain information from investigators

- x (1) Signed Form FDA-1572
- x (2) CV or other qualification statement
- x (3) Clinical protocol outline
- x (4) Financial disclosure information

x (d) Select qualified monitors

Sec. 312.54: Emergency research

o (a) Monitor the progress of all studies involving an exception from informed consent.

o (b) Monitor such studies to identify when an IRB determines that it can't approve the research.

Sec. 312.55: Informing investigators

x (a) Provide sites with the current Inv. Brochure.

x (b) Inform investigators of new observations on the drug, particularly with respect to AEs and safe use.

Sec. 312.56: Review of ongoing investigations

o (a) Monitor the progress of all IND studies.

x (b) Secure compliance from noncompliant investigators or discontinue drug shipments and end the investigator's participation in the study.

o (c) Review and evaluate the safety and efficacy results as it is obtained from the investigator.

x (d) Discontinue use of the investigational drug if it is determined to present an unreasonable and significant risk to subjects, notify all IRBs and investigators, and assure the return or alternate disposition of the drug from the investigators.

Sec. 312.57: Record keeping and record retention

x (a) Maintain adequate records showing investigational drug receipt, shipment, or other disposition. *Master Drug Logs will include the name of the Investigator to whom the drug is shipped, the date, and the quantity and batch of each such shipment.

x (b) Maintain complete and accurate records showing any financial interests of the investigator subject to 21 CFR 54.

x (c) Retain the records and reports required by the regulations for 2 years after the marketing application is approved, or if not approved, until 2 years after investigational drug shipment is discontinued and FDA has been notified.

o (d) Retain reserve samples of any test article and reference standard identified and used in bioequivalence or bioavailability studies.

Sec. 312.58: Inspection of sponsor's records and reports

x (a) Permit FDA personnel to have access to and copy and verify any records and reports related to the clinical investigation.

x (b) Permit DEA personnel to have access to and copy records related to the shipment, delivery, receipt and disposition of any investigational controlled substance. Assure adequate storage precautions are taken for investigational new drug substances listed in any schedule of the Controlled Substances Act.

Sec. 312.59: Disposition of unused supply of investigational drug

x Assure the return (or alternate disposition) of all unused supplies of the investigational drug from each discontinued/terminated investigator; maintain written records of any disposition of the investigational drug.

Other

o Please describe any other applicable transfers below:

September 7, 2007

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MEDPACE
VIVUS Task Order #03

EXHIBIT A

Qnexa OB-303 TASK ORDER

MEDPACE Task Order Number: 03

MEDPACE Project Number: VOB303

This Task Order, dated September 12, 2007, is between Medpace, Inc. (**"MEDPACE"**), and VIVUS, Inc. (**"VIVUS"**).

RECITALS:

WHEREAS, MEDPACE and VIVUS have entered into that certain Master Services Agreement dated September 12, 2007 (the "Master Services Agreement"); and

WHEREAS, pursuant to the Master Services Agreement, MEDPACE has agreed to perform certain Services in accordance with Task Orders from time to time entered into by the Parties and VIVUS and MEDPACE now desire to enter into such a Task Order; and

WHEREAS, MEDPACE and VIVUS desire that MEDPACE provide certain services with respect to a phase III randomized, double blind, placebo controlled multicenter study to determine the safety and efficacy of VI-0521 in the treatment of obesity in adults with obesity-related comorbid conditions (the **"**Study") for the study of the product VI-0521 (**"**Study Product") as set out in the Protocol Number: OB-303, which is attached hereto as Appendix 1;

NOW, THEREFORE, in consideration of the mutual covenants contained herein, the Parties hereby agree as follows:

1. Scope of Work: MEDPACE shall perform the services described in the Scope of Work, attached hereto as Appendix 2, in accordance with the Project Schedule, attached hereto as Appendix 3 and any other documents attached to and specifically referenced in this Task Order ("Services")

2. Compensation: For performance of these Services, VIVUS shall pay to MEDPACE an amount equal to the Project Budget set forth in Appendix 4, which amount shall be payable pursuant to the Payment Schedule set forth in Appendix 5.

3. Transfer of Obligations: Sponsor Obligations transferred to MEDPACE by VIVUS (consistent with the regulations set forth in 21 C.F.R. Section 312, Subpart D) are identified in Appendix 6.

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4. MSA. The provisions of the Master Services Agreement are hereby expressly incorporated by reference into and made a part of this Task Order.

IN WITNESS WHEREOF, the Parties have hereunto signed this Task Order effective as of the day and year first written above.

MEDPACE, INC.

Signature: /s/ August J. Troendle

By: August J. Troendle
(Print Name)

Title: President

Date: September 12, 2007

SPONSOR

Signature: /s/ Wesley W. Day

By: Wesley W. Day
(Print Name)

Title: Vice President, Clinical Development

Date: September 10, 2007

List of Appendices:

Appendix 1: Protocol
Appendix 2: Scope of Work
Appendix 3: Project Schedule
Appendix 4: Project Budget
Appendix 5: Payment Schedule
Appendix 6: Transfer of Obligations

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VI-0521
Protocol No. OB-303
***

CLINICAL PROTOCOL

A PHASE III RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED MULTICENTER STUDY TO DETERMINE THE SAFETY AND EFFICACY OF VI-0521 IN THE TREATMENT OF OBESITY IN ADULTS WITH OBESITY-RELATED CO-MORBID CONDITIONS

Compound:	VI-0521
Compound Name (if applicable):	Phentermine plus Topiramate
US IND Number (if applicable):	***
Protocol Number:	OB 303
Phase:	3
Medical Monitor:	***
Sponsor:	VIVUS, Inc. 1172 Castro St. Mountain View, CA 94040 Tel: (650) 934-5200 Fax: (650) 934-5209
Version and Date:	***

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INTERNAL PROTOCOL APPROVAL

Protocol Number: OB-303

Title: A Phase III Randomized, Double-Blind, Placebo Controlled Multicenter Study to Determine the Safety and Efficacy of VI-0521 in the Treatment of Obesity in Adults with Obesity-Related Co-Morbid Conditions

The signature below documents that the reviewer has read and approved the attached protocol.

	Signature	Date
Author: Charlene Wisdom, PhD, MPH **Clinical Consultant**		
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PRINCIPAL INVESTIGATOR SIGNATURE

Protocol Number: OB-303

Title: A Phase III Randomized, Double-Blind, Placebo Controlled Multicenter Study to Determine the Safety and Efficacy of VI-0521 in the Treatment of Obesity in Adults with Obesity-Related Co-Morbid Conditions

The signature below indicates that the principal investigator has read and understands the protocol and agrees to conduct the study in accordance with the protocol, applicable guidelines for Good Clinical Practices, the Declaration of Helsinki and all applicable regulatory guidelines and requirements. Please return one copy of this executed page to VIVUS, Inc.

Printed Name: _____

Signature: _____ Date: _____

Facility Name: _____

Address: _____

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PROTOCOL SYNOPSIS

Rationale:

Obesity leads to the development of co-morbidities such as hypertension, type 2 diabetes, dyslipidemia, coronary artery disease (CAD) and stroke. Weight reduction in obese individuals has been shown to delay or prevent the onset of these co-morbidities, or even reverse the damage caused by these co-morbidities. Diet, exercise and behavior modification therapy can be effective short-term treatments; however, many people experience difficulty in achieving and maintaining weight reduction without pharmacotherapy. VI-0521 is an investigational weight loss therapy that is a new combination of two currently approved drugs, phentermine and topiramate. This novel combination treatment may provide a safe and effective option for the achievement and maintenance of weight loss in obese adults.

Objectives:

The objectives of this study are to evaluate the safety and efficacy of two doses of VI-0521 compared to placebo in the treatment of overweight and obesity in adults with at least *** obesity-related co-morbid conditions.

Trial Design:

The study is a randomized, double blind placebo-controlled prospective trial with subjects randomized to receive daily treatment with VI-0521 *** or *** or ***, with the total duration of treatment being 56 weeks. Randomization will be stratified by ***, and at least *** of the subjects must be ***. Approximately 2500 subjects will be treated under the protocol with *** subjects randomized to ***, and ***. Up to *** study sites in the USA will be employed.

At randomization, subjects will be instructed to follow a hypocaloric diet representing a 500-calorie/day deficit and advised to implement a lifestyle modification program, as tolerated, throughout the study period. During the first 4 weeks of treatment (weeks 1-4), study medication will be titrated to the desired level, with the dosage level increased each week as determined by randomization group. During treatment weeks 5-56, the dose will be maintained at the final dose level. Subjects who are unable to tolerate the assigned dosage may be treated at a reduced dose level and/or interrupt dosing for up to ***.

Subjects will return at 4-week intervals for measurement and evaluation. Female subjects of child bearing potential will undergo a urine pregnancy test at each study visit. Subjects who discontinue the study during treatment will be encouraged to return at the 56-week time point for evaluation.

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Study Subjects:

The study population will consist of *** (BMI $\geq$ *** and $\leq$ ***) adults $\leq$ 70 years of age with at least *** of the following obesity-related comorbid conditions:

- ***;
- ***;
- ***;
- ***.

Major exclusion criteria include: type 1 diabetes; diabetes medications other than metformin; known or suspected valvular heart disease; clinically significant ECG abnormality, physical exam, vital signs or laboratory abnormality; clinically significant hepatic or renal disease; creatinine clearance < 60 mL/minute; clinically significant thyroid dysfunction as evidenced by signs, symptoms, or TSH > 1.5 x ULN; obesity of known genetic or endocrine origin; history of bipolar disorder or psychosis, depression of moderate or greater severity, or presence or history of suicidal behavior or active suicidal ideation; recent weight instability; history of glaucoma or increased intraocular pressure; prior bariatric surgery; or smoking cessation within 3 months prior to enrollment. Female subjects of childbearing potential must agree to use adequate contraception (a double barrier method, stable hormonal contraception plus single barrier or tubal ligation) for the duration of treatment.

Efficacy Endpoints:

The primary endpoints are the differences between *** and *** groups in mean percent loss of baseline body weight, determined by weight at randomization (baseline) and weight at end of treatment (week 56), and percent of subjects with weight loss of 5% or more at end of treatment (week 56). Percent weight loss will be calculated as ***.

Secondary efficacy endpoints are:

- The difference in absolute weight loss between randomization (baseline) and end of treatment (week 56) for *** and *** groups;
- The difference in percent of subjects who achieve a reduction in total body weight of at least 10% between randomization (baseline) and end of treatment (week 56) for *** and *** groups; and
- The difference in change in waist circumference (randomization to week 56) for *** and *** groups.

Additional efficacy endpoints include:

- Effect on ***;

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- Effect on body composition as indicated by ***. *** assessments will be performed at only at a ***.

- Effect on *** of *** and ***;

- Change from baseline to week 28 and week 56 in BMI;

- The change in obesity-associated risk factors (HgbA1c, total cholesterol, triglycerides, LDL-C, HDL-C, fasting glucose, fasting insulin, a measure of insulin sensitivity, systolic blood pressure, diastolic blood pressure, C-reactive protein);

- Change in urinary microalbumin and albumin/creatinine ratio (ACR) from screening to week 28 and week 56;

- Change from baseline in medication number and dosages for medication to treat cardiovascular or metabolic risk factors;

- Difference between *** and *** groups in the rate of progression to type 2 diabetes (subjects non-diabetic at screening); and

- Baseline adjusted change in Framingham 10-year risk score at weeks 28 and 56.

The change in weight loss (absolute, percent, percent of subjects achieving weight loss of $\geq$ 5% and $\geq$ 10% of starting weight), waist circumference and obesity associated risk factors will also be assessed over time. Subgroup analyses, including but not limited to analysis by gender, age and race, may be performed.

***** Assessment:**

*** will also be evaluated. Data will be obtained using a multiple trough sampling scheme with samples collected at *** and ***. Effects of various cofactors including (but not limited to) ***, gender, race, *** and age will be evaluated.

Safety Endpoints:

Safety will be assessed by an evaluation of adverse events, including eye symptoms (collected at each study visit); ***. All subjects will be screened for the *** using a validated survey instrument ***, and for *** using the ***. Follow-up *** assessments will be done at *** after ***.

Statistical Methods:

All subjects who are randomized, take one or more doses of test material and have at least one post treatment efficacy measurement will be included in the analysis. Comparisons between treatments will be assessed using an *** with factors of ***, *** and *** and with *** for percent weight loss, and *** for percentage of subjects with at least 5% weight loss. A step-down multiple comparison procedure will be used to compare each dose group with ***. That is, comparison with *** will start at the ***. If the statistical test is significant at *** for

both co-primary endpoints, then the test will proceed to the *** also at the ***. If the statistical comparison is not significant at the ***, then the statistical test will be stopped and the *** will not be tested. If both dose groups are significantly better than ***, then the two active dose groups will be compared. A *** of difference in response rate between treatment groups will be derived. The *** for subjects who discontinue treatment prior to completion of the study, ***.

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LIST OF ABBREVIATIONS

ACE	angiotensin converting enzyme
ACR	albumin/creatinine ratio
***	***
***	***
***	***

CAD	coronary artery disease
Cl	apparent clearance
cm	centimeter
CRFs	case report forms
***	***
***	***
DSM-IV	Diagnostic and Statistical Manual IV
ECG	electrocardiogram
FDA	Food and Drug Administration
***	***
GCP	Good Clinical Practices
***	***
gm	gram
HBsAg	hepatitis B surface antigen
HCV	hepatitis C virus
HDL-C	high density lipoprotein cholesterol
HIV	human immunodeficiency virus
I-CAM	Intercellular Cell Adhesion Molecule
ICH	International Conference on Harmonization
IEC	Independent Ethics Committee
IND	Investigational New Drug
IRB	Institutional Review Board
IVRS	Interactive Voice Response System
***	***
kcal/day	kilocalories per day
kg	kilogram
kg/m^2	kilogram per square meter
***	***
LDL-C	low density lipoprotein cholesterol
µU/mL	microunits per milliliter
MedDRA	Medical Dictionary for Regulatory Activities
mg	milligram
mg/day	milligram per day
mg/dL	milligram per deciliter
mmHg	millimeters of mercury
NYHA	New York Heart Association
OGTT	oral glucose tolerance test
PAI-1	Plasminogen Activator Inhibitor 1
***	***
***	***
QOD	every other day
RBC	red blood cell
RBP-4	Retinol Binding Protein 4
***	***
***	***

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TSH	thyroid stimulating hormone
ULN	upper limit of normal
***	***
V-CAM	Vascular Cell Adhesion Molecule
WBC	white blood cells
WHO	World Health Organization
WNL	within normal limits

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1. INTRODUCTION

VI-0521 is an investigational weight loss therapy that is a combination of two approved drugs, phentermine and topiramate. Phentermine hydrochloride (phentermine), an anorectic agent, has sympathomimetic actions and stimulates the central nervous system.(1), (2) It is postulated that ***, and there is a ***.(3), (4) Topiramate, an anticonvulsant agent that has been shown to induce weight loss, is known to ***.(5) However, the specific mechanism mediating the weight loss is not known. The present study is being conducted to evaluate the combined use of phentermine and topiramate at doses of 7.5 mg phentermine/46 mg topiramate and 15 mg phentermine/92 mg topiramate in the treatment of obesity in adult subjects.

1.1. Background

Recent studies have shown that about 129 million adults in the United States are clinically overweight or obese.(6) In recent years, there has been a dramatic increase in obesity in both children and adults.(7), (8) Results from the National Health and Nutrition Examination Survey showed an overall 32.2% prevalence of obesity during 2003-2004, with obesity increasing from 27.5% in 1999-2000 to 31.1% in 2003-2004 in men but remaining relatively unchanged in women (1999-2000, 33.4%; 2003-2004, 33.2%).(8)

Obesity is associated with numerous co-morbidities including dyslipidemia, coronary artery disease (CAD), hypertension, stroke and type 2 diabetes.(7), (9) Epidemiological data indicate that obesity is associated with increased mortality,(10) and a recent study of over 500,000 individuals concluded that excess body weight during midlife, was associated with an increased risk of death.(11) A modest weight loss (5-10%) can result in a marked reduction in obesity-related metabolic and cardiovascular risk factors.(12), (13), (14) Diet, exercise and behavior modification are standard treatments for obesity although most obese individuals do not achieve prolonged weight reduction without supplemental pharmacotherapy. However, the medications currently approved by the Food and Drug Administration (FDA) for weight loss are often poorly tolerated due to side effects and often fail to maintain long-term efficacy.(15)

Phentermine hydrochloride, a synthetic sympathomimetic amine, is an anorectic agent approved by the FDA as a short-term adjunct to a weight loss regimen based on exercise, behavior modification and caloric restriction. The usual adult dosage is *** administered either once daily or in divided doses.(1) The mechanism of action of phentermine for weight loss is similar to that of other anorectic agents; it decreases appetite and stimulates the central nervous system. (1) It is postulated that ***, and there is a ***.(3), (4) Additionally, increased *** levels may result in a decrease in *** that may result in increased satiety and decreased appetite.

Topiramate, a sulfamate-substituted monosaccharide, is an anticonvulsant agent indicated as adjunctive therapy for partial onset seizures, primary generalized tonic-clonic seizures, seizures associated with Lennox-Gastaut syndrome and for migraine headache prophylaxis.(5) The

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recommended total daily dose of topiramate for treatment of seizures in adults is *** administered in two divided doses; ***. Topiramate is known to ***. (5) Recent clinical studies have shown that topiramate can promote weight loss in ***.(16),(17),(18) However, the exact mechanism by which topiramate exerts its anorectic effect is unknown although it is postulated to ***.

A detailed summary of the clinical and nonclinical toxicology, pharmacokinetics and metabolism of phentermine and topiramate is provided in the Investigator Brochure.

VI-0521 has been studied in a Phase 2, randomized, double-blind clinical trial of 200 otherwise healthy obese adults under an Investigator-Initiated investigational new drug application (IND).(19) In this study, subjects were randomized into 1 of 4 treatment groups: ***. Treatment was continued for *** (including ***). Weight loss (percent of total body weight) among subjects treated with VI-0521 ***, compared to *** among *** among ***, and *** among ***. Subjects treated with VI-0521 *** than subjects in the other treatment groups. Significant decreases vs *** and *** were observed in subjects receiving VI-0521. Of the 200 subjects randomized, *** completed treatment to *** group completed treatment. No deaths or serious adverse events were reported during the study and no significant changes in heart valve morphology were observed. The most commonly reported adverse events in subjects treated with VI-0521 were ***.

1.2. Rationale

VI-0521 is an investigational weight loss therapy that is a combination of two currently approved drugs, phentermine and topiramate. As such, VI-0521 represents a potential advance in the medical treatment of obesity since the two agents comprising this combination product affect weight loss through different mechanisms. Additionally, some of the expected side effects of the two drugs may be mitigated by complementary effects of the other. Thus, combining phentermine with topiramate may produce a similar or better adverse event profile compared to either of these agents individually. Topiramate therapy has been associated with ***. Due to the ***, it is mechanistically possible that ***. Thus, the dual mechanisms and low drug doses employed in VI-0521 may provide a safe and effective pharmacotherapy for the achievement and maintenance of weight loss in obese adults.

2. TRIAL OBJECTIVES

The objectives of this study are to evaluate the safety and efficacy of two doses of VI-0521 compared to placebo in the treatment of overweight and obesity in adults with at least *** obesity-related co-morbid conditions.

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3. TRIAL DESIGN

In this prospective, randomized, double-blind, placebo-controlled trial, overweight and obese male and female subjects with at least *** obesity-related co-morbidities who meet the eligibility criteria will be randomly assigned among *** treatment groups shown in Figure 1.

***

Figure 1. Schematic Representation of Study Design.

Approximately 2500 subjects will be randomized *** at up to *** study sites in the United States. The randomization schedule will be stratified by *** to ***; at least *** of subjects will be ***.

Subjects will initiate treatment with a dose titration during weeks 1-4 with doses gradually increased at *** intervals, as determined by randomization assignment, until the specified dose is reached and will be treated for 52 weeks (weeks 5-56) at the assigned dose level. Subjects will return to the site at the end of weeks 2 and 4 during titration and at 4-week intervals thereafter. A schedule of events is provided in Appendix 1.

The primary endpoints are differences between *** and *** groups in mean percent loss of baseline body weight, determined by weight at randomization (baseline) and weight at end of treatment (week 56), and percent of subjects with weight loss of 5% or more at end of treatment (week 56). Percent weight loss will be calculated as ***.

Secondary efficacy endpoints are:

- The difference in absolute weight loss between randomization (baseline) and end of treatment (week 56) for *** and *** groups.
- The difference in percent of subjects who achieve a reduction in total body weight of at least 10% between randomization (baseline) and end of treatment (week 56) for *** and *** groups.
- The difference in change in waist circumference (randomization to week 56) for *** and *** groups.

Additional efficacy endpoints will include the following:

- Effect on ***;
- Effect on *** of *** and ***; ***, *** and ***;
- Change from baseline to week 28 and week 56 in BMI;

- The change in obesity-associated markers (total cholesterol, triglycerides, LDL-C, HDL-C, HgbA1c, fasting glucose, fasting insulin, a measure of insulin sensitivity, systolic blood pressure, diastolic blood pressure, C-reactive protein);
- Change in *** from screening to *** and ***;
- Change from baseline in medication number and dosages for medications to treat cardiovascular or metabolic co-morbidities;
- Difference between *** and *** groups in the rate of progression to type 2 diabetes (subjects non-diabetic at screening); and
- Baseline adjusted change in Framingham 10-year risk score at weeks 28 and 56;
- Change from *** to *** and *** in body composition [assessed by *** at ***].

The change in weight loss (absolute, percent, percent of subjects achieving weight loss of $\geq$ 5% and $\geq$ 10% of starting weight), waist circumference and obesity associated risk factors will also be assessed over time. Subgroup analyses, including but not limited to analysis by gender, age and race, may be performed.

Safety evaluations will include assessment of adverse events, including eye symptoms, ***.

*** will also be obtained, and effects of various cofactors including (but not limited to) ***, gender, race, ***, and age will be evaluated. ***.

4. SUBJECT SELECTION

This study is designed to assess the effect of treatment with VI-0521 on overweight and obese adult subjects with *** or more obesity-related co-morbid conditions either currently uncontrolled or requiring measures beyond first line drug treatment to control.

The following eligibility criteria are designed to select subjects for whom protocol treatment is considered appropriate. All relevant medical and non-medical conditions should be taken into consideration when deciding whether this protocol is suitable for a particular subject.

4.1. Inclusion Criteria

To be eligible for enrollment into this trial, subjects must meet all of the following criteria. Specifically, subjects must:

1. Be adults 70 years of age or less;

2. Have a BMI ≥ *** and ≤ *** (for diabetic subjects, there is no lower limit on BMI for study inclusion);

3. Have *** or more of the following obesity-related co-morbid conditions:

- ***:
  - ***;
  - ***;
  - ***.
- ***;
- ***:
  - ***;
  - ***
  - ***.
- ***;

4. If females of child-bearing potential, be using adequate contraception, defined as double barrier methods, stable hormonal contraception plus single barrier method, or tubal ligation. Females are considered to be of child-bearing potential unless they have undergone a hysterectomy or bilateral oophorectomy, are 55 years of age or greater and have experienced spontaneous cessation of menses for at least 1 year, or have a documented follicle stimulating hormone level ≥40 IU/L;

5. Provide written informed consent;

6. Be willing and able to comply with scheduled study visits, treatment plan, laboratory tests and other study procedures.

4.2. Exclusion Criteria

Subjects presenting with any of the following will not be included in the trial:

1. Known allergy or hypersensitivity to phentermine or topiramate, any prior use of a combination of phentermine and topiramate for weight loss or use of phentermine or topiramate for any indication within the past 3 months;

2. Weight gain or loss of greater than 5 kg, use of a very low-calorie diet, or participation in a formal weight loss program (investigational or otherwise) within the past 3 months (this includes: Weight Watchers and related dietary/lifestyle intervention programs; prepared food programs; prescribed or over-the-counter weight loss medications; dietary supplement or herbal preparations, teas, or tinctures intended for weight loss; or any supervised fast or very low calorie diet);

3. Obesity of a known genetic or endocrine origin;

4. History of any eating disorders (e.g. bulimia, binge eating disorder) within the past year;

5. History of drug abuse within the past year;

6. History of alcohol abuse (defined as >14 drinks per week) within the past year;

7. Previous bariatric surgery;

8. Smoking cessation within the previous 3 months or plans to quit smoking during study participation;

9. History of glaucoma, history of increased intraocular pressure or any past or present use of medications to treat increased intraocular pressure;

10. Clinically significant thyroid dysfunction as evidenced by signs or symptoms of hypothyroidism, a TSH > 1.5 x ULN, or use of thyroid hormone treatment that has not been stable for at least 3 months;

11. Use of chronic systemic glucocorticoid therapy, or any other steroid hormone therapy that has not been stable for at least 3 months;

12. Any history of bipolar disorder or psychosis, greater than one lifetime episode of major depression, current depression of moderate or greater severity (PHQ-9 score of 10 or more), presence or history of suicidal behavior or ideation with some intent to act on it, or antidepressant use that has not been stable for at least 3 months;

13. Diagnosis of type 1 diabetes or use of any antidiabetic medication other than metformin within the past month;

14. Stroke, myocardial infarction, life-threatening arrhythmia, coronary re-vascularization within the past 6 months;

15. Unstable angina, congestive heart failure (NYHA Class II, III or IV), or known or suspected clinically significant cardiac valvulopathy;

16. Systolic blood pressure >160 mmHg, diastolic blood pressure > 100 mmHg or antihypertensive medication that has not been stable for at least 1 month;

17. Any history of malignancy within 5 years other than surgically excised basal or squamous cell carcinoma of the skin or cervical cancer;

18. Cholelithiasis within the past 6 months;

19. Any history of nephrolithiasis;

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20. Creatinine clearance < 60 mL/minute;

21. For female subjects of childbearing potential, pregnancy, breastfeeding or plans for pregnancy during the study period;

22. Use of any investigational medication or device for any indication within the last month;

23. Evidence of any clinically significant renal, pulmonary, hepatic, psychiatric or other condition by history, physical examination or laboratory studies that, in the opinion of the investigator, would contraindicate the administration of study medications, affect compliance, interfere with study evaluations or confound the interpretation of study results.

4.3. Randomization Criteria

The following additional criteria must be met prior to randomization and dispensing of study medication to subjects:

1. Baseline physical examination, ECG and laboratory findings with no abnormalities that are considered clinically significant by the principal investigator;

2. Laboratory values that are within the ranges specified below:

***

4.4. Life Style Guidelines

Subjects randomized into the study will receive counseling on how to reduce their caloric intake by 500 kcal/day and will be advised to increase their daily water intake. Subjects will be advised to initiate a lifestyle modification program utilizing the LEARN® Program for Weight Management.(20) The LEARN® program is designed as a 16-week program to aid in weight management by providing tools to facilitate lifestyle, exercise, attitude, relationship and nutrition changes. Each subject will be provided with a LEARN® manual and advised to read and implement the material as appropriate to their individual situation between study visits. Site personnel will discuss these materials with subjects at their regularly scheduled visits. However, no data will be collected to document the level of compliance with the program's dietary, lifestyle and/or exercise recommendations.

To facilitate discussions between study subjects and research staff, subjects will complete a 24-hour dietary recall at their randomization visit (Visit 2); however, information provided as part of this exercise will be used only for discussions related to recommended dietary modification and will not be retained as documentation. No data will be collected during the study to document the level of compliance with dietary recommendations.

5. TRIAL TREATMENTS

5.1. Allocation to Treatment

Subjects meeting the randomization requirements specified in Section 4.3 will be randomized to study treatment at visit 2 using a centralized computer-generated randomization system. Eligible subjects will be randomly assigned to *** or *** at a ratio of ***. Randomization will be stratified by ***, and at least *** of subjects will be ***. Both the subject and the study site will be blinded as to subject randomization.

To implement subject randomization among treatment groups, each participating site will be pre-stocked with titration kits corresponding to each treatment group. When a subject qualifies for randomization, site personnel will contact an Interactive Voice Response System (IVRS) and provide the information required regarding the study subject. The randomization assignment will then be made, and the site will be instructed to dispense a specific kit number to the study subject. Additional kits will be shipped to the site to replace those dispensed according to the randomization schedule. When subjects return for subsequent study visits, the IVRS system will also be used to dispense appropriate treatment kits.

5.2. Breaking the Blind

Study medication must not be unblinded during the study unless it is considered absolutely necessary by the investigator for the management of an adverse event or other medical emergency. Under such conditions, the identity of the study treatment will be obtained by contacting the IVRS. Any subject whose treatment assignment has been unblinded must discontinue participation in the study.

VIVUS will be notified of any unblinding of subject treatment group ***. Additionally, investigators are required to ensure that any potential serious adverse events are reported according to the requirements outlined in Sections 8.2 and 8.5 and to provide a written report on the reason for unblinding within ***.

5.3. Drug Supplies

5.3.1. Formulation and Packaging

Medications for this trial will consist of ***. Doses specified for each treatment group will be achieved by varying the *** added to each capsule. Regardless of the dosage assignment, all study treatments will be administered as a ***.

Clinical supplies will be manufactured for VIVUS, Inc. by *** in accordance with current Good Manufacturing Practices. All clinical supplies will be labeled with information required by national regulations. Study drug will be packaged into 2 types of kits; titration kits for use during the first 4 weeks of study therapy when doses are being increased gradually to the final

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assigned dose, and treatment kits, for use once subjects have been titrated to their assigned dosage of medication. Each titration kit will contain *** for use during weeks 1 through 4 of titration, with each ***. Each *** on the *** will be labeled with the *** and will contain capsules with the dose specified for that week of treatment, as outlined in Table 1.

Table 1: VI-0521 Dosage Strengths by Titration Week for Each Treatment Group

	***	***			
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***

Titration kits will be labeled with the ***. *** will be labeled with the ***.

Each treatment kit will consist of a single bottle *** of study medication at the final treatment dosages shown in Table 1. Each bottle will be labeled with the ***.

5.3.2. Preparation and Dispensing

Clinical supplies provided by the sponsor are to be dispensed only by or under the direct supervision of qualified investigators to subjects meeting the criteria for study entry and in accordance with this protocol. Assignment of specific titration and treatment drug kits to study subjects will require the use of the IVRS; however, no other preparation of clinical supplies is required of the investigational staff.

5.3.3. Administration

Investigators will instruct subjects to take 1 capsule of study medication every morning. When dispensing titration kits, investigators should ensure that subjects understand that each card contains a 4-week supply of medication, and that the capsules must be taken in ***. Investigators will also instruct subjects to return the study medication kit to the site at each site visit. For the week 2 visit, the site will perform drug accountability and redispense *** to the subject for use during titration weeks 3 and 4.

5.3.4. *

*** is an option for subjects who experience ***. *** is implemented through the ***, and will be done without ***. *** is not an option for subjects who experience ***.

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When *** is not appropriate or when *** may be required due to events unrelated to subject treatment, subjects may ***. *** are possible with agreement from the medical monitor. All subjects undergoing *** for *** may be *** based on discretion of the PI. If dosing has been ***, a new titration kit should be ordered through *** to ***. Subjects who have a ***. For subjects having a ***. For ***, subjects may ***.

If ***, subjects may be ***. Subjects *** will be encouraged to *** and to continue to make site visits at the regularly scheduled intervals. The last date on which the subject ***. If the subject ***. If the subject elects to withdraw completely from the trial (Section 6.4), the end of treatment (Visit 17) testing should be completed.

5.3.5. Compliance

Subject compliance with study medication will be assessed by ***, and *** should implement any corrective action necessary. Subjects who remain noncompliant with study dosing despite corrective actions by site personnel may be discontinued from the trial.

5.4. Drug Storage and Drug Accountability

All unused study drug must be stored in its packaging at room temperature in a dry, secure area. Access to drug storage areas should be limited to the investigator and designated staff involved with the study. All used and unused drug must be maintained at the study site and made available for audits by VIVUS personnel or their designee.

It should be noted that one component of the study drug combination is a Schedule IV controlled substance. The investigator should take all appropriate measures to control access to and dispensing of study drug.

The investigator must maintain records documenting the amount, condition and date of delivery of all study drug received from the sponsor. In addition, all drug dispensed to study subjects during the course of the study must be ***. Subjects must be instructed to *** by each subject. No investigational drug or packaging, used or unused, may be discarded. All packaging and used and unused drug must be returned to the sponsor upon completion of the study.

5.5. Concomitant Medication(s)

5.5.1. Excluded Medications

Subjects must not take the following medications during their participation in this trial:

- ***;
- ***;
- ***;

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- ***;
- ***.

Although subjects requiring antidiabetic medications other than metformin may not be entered into the study, subjects who develop the need for other antidiabetic medications during the course of the trial need not be discontinued. Refer to Section 5.6 for treatment and monitoring recommendations.

5.5.2. Other Restricted Medications

Subjects using *** or allowed *** must be on doses that have been stable for at least 3 months prior to screening. Subjects who develop symptoms indicative of *** during the course of the study need not withdraw but should be evaluated and managed as indicated (Section 5.8).

*** and *** are permitted, provided that the dosage has been stable for at least 1 month prior to screening, and the frequency of use does not exceed twice a week.

All other medications used for the treatment of *** associated with *** must be stable for at least 1 month prior to screening. However, adjustment of these medications is permitted during the trial if the subject's requirements for treatment change.

5.5.3. Documentation of Concomitant Medication Use

All concomitant medications, including over-the-counter products, vitamins and nutritional/herbal supplements, must be listed on the appropriate case report form (CRF) at trial entry. Any changes in concomitant medication during the course of the trial must be noted on the appropriate CRF.

5.6. Treatment of Diabetes

Subjects who are diabetic at study entry or who become diabetic during the course of the study will be provided with ***. Subjects will be instructed to ***. Diabetic subjects will ***.

*** is suggested as the initial therapy for *** type 2 diabetes ***. ***, including ***, should be reserved for subjects who cannot achieve adequate control with other modes of treatment. *** are prohibited, and subjects requiring treatment with these medications must be discontinued from the trial.

Subjects with consistently elevated fasting blood glucose values should ***. For this study, actionable levels for glucose values are ***. Subjects who note *** fasting glucose values *** in daily glucose monitoring logs during the week prior to a study visit would be considered appropriate for ***. Subjects whose fasting blood glucose ***, or whose blood glucose cannot be adequately controlled with the concomitant treatments allowed in this trial should be

discontinued from study treatment and referred back to their primary healthcare provider for additional glycemic management. Subjects may continue attending study visits ***.

During treatment, subjects whose fasting blood glucose is ***.

When discontinuing medications, *** should be discontinued first, followed by ***, and finally ***.

5.7. Treatment of ***

For subjects whose ***. If these medications are already present, ***.

Subjects whose ***, should be discontinued from study treatment and referred back to their primary healthcare provider for more intensive management. Subjects may continue attending study visits ***.

For subjects whose ***. For this trial, it is recommended that *** be the first medications to be reduced or withdrawn followed by ***, and lastly, ***.

5.8. Treatment of ***

Subjects who *** need not be discontinued from therapy. These subjects should be assessed clinically and with laboratory testing ***. Following evaluation, subjects found to be *** may be ***, as appropriate.

6. TRIAL PROCEDURES

This trial is being conducted in conjunction with a companion study (OB-302: A Phase III Randomized, Double-Blind, Placebo-Controlled Multicenter Study to Determine the Safety and Efficacy of VI-0521 in the Treatment of Obesity in an Adult Population with BMI $\geq$ ***) that is of similar design. The distinguishing factors between the two trials are related to the subject populations, specifically, the subjects enrolled into this trial will have a *** associated with obesity than the subjects enrolled into study OB-302. Because there is little overlap between the populations for these two trials, the majority of sites participating in this trial will also be conducting study OB-302. Because results of the screening evaluations may be required to determine which trial a particular subject qualifies for, the initial screening procedures for both of these trials are identical, and will be done under a generic screening informed consent. Once the determination of trial placement has been made a specific informed consent document for that study will be obtained and specific trial evaluations will continue. A schedule of study activities by visit is presented in Appendix 1. A detailed list of these activities is provided in the following sections.

6.1. Screening

Screening activities will take place at Visit 1 (generic) and Visit 1a (additional screening activities specific for this study). An oral glucose tolerance test (OGTT) will be performed at Visit 1a for all subjects eligible for study participation based on results from Visit 1 screening studies. The screening OGTT test should not be performed until initial screening results have been reviewed.

The screening physical examination and screening ECG may be performed at either Visit 1a or Visit 2 (prior to final evaluation and randomization). These studies should not be performed until initial screening results from Visit 1 have been reviewed.

For purposes of this study, Visit 1a is considered to be a part of Visit 1. In consequence, it is not necessary to obtain information on subject weight, waist circumference, vital signs, pregnancy test, ***, concomitant medications or adverse events at Visit 1a.

6.1.1. Visit 1

Activities at screening (Visit 1) are:

- Obtain written informed consent for screening evaluations;
- Obtain demographics (including age, race, gender, ethnicity, education, history of smoking, hypertension and dyslipidemia and family history of hypertension, smoking and premature cardiovascular disease) and medical history;
- Assess weight (kg), height (cm), waist circumference (cm) and BMI (note: the BMI calculation must be obtained from the IVRS following informed consent and should be obtained prior to initiating the testing described below);
- Assess vital signs;
- Record baseline concomitant medications;
- Administer *** and ***;
- Administer ***;
- Assess Inclusion/Exclusion Criteria;
- Obtain blood and urine samples for laboratory testing;
- Collect urine sample for pregnancy test (females of childbearing potential only) and perform pregnancy test;
- Schedule Visit 1a for OGTT testing in 1 week (± 2 days).

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6.1.2. Visit 1a

- Obtain study-specific written informed consent;
- Administer ***;
- Perform OGTT for all subjects eligible for participation by results of Visit 1 screening tests;
- Obtain blood and urine samples for biomarkers testing [C-reactive protein, microalbumin (urine) and creatinine (urine)];
- Collect blood sample for HgbA1c and C-peptide;
- Schedule the randomization visit (Visit 2) in 1 week (± 2 days).

6.2. Trial Period

6.2.1. Randomization (Visit 2)

Subjects eligible for treatment will be randomized and study drug dispensed at Visit 2. Activities at randomization are:

- Collect urine sample for pregnancy test (females of childbearing potential only) and perform pregnancy test;
- Perform complete physical examination (including neurological examination and auscultation for heart sounds);

- Obtain written informed consent for *** procedures and perform *** scan ***. *** scans may be performed between Visits 1 and 2, after results from Visit 1 indicate subject may be eligible to participate;
- Perform 12-lead electrocardiogram;
- Assess adverse events (including eye symptoms), if any;
- Obtain vital signs;
- Obtain weight and waist circumference measurements;
- Assess changes in concomitant medications;
- Evaluate randomization criteria (Section 4.3);
- Obtain 5 mL serum sample to be retained for possible use for scientific exploratory testing;
- Contact IVRS and obtain subject study medication identification;
- Administer *** for *** and ***;

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- Complete 24 hour dietary recall, distribute LEARN® materials and perform lifestyle counseling;
- Dispense study medication *** from the assigned kit and provide instructions for proper use;
- Schedule the next study visit in 2 weeks (± 2 days).

6.2.2. Titration (Visit 3)

Subjects will visit the study site at the end of the second week of titration (Visit 3). Activities at Visit 3 are:

- Obtain weight and waist circumference measurements;
- Obtain vital signs;
- Assess adverse events (including eye symptoms), if any;
- Assess concomitant medications;
- Administer *** and ***;
- Collect urine sample for pregnancy test (females of childbearing potential only) and perform pregnancy test;
- Review the study medication used since Visit 2; assess treatment compliance and perform drug accountability. Re-dispense the titration card to the subject for use during weeks 3 and 4;
- Perform brief review of lifestyle counseling and answer questions, if any;
- Schedule the next study visit in 2 weeks (± 2 days).

6.2.3. Treatment (Visits 4 through 16)

Subject titration will be completed on Visit 4; subsequently, subjects will return to the site at 4-week intervals for evaluation and to obtain additional study medication. Activities will be as follows:

- Obtain weight and waist circumference measurements;
- Obtain vital signs;
- Assess adverse events (including eye symptoms), if any;
- Assess concomitant medications;
- Administer *** and ***;

- Perform OGTT *(Visit 4 only)*;
- Collect urine sample for pregnancy test (females of childbearing potential only) and perform pregnancy test;
- Perform brief review of lifestyle counseling and answer questions, if any;
- Obtain fasting blood samples for blood chemistry testing *(Visits 4, 5, 7, 10 and 13 only).*
- Ensure that the previous dose of trial medications was taken between 20 and 28 hours ago, and obtain a *** blood sample for *** evaluations (if the previous dose of trial medications is outside this window, *** should be postponed for 1 day) *(Visits 7 and 10 only)*;
- Obtain samples for biomarkers: C-reactive protein (blood), microalbumin (urine) and creatinine (urine) *(Visit 10 only);*
- Obtain samples for HgbA1c **for diabetic subjects only** *(Visits 7 and 13 only);*
- Obtain samples for HgbA1c for all subjects *(Visit 10 only);*
- Obtain blood samples for hematology testing *(Visit 10 only);*
- Administer *** for *** and *** *(Visits 4, 7 and 10 only);*
- Administer *** and *** *(Visit 10 only);*
- Perform *** scan *** *(Visit 10 only);*
- Collect study medication from previous visit; assess for treatment compliance and perform drug accountability;
- Dispense study medication for the upcoming study interval and provide the proper instructions for use;
- Schedule the next study visit in 4 weeks (± 1 week).

6.2.4. End of Treatment (Visit 17 or Withdrawal from Study)

The end of treatment for subjects completing the study is Visit 17. End of treatment testing will also be performed for subjects who are withdrawn from treatment prior to completion of the study at the time of their treatment termination. For subjects who withdraw from the study prior to completion, the site will also attempt to contact the subject at or about the 56-week time point to obtain a weight measurement, waist circumference, blood chemistry panel and vital signs.

Activities at the end of treatment visit include:

- Obtain weight and waist circumference measurements;
- Obtain vital signs;

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- Assess adverse events (including eye symptoms), if any;
- Assess concomitant medications;
- Administer ***;
- Collect urine sample for pregnancy test (females of childbearing potential only) and perform pregnancy test;
- Administer ***;
- Administer *** and ***;
- Perform *** scan ***;
- Administer *** for *** and ***;

- Complete End of Treatment Questions: ***;
- Obtain fasting blood and urine samples for laboratory testing;
- Obtain samples for biomarkers: C-reactive protein (blood), HgbA1c (blood), microalbumin (urine) and creatinine (urine);
- Perform complete physical examination (including neurological examination and auscultation for heart sounds);
- Perform 12-lead electrocardiogram;
- Collect study medications dispensed at previous visit, assess treatment compliance and perform drug accountability;

6.3. Study Period

The study period for each subject will begin when written informed consent is provided and will continue until Visit 17 (week 56 or early termination) is completed. Sites should link the scheduling of visits to the randomization visit (Visit 2, week 0). Visit windows are provided to allow subject and site scheduling convenience. However, every effort should be made to ensure that visits occur within these windows so that the overall treatment duration is 56 weeks, including titration period, for subjects who complete all visits. In certain instances, adverse event information may be required for events occurring after the study period (Section 8.4).

6.4. Subject Withdrawal

Subjects may withdraw from the trial at any time and for any reason. Additionally, the subject may be withdrawn because of:

- Adverse event;
- Subject lost to follow-up;

- Requirement for other medical treatment excluded by the protocol;
- Lack of compliance with the provisions of the protocol;
- Treatment unblinded by investigator;
- Pregnancy;
- Lack of efficacy;
- Termination of trial.

Withdrawn subjects will not be replaced.

Subjects discontinued from treatment should be encouraged to remain in the trial off-treatment and to continue site visits at the scheduled intervals (Section 5.3.3). Subjects who withdraw completely from the trial at any point should complete the end of treatment (Visit 17, week 56) testing. The date of last dose should be recorded.

Every effort should be made to document subject outcome. For subjects who elect to withdraw from the trial without continuing site visits, the investigator should ***.

At about the 56 week time point, withdrawn subjects who have not continued site visits should be asked to return to the site to obtain weight and waist circumference measurements at a minimum and, if possible, the following additional information: adverse events, vital signs, laboratory tests (chemistry, hematology, urinalysis), concomitant medications, questionnaires ***.

If a subject withdraws from the trial and also withdraws consent for disclosure of future information, ***.

Investigators must discontinue trial participation for all subjects if the sponsor terminates the trial, and evaluations that would normally be performed upon trial completion should be made at that time. For subjects who have received ***, this includes obtaining information requested for the Visit 17 (week 56) end of treatment visit.

7. ASSESSMENTS

7.1. Weight Assessment and Waist Measurement

Subjects will be weighed (kg) and a waist circumference (cm) measurement obtained at each study visit (Visits 1-17). Height (cm) and BMI will be obtained at the screening visit (Visit 1) only.

7.1.1. Weight Assessment

Subjects should be weighed in kilograms using a calibrated digital scale. The same scale should be used for each measurement and measurements should be evaluated by the same site personnel at each visit, whenever possible. Subject weights should be obtained, whenever possible, under the same conditions (no shoes, clothing of similar weight) that were employed at the first (screening) weighing. Subjects should be encouraged to complete their weigh-in visits in the morning and should be fasting prior to weigh-in.

7.1.2. Waist Measurement

Waist circumference measurements (cm) will be performed using a measuring tape provided by VIVUS, Inc and should be obtained by the same individual at each visit, when possible. To measure the waist circumference, locate the top of the right iliac crest. Place the measuring tape in a horizontal plane (parallel to the floor) around the abdomen at the level of the top of the iliac crest as shown in Figure 2.

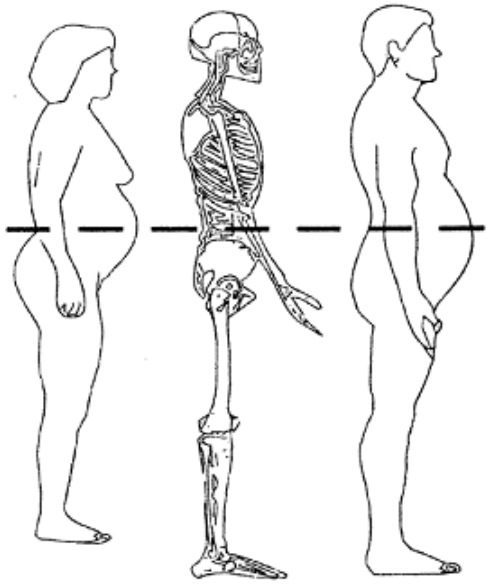

Figure 2. Measuring Tape Position for Waist Circumference Assessments

Ensure that the subject is relaxed. Ensure that the tape is snug but does not indent or compress the skin, and make the measurement (in centimeters) at the end of a normal expiration.(21)

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7.1.3. Height and BMI

Height measurements (cm) and BMI will be determined by the site at screening only. Height measurements should be made without shoes.

BMI will be calculated for purposes of screening using the IVRS. A printed copy of the BMI obtained from the IVRS should be retained as part of the subject's source documentation. Manual BMI calculations should not be performed.

If a subject does not meet the BMI criterion for inclusion into the study, no further screening procedures should be undertaken.

7.2. Vital Signs

Vital signs (systolic blood pressure, diastolic blood pressure, heart rate, respiration rate, temperature) will be assessed at screening and each study visit. Subjects should be seated comfortably for at least *** prior to assessing vital signs. Pulse rate and respiratory rate measurements should be made by counting events (heartbeats or breaths) for a period of 30 seconds and multiplying these values by 2 to obtain the rates per minute. A calibrated cuff should be employed for blood pressure measurements. Whenever possible, the same person should perform all assessments for a given subject.

7.3. Questionnaires

7.3.1. *

The *** for the assessment of ***.(22)-(24)

Because this instrument is intended to be completed ***, it is important that *** on this questionnaire in any way. Should subjects ***. Because this questionnaire assesses the ***. Site personnel, therefore, must carefully review questionnaires for completeness before ***, and assure that questionnaires are properly completed.

The *** is being used ***. This questionnaire will be completed at ***, and at ***after the ***. Answers to the questionnaire may reveal evidence of ***, including the ***. It is the responsibility of the investigator to evaluate ***. The evaluation by the Investigator will be guided by the ***. Investigators should document any such problems ***. It is expected that any randomized ***.

7.3.2. *

The ***(25) is an ***. Each of the ***, and is answered on a yes/no basis. This assessment will be administered to all *** at *** in order to confirm the *** included in the treatment program. Subsequent *** evaluations will be done at *** after ***. All *** assessments must be

administered by a trained interviewer. If any assessments reveal ***, then the results must be reviewed by a physician investigator prior to ***.

7.3.3. *

The *** that will be completed at *** and ***.

This questionnaire is designed to evaluate the ***.(26), (27) This instrument is intended to be completed ***.

Site personnel must ***. It is critical, therefore, that site personnel review questionnaires for completeness at the time they are initially filled out, and that any missing answers are completed before the ***.

7.3.4. *

The *** is a *** designed to evaluate ***.(28) This questionnaire is to be completed ***.

As with other questionnaires, site personnel ***.

Site personnel must also ***. It is critical, therefore, that site personnel review questionnaires for completeness at the time they are initially filled out, and that any missing answers are completed before the ***.

7.4. * and End of Treatment Questions**

7.4.1. *

*** for *** and *** will be assessed at *** and at the ***. For the *** assessment, subjects will *** For the *** assessment, a ***

7.4.2. End of Treatment Questions

At the end of treatment, subjects will be asked to respond to *** questions assessing ***. These questions are:

- ***.
- ***.
- ***

7.5. Laboratory Tests

Laboratory tests will be performed at a licensed, certified central testing laboratory identified by the sponsor. Urine pregnancy tests will be performed at the site using kits supplied by VIVUS,

Inc. Testing will be conducted according to the schedule provided below. For blood chemistry tests, the subject must have fasted for a minimum of 8 hours before the sample can be drawn.

Testing for phentermine and topiramate will be conducted in a sponsor-approved central laboratory using validated laboratory assays.

7.5.1. Blood Chemistry

Fasting blood chemistries will be evaluated at screening (Visit 1), Visit 4 (week 4), Visit 5 (week 8), Visit 7 (week 16), Visit 10 (week 28), Visit 13 (week 40) and end of treatment (Visit 17 or study withdrawal). Tests will be made for the following: albumin, alkaline phosphatase, alanine transaminase (ALT), aspartate amino transferase (AST), blood urea nitrogen (BUN), serum calcium, serum chloride, serum sodium, bicarbonate, creatinine, creatinine clearance, direct bilirubin, gamma-glutamyl transferase (GGT), glucose, lactate dehydrogenase (LDH), serum phosphorus, serum potassium, total bilirubin, total cholesterol, total protein, uric acid, triglycerides, HDL cholesterol (HDL-C) and LDL cholesterol (LDL-C).

7.5.2. Oral Glucose Tolerance Test

An oral glucose tolerance test (OGTT) will be obtained at Visit 1a (after results from Visit 1 indicate the subject may be eligible for participation), at Visit 4 (week 4) and at end of treatment (Visit 17 or study withdrawal) for all subjects.

The OGTT will use a 75 g glucose loading dose; samples will be obtained at baseline and at 2 hours post dose for evaluation of both glucose and insulin levels.

7.5.3. Hematology

Hematology studies will be evaluated at screening (Visit 1), Visit 10 (week 28) and end of treatment (Visit 17 at week 56 or study withdrawal) for hemoglobin, hematocrit, red blood cell count (RBC), total white blood cell count (WBC), WBC differential (neutrophils, lymphocytes, monocytes, eosinophils, basophils) and platelet count.

7.5.4. Urinalysis

A routine midstream urinalysis with reflex microscopic evaluation will be obtained at screening (Visit 1) and end of treatment (Visit 17 or study withdrawal).

7.5.5. Biomarkers

Appropriate blood and urine biomarkers [C-reactive protein, microalbumin (urine) and creatinine (urine)] will be evaluated at screening (Visit 1a), Visit 10 (week 28) and end of treatment (Visit 17 or study withdrawal). Additionally, adiponectin, intercellular cell adhesion molecule (I-CAM),

vascular cell adhesion molecule (V-CAM), retinal binding protein 4 (RBP-4), plasminogen activator inhibitor 1 (PAI-1) and fibrinogen will be evaluated at screening (Visit 1a) and end of treatment (Visit 17 or study withdrawal). With the exception of urine microalbumin and creatinine, all post-screening biomarker results will be blinded to investigators and sponsor.

7.5.6. Hemoglobin A1c

Hemoglobin A1c (HgbA1c) testing will be performed at screening (Visit 1a) Visit 10 (week 28) and end of treatment (Visit 17 or study withdrawal) for all subjects. Additionally, HgbA1c testing will be performed at Visit 7 (week 16) and Visit 13 (week 40) for diabetic subjects.

7.5.7. Urine Pregnancy Test

A urine pregnancy test will be obtained for females of childbearing potential at each study visit (Visits 1-17). Urine pregnancy testing will be performed at the site and results reported on the appropriate CRF.

Female subjects who have undergone a hysterectomy or bilateral oophorectomy, who have a follicle stimulating hormone level > 40 IU/L or who are 55 years of age or greater and have experienced cessation of menses for at least 1 year are considered to not be of childbearing potential. Urine pregnancy testing is not required in these subjects.

Management of any subject who becomes pregnant during this study is described in Section 8.5.3.

7.5.8. Thyroid Stimulating Hormone (TSH)

A test for thyroid stimulating hormone (TSH) will be conducted at screening (Visit 1).

7.5.9. Antibody to HIV, HCV, HBsAg

Testing for hepatitis B surface antigen (HBsAg) and antibodies to human immunodeficiency virus (HIV) and hepatitis C virus (HCV) will be conducted at screening.

7.5.10. C-Peptide

A test for C-peptide will be conducted at screening (Visit 1a).

7.5.11. Screening Serum Sample (Retain)

A 5.0 mL serum sample will be obtained at Visit 2 to be retained at the central laboratory for possible use in scientific experimental studies.

7.5.12. Urine Drug Screen

A urine drug screen will be conducted at screening. Subjects will be tested for cannabinoids, cocaine, amphetamines, opiates and phencyclidine.

7.6. * Evaluation**

Samples for the evaluation of *** will be obtained at ***.

Subjects should be advised at the previous visit to refrain from dosing with study medication until after the clinic visit on *** and should be reminded about 1 week prior to the visit to delay dosing on the days of *** until after testing at the site. If the subject has taken study medication < 20 hours prior to the clinic visit, *** should be postponed until the next day.

7.7. Physical Examination

A complete physical examination will be performed at Visit 2 (prior to review for randomization) and at Visit 17 (week 56) or early withdrawal. The screening examination should not be performed until results of testing at Visit 1 have been reviewed to confirm that the subject may be eligible for treatment.

The physical examination will consist of the following: general appearance, skin, head, eyes, ears, nose, throat, neck (including thyroid), lymph nodes, chest, heart (including auscultation for heart sounds and murmurs), abdomen, extremities, and neurological examination. Subjects will be evaluated for clinically significant abnormalities that would prevent entry into the study and for clinically significant differences between screening and end of treatment.

7.8. Electrocardiogram (ECG)

Twelve-lead electrocardiographic studies will be obtained at Visit 2 (prior to review for randomization) and the end of treatment (Visit 17 or early withdrawal). Screening ECG studies should not be performed until results of testing at Visit 1 have been reviewed to confirm initial subject eligibility for treatment. Whenever possible, ECGs should be obtained in the morning with the timing of the studies matched as closely as possible. Studies will be evaluated for clinically significant abnormalities that would prevent entry into the study and for clinically relevant changes between screening and end of treatment. Parameters including R-R, QRS, QT, and QTc intervals will also be recorded.

7.9. Framingham Risk Score

The Framingham risk assessment evaluates the 10-year risk for development of coronary heart disease.(29) In order to calculate the Framingham risk, the following information will be recorded at screening: demographics (age, gender, race, and ethnicity), medical history (including histories of smoking, diabetes, congestive heart failure, myocardial infarction, hypertension, and

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dyslipidemia) and family history of premature cardiovascular disease. The Framingham risk assessment will be calculated by VIVUS, Inc. or its designee based on data provided on the CRF.

7.10. Body Composition

At a selected subset of study sites, body composition assessments will be made at baseline (Visit 2), week 28 (Visit 10) and week 56 (Visit 17) using ***. Scans will be collected at a sufficient number of study sites to provide body composition data on approximately *** subjects from this study combined with protocol OB-302. Equipment and procedures used to obtain *** data will be standardized as described in a separate document. All sites will be trained on these procedures prior to performing scans on study subjects. Scans will be read at a central facility and the reader will be blinded.

8. Adverse Event Reporting

8.1. Adverse Events

Adverse events (AEs) are defined as any untoward medical occurrences in subjects administered the trial treatment, whether or not they have a causal relationship to the treatment. All observed or volunteered adverse events regardless of suspected causal relationship to the investigational product must be reported as described in the following sections.

The investigator must pursue and obtain information adequate to describe adverse events, their severity and relationship to study treatment, and their outcomes. Descriptions of neurological or psychological adverse events should be consistent with standard diagnostic criteria and terminology (such as DSM-IV) rather than general reports of symptoms. For adverse events with a causal relationship to the investigational product, follow-up by the investigator is required until the events or their sequelae resolve or stabilize at a level acceptable to the investigator, and VIVUS concurs with that assessment. Investigators must also assess whether adverse events meet the criteria for classification as serious adverse events (see Section 8.2) requiring immediate notification to VIVUS or its designated representative.

8.1.1. Severity Assessment

The investigator will assess the severity of all adverse events using the ***, ***, or *** to describe the maximum intensity of each adverse event. For purposes of consistency, these intensity grades are defined as follows:

- ***;
- ***;
- ***.

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Note the distinction between the severity and the seriousness of an adverse event. A *** is not necessarily a ***. For example, a headache may be *** but would not be classified as serious unless it met one of the criteria for ***.

8.1.2. Causality Assessment

Trial investigators are required to provide an assessment of causality for all adverse events (serious and non-serious) observed during this trial. This assessment will provide a determination of whether, in the investigator's judgment, there exists a reasonable possibility that the investigational product caused or contributed to an adverse event. For this assessment, investigators must categorize the causality as either "related" or "not related." For an adverse event to be considered "related" to the trial treatment, there should be evidence that the event follows a reasonable temporal sequence from the administration of trial treatment or that the event follows a known response pattern to the drug. Causality would be further confirmed by improvement in the adverse event upon stopping the trial treatment and reappearance of the event upon rechallenge.

8.1.3. Abnormal Test Findings

The criteria for determining whether an abnormal objective test finding should be reported as an adverse event are as follows:

- Test result is associated with accompanying symptoms, and/or
- Test result requires additional diagnostic testing or medical/surgical intervention, and/or
- Test result leads to a change in trial dosing or discontinuation from the trial, significant additional concomitant drug treatment, or other therapy, and/or
- Test result is considered by the investigator or sponsor to represent a clinically significant finding.

Merely repeating an abnormal test, in the absence of any of the above conditions, does not constitute an adverse event. Any abnormal test result that is determined to be an error does not require reporting as an adverse event.

8.2. Serious Adverse Events

As defined in the Code of Federal Regulations (21 CFR 312.32), a serious adverse event or serious adverse drug reaction is any untoward medical occurrence at any dose that:

- Results in death;
- Is life-threatening (immediate risk of death);
- Requires inpatient hospitalization or prolongation of existing hospitalization;

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- Results in persistent or significant disability/incapacity;
- Results in congenital anomaly/birth defect.

Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious adverse drug experiences when, based on appropriate medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed above. Adverse events that, in the investigator's judgment, significantly jeopardize trial subjects or require medical or surgical intervention in order to prevent any of the outcomes listed above should therefore be reported as serious adverse events.

8.2.1. Definition of Hospitalization

Adverse events reported from clinical trials that result in hospitalization or prolong an existing hospitalization are considered serious. Any initial admission (even if less than 24 hours) to a healthcare facility meets these criteria.

Outpatient ambulatory surgical procedures (same day surgeries) and routine emergency room treatment do not qualify as hospitalizations. Additionally, hospitalization in the absence of a precipitating, clinical adverse event is not in itself a serious adverse event. Examples include, but are not limited to:

- Admission for treatment of a preexisting condition not associated with the development of a new adverse event or with a worsening of the preexisting condition (e.g., for work-up of persistent pre-treatment lab abnormality);
- Administrative admission (e.g., for yearly physical exam);
- Optional admission not associated with a precipitating clinical adverse event (e.g., for elective cosmetic surgery);
- Pre-planned treatments or surgical procedures should be noted in the baseline documentation for the entire protocol and/or for the individual subject.

Diagnostic and therapeutic non-invasive and invasive procedures, such as surgery, should not be reported as adverse events. However, the medical condition for which the procedure was performed should be reported if it meets the definition of an adverse event. For example, an acute appendicitis that begins during the adverse event reporting period should be reported as the adverse event, and the resulting appendectomy should be recorded as treatment of the adverse event.

8.3. Eliciting Adverse Event Information

The investigator is to report all directly observed adverse events and all adverse events spontaneously reported by the trial subject. In addition, trial subjects should be ***

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Certain adverse events require prompt and specific action by the investigator in any clinical trial. The following sections describe additional requirements to ensure ***.

8.3.1. Eye Pain

At each visit, subjects will be queried regarding eye symptoms, *** Subject responses will be recorded as adverse events, where appropriate. If any subject reports eye pain and/or ***, the subject should be referred to ***. Treatment with study drug should be discontinued until the ***.

8.3.2. *

All subjects will be screened for the presence and *** at *** and subsequently at *** after the *** using a validated survey instrument *** designed for assessment of *** in a primary care setting. The *** is a *** module based directly on the diagnostic criteria for ***. *** will also be assessed at *** and at *** following the *** using the ***.

Should this additional assessment indicate the presence of ***. Any such event must be ***. Subjects must be ***.

Any *** must be ***.

8.3.3. Hypoglycemia

Guidelines for the reporting of adverse events based on results obtained in *** maintained by *** are summarized in Table 2.

Table 2. Guidelines for adverse event reports based on *.**

***	***	***	***	***
***	***	***	***	***
***	***	***	***	***
***	***	***	***	***

***	***	***	***	***
***	***	***	***	***
***	***	***	***	***

8.4. Reporting Period

The reporting period for adverse events begins when the subject provides written informed consent and extends until *** after the last dose of the investigational product is administered. All adverse events that occur during this period and are known to the investigator must be reported according to the requirements outlined in Section 8.5.

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8.5. Reporting Requirements

All adverse events will be reported on the adverse event page(s) of the CRF. In addition, serious adverse events must also be reported on a separate Serious Adverse Event form. Where the same data are collected, the forms must be completed in a consistent manner. For example, the same adverse event term should be used on both forms. Adverse events should be reported using concise medical terminology on the CRFs as well as on the form for collection of serious adverse event information.

8.5.1. Serious Adverse Event Reporting Requirements

If a serious adverse event occurs, VIVUS, Inc. or designee is to be notified within 1 business day of awareness of the event by the investigator. In particular, if the serious adverse event is fatal or life-threatening, notification to VIVUS, Inc. or designee must be made immediately, irrespective of the extent of available adverse event information. This timeframe also applies to additional new information (follow-up) on previously forwarded serious adverse event reports.

***

For all serious adverse events, the investigator is obligated to pursue and provide information to VIVUS, Inc. or designee in accordance with the timeframes for reporting specified above. In addition, an investigator may be requested by VIVUS, Inc. or designee to obtain specific additional follow-up information in an expedited fashion. This information may be more detailed than that captured on the adverse event case report form. In general, this will include a description of the adverse event in sufficient detail to allow for a complete medical assessment of the case and independent determination of possible causality. Information on other possible causes of the event, such as concomitant medications and illnesses, must be provided. In the case of a subject death, a summary of available autopsy findings must be submitted as soon as possible to VIVUS, Inc. or its designated representative.

8.5.2. Non-Serious Adverse Event Reporting Requirements

Non-serious adverse events are to be reported on the adverse event CRFs, which are to be submitted to VIVUS, Inc. or its designee.

8.5.3. ***

If any trial subject becomes or is found to be *** while receiving the investigational product, the investigator must submit this information to VIVUS, Inc. on an ***.

The investigator will follow the *** and then notify VIVUS, Inc. or its designee of the outcome. The investigator will provide this information as a follow up to the ***.

For reported ***. The status of an ***.

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If *** meet the criteria for immediate classification as a serious adverse event ***, the investigator should follow the procedures for reporting serious adverse events. Similarly, any *** that are considered to be adverse events should be reported as such on the appropriate CRF. However, *** need not be reported as an adverse event if there is no associated adverse outcome.

For reporting purposes, *** should be reported as serious adverse events, but because the ***.

9. DATA ANALYSIS/STATISTICAL METHODS

9.1. Sample Size Determination

In a previous *** study evaluating the effects of VI-0521, subjects treated with a *** had a mean (SD) weight loss of *** for subjects receiving *** treated subjects. If similar standard deviations are achieved in the present trial, the planned sample size of at least 500 subjects per treatment group should provide *** power to detect these differences.

9.2. Efficacy Analysis

9.2.1. Analysis of Primary Endpoints

The primary hypotheses are:

***

The primary calculated endpoints for the trial are the percent weight loss at week 56 calculated as *** and the percentage of subjects achieving at least 5% weight loss at week 56.

The intent to treat (ITT) population (Section 9.2.1.3) is the primary analysis population. For subjects who discontinue treatment prior to trial completion, every attempt will be made to have them return to the clinic at week 56 for a final weight assessment, regardless of when they discontinued treatment. For subjects who ***.

Comparisons between treatments for percent weight loss will be assessed using an *** with factors of ***, ***and ***, and with ***. Comparisons between treatments for the percentage of subjects achieving at least 5% weight loss will be assessed by *** with ***, ***, and *** and ***. A step-down multiple comparison procedure will be used to compare each dose group with ***. That is, comparison with *** will start at the ***. If the statistical test is significant for both co-primary end points at ***, then the test will proceed to the *** also at ***. If the statistical comparison is not significant at the *** for the *** when compared with ***, then the statistical test will be stopped and the *** will not be tested.

If both dose groups are significantly better than ***, then the *** and *** dose groups will be compared. The *** for the difference in the mean percent body weight reduction between treatment groups will be derived.

The cumulative probability distribution as a function of percentage change in body weight for each treatment group will be plotted.

9.2.2. Analysis of Secondary Endpoints

Secondary efficacy endpoints are:

- The difference in absolute weight loss between randomization (baseline) and end of treatment (week 56) for *** and *** groups.
- The difference in percent of subjects who achieve a reduction in total body weight of at least 10% between randomization (baseline) and end of treatment (week 56) for *** and *** groups.
- The difference in change in waist circumference (randomization to week 56) for *** and *** groups.

The ITT population will be employed to evaluate all secondary efficacy endpoints, and a step down strategy analogous to that used for the primary endpoint will be implemented to protect the overall alpha levels for these.

The difference in absolute weight reduction and the difference in waist reduction at week 56 from baseline will also be compared using the same *** as the primary end point. *** with ***, *** and *** and ***, will be used to compare the probability of reaching 5% and 10% body weight reduction from baseline to week 56 between treatment groups.

9.3. Analysis of Other Endpoints

9.3.1. Other Efficacy Endpoints

The changes in primary and secondary outcomes over monthly intervals during the study will be evaluated. The methodology for these comparisons will be similar to that used for primary and secondary endpoints. Details of these analyses will be provided in the Statistical Analysis Plan.

The *** data will consist of ***, each of which will be analyzed separately, and a ***. Similarly, the *** will consist of ***. These ***. Changes from baseline will be summarized using *** and ***. Effect sizes (change divided by baseline standard deviation) will also be summarized. Changes from baseline will be compared between treatment groups using *** as appropriate for *** and for *** assessments of eating behavior. Results of the *** questions will be calculated for each study group and compared.

Changes in BMI between baseline and Visits 10 and 17 (weeks 28 and 56) and change in Framingham 10-year risk assessments between baseline and Visits 10 and 17 (weeks 28 and 56) will be evaluated. For these analyses, BMI and Framingham risk scores will be calculated by the central analysis group.

The change from baseline to Visit 17 (week 56) in the number and dosage of medications used to treat cardiovascular or metabolic risk factors will be calculated.

In the *** of subjects treated at ***, changes from *** to *** and *** in percent lean body mass and percent *** will be evaluated. Differences between treatment groups will be evaluated using methods similar to those used to evaluate other continuous variables. For these evaluations, data will be pooled from protocols OB-302 and OB-303.

9.3.2. * Analysis**

*** will be obtained during this trial using a multiple trough sampling scheme, where samples are obtained from each subject at ***. These data will be combined for analyses with data from other Phase 3 trials that will utilize similar sampling schemes. *** analyses will characterize the *** for both drugs. The effects of various covariates including (but not limited to) ***, gender, race, *** and age will be evaluated.

9.4. Analysis Populations

Intent-to-treat (ITT) and safety populations: All subjects who are randomized, take one or more doses and have at least one post dosing assessment will be included in the ITT and safety populations.

9.5. *

For those subjects who ***. If a subject ***.

9.6. *

***

9.7. Safety Analysis

Safety analyses will be performed on the safety population and will include all data on all doses reported during the study.

9.7.1. Adverse Events

Adverse events will be coded using a MedDRA coding dictionary. The number and percentage of subjects who reported at least one adverse event in each system organ class and preferred term

category, and the total number and percentage of subjects with any AE over all system organ classes will be summarized by treatment group.

Subsets of AEs that are considered serious or required discontinuation of the study medication will be listed by subject and presented separately.

9.7.2. Clinical Laboratory Tests

A summary of observed values and change from baseline will be presented for all laboratory parameters with numerical measures using descriptive statistics. Shift tables displaying low-normal-high at baseline versus low-normal-high at end of treatment in a 3-by-3 contingency table will be provided. For selected laboratory parameters, scatter plots of baseline versus week 56 results, will be produced by treatment group.

A laboratory value that is above or below normal range will be considered an abnormal value. For selected laboratory parameters, threshold limits of clinical concern will be defined as multiplicative factors of the normal ranges. The list of multiplicative factors for each laboratory parameter will be included in the Statistical Analysis Plan. The frequency and percentage of subjects with laboratory results above or below the normal range and threshold limits at each scheduled assessment or any time during the treatment will be summarized by treatment group.

9.7.3. Vital Signs and Other Safety Evaluations

Mean blood pressures, heart rate, respiration rate and temperature, obtained at each visit, will be summarized and plotted by treatment group. Medications, other than study medication, taken during the study will be considered as concomitant medications. They will be summarized by treatment group according to the preferred terms, using the World Health Organization (WHO) Drug Dictionary.

9.7.4. Questionnaire Assessments

Changes in total *** will be summarized by treatment group *** and ***. Since the proposed indication for the study medication is weight loss, ***. Descriptive summaries of individual questionnaire items will also be presented.

9.8. Interim Analysis

An interim analysis may be conducted once approximately half of the study subjects have completed the intended course of treatment to provide information for the planning of future clinical trials that may be designed or commenced prior to the completion of this trial. No changes will be made to the conduct of the present study, including premature termination or increased sample size, based on the results of this interim analysis and no adjustments to the significance level for the primary hypothesis will be made if this interim analysis is conducted.

9.9. ***

***

10. QUALITY CONTROL AND QUALITY ASSURANCE

During trial conduct, VIVUS, Inc. or its agent will conduct periodic monitoring visits to ensure that the protocol and GCPs are being followed. The monitors may review source documents to confirm that the data recorded on CRFs are accurate. The investigator and institution will allow VIVUS, Inc. monitors or its agents and appropriate regulatory authorities direct access to all appropriate source documents to perform this verification.

The trial site and trial-related documents may be subject to review by the institutional review board (IRB)/independent ethics committee (IEC), and/or to quality assurance audits performed by VIVUS, Inc. or its agents and/or to inspection appropriate regulatory authorities. Refer to Section 13.

It is important that the investigator(s) and their relevant personnel are available during the monitoring visits and possible audits or inspections and that sufficient time is devoted to the process by the investigator and site personnel.

11. DATA HANDLING AND RECORD KEEPING

11.1. Case Report Forms / Electronic Data Record

As used in this protocol, the term case report form (CRF) should be understood to refer to either a paper form or an electronic data record or both, depending on the data collection method used in this trial.

A CRF is required and should be completed for each included subject. The completed original CRFs are the sole property of VIVUS, Inc. and should not be made available in any form to third parties, except for authorized representatives of VIVUS, Inc. or appropriate regulatory authorities, without written permission from VIVUS, Inc.

It is the investigator’s responsibility to ensure CRF completion and to review and approve all CRFs. CRFs must be signed by the investigator or by an authorized staff member. These signatures serve to attest that the information contained on the CRFs is complete and accurate. At all times, the investigator has final personal responsibility for the accuracy and authenticity of all clinical and laboratory data entered on the CRFs. Subject source documents are the physician’s subject records maintained at the trial site. In most cases, the source documents will be the hospital’s or the physician’s chart. In cases where the source documents are the hospital or the physician’s chart, the information collected on the CRFs must match those charts.

11.2. Record Retention

To enable evaluations and/or audits from regulatory authorities or VIVUS, Inc., the investigator will keep records, including the identity of all participating subjects (sufficient information to link records, eg, CRFs and hospital records), all original signed informed consent forms, copies of all CRFs, serious adverse event forms, source documents, and detailed records of treatment disposition. The records should be retained by the investigator according to specifications in the ICH guidelines, local regulations, or as specified in the Clinical Study Agreement, whichever is longer. The investigator must obtain written permission from VIVUS before disposing of any records, even if retention requirements have been met.

If the investigator relocates, retires, or for any reason withdraws from the trial, VIVUS, Inc. should be prospectively notified. The trial records must be transferred to an acceptable designee, such as another investigator, another institution, or to VIVUS, Inc.

12. ETHICS

12.1. Institutional Review Board (IRB)/Independent Ethics Committee (IEC)

Regulations require that an IRB/IEC oversee all investigational drug studies. This board or committee, the makeup of which must conform to local and regional regulations, will approve all aspects of the study, including the protocol, advertising and written informed consent form to be used prior to initiation of the study. It is the responsibility of the investigator to have prospective approval of the trial protocol, protocol amendments, informed consent forms and other relevant documents, eg, advertisements, if applicable, from the IRB/IEC. All correspondence with the IRB/IEC should be retained in the Investigator File. Copies of IRB/IEC approvals should be forwarded to VIVUS, Inc. or designee. All correspondence with the IRB/IEC should be retained in the Investigator file and copies forwarded to VIVUS, Inc. or designee.

All amendments to the protocol must be reviewed and approved by VIVUS, Inc. and the IRB/IEC prior to implementation. The only circumstance in which an amendment may be initiated prior to IRB/IEC approval is where the change is necessary to eliminate apparent immediate hazards to the subjects. In that event, the investigator must notify the IRB/IEC and VIVUS, Inc. in writing within 5 working days after the implementation.

The investigator is responsible for obtaining annual (at a minimum) IRB/IEC renewal for the duration of the study. The investigator is also responsible for keeping the IRB/IEC advised of the progress of the study, of any changes made to the protocol as deemed appropriate, but at least once a year. Copies of the investigator's report and of the IRB/IEC extension approval must be forwarded to VIVUS, Inc. or designee.

12.2. Ethical Conduct of the Trial

The trial will be performed in accordance with the protocol, International Conference on Harmonization Good Clinical Practice (ICH-GCP) guidelines and applicable local regulatory requirements and laws.

12.3. Subject Information and Consent

The informed consent form and any changes to the informed consent form made during the course of the trial must be agreed to by VIVUS, Inc. or designee and the IRB/IEC prior to its use and must be in compliance with all ICH-GCP, local regulatory requirements and legal requirements.

The investigator must ensure that each trial subject is fully informed about the nature and objectives of the trial and possible risks associated with participation and must ensure that the subject has been informed of his/her rights to privacy. The investigator will obtain written informed consent from each subject before any trial-specific activity is performed and should document in the source documentation that consent was obtained prior to enrollment in the trial. The original signed copy of the informed consent form must be maintained by the investigator and is subject to inspection by a representative of VIVUS, Inc., their representatives, auditors, the IRB/IEC and/or regulatory agencies. A copy of the signed informed consent form will be given to the subject.

12.4. Disclosure of Data

Data generated by this trial must be available for inspection by the U.S. Food and Drug Administration (FDA), by the sponsor or a designate acting on behalf of the sponsor, by applicable foreign health authorities, and by the IRB or IEC as appropriate. At a subject's request, medical information may be given to their personal physician or other appropriate medical personnel responsible for their welfare.

Subject medical information obtained during the course of this trial is confidential and disclosure to third parties other than those noted above is prohibited.

13. REGULATORY CORRESPONDENCE

The trial site and trial-related documents may be subject to review by the IRB/IEC and/or to quality assurance audits performed by VIVUS, Inc. or its designee and/or to inspection by the FDA and/or applicable foreign health authorities. The investigator will notify VIVUS, Inc. within *** working days following any FDA or other regulatory agency contact with the investigative site regarding this study. The investigator will provide VIVUS with copies of all correspondence with the FDA or other regulatory agency which may affect the review of the current study (e.g., Form 483, Inspection Observations) or their qualification as an investigator in studies conducted by VIVUS, Inc. (e.g., warning letters).

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14. Definition of end of trial

The end of trial is defined as the date when the last subject completes the last trial visit.

Additionally, data and materials that are required by the Sponsor before any trial site's activity can be considered complete include:

- All completed Case Report Forms, appropriately signed by the investigator;
- All laboratory findings, clinical data and special test results collected during the trial period;

- Completed drug accountability and investigational materials return records;
- Statement of outcome for any serious adverse events reported during the study;
- Copy of notification to IRB or IEC indicating study completion.

15. SPONSOR DISCONTINUATION CRITERIA

Premature termination of this clinical trial may occur because of a regulatory authority decision, change in opinion of the IRB/IEC, drug safety problems, or at the discretion of VIVUS, Inc. In addition, VIVUS, Inc. retains the right to discontinue development of VI-0521 at any time.

If a trial is prematurely terminated or discontinued, VIVUS, Inc. will promptly notify the investigator. After notification, the investigator must contact all participating subjects within 15 days. As directed by VIVUS, Inc., all trial materials must be collected and all CRFs completed to the greatest extent possible.

16. PUBLICATION OF TRIAL RESULTS

All information and data, including the terms of this protocol, and all data, clinical results, and research conducted hereunder concerning VIVUS, Inc's products and operations including VIVUS, Inc. patent applications, formulas, manufacturing processes, basic scientific data, and formulation information that has been supplied by VIVUS, Inc. and not previously published are considered confidential by VIVUS, Inc. and will remain the sole property of VIVUS, Inc. The investigator understands and agrees that said proprietary and/or confidential information disclosed to or produced by him/her thereunder is highly valuable to VIVUS, Inc. and will be used exclusively by the investigator in accomplishing this study and will not be used for any other purposes without VIVUS, Inc's prior written consent. The investigator agrees that he/she will not use any such proprietary and/or confidential information for any other purpose. The investigator also understands and agrees that such disclosure will not be deemed to grant to the investigator a license for use of said proprietary and/or confidential information, except as expressly provided herein.

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It is understood by the investigator that the information developed in the clinical study will be used by VIVUS, Inc. in connection with the development of this product. This information, therefore, may be disclosed and used solely by VIVUS, Inc. as required to such third parties and agencies as VIVUS, Inc., in its sole discretion, warrants. In order to allow for the use of the information derived from the clinical studies, it is understood that there is an obligation to provide to VIVUS, Inc. complete test results and all data developed in this study. The investigator agrees to promptly answer all inquires from VIVUS, Inc. regarding completion, legibility or accuracy of trial data in the case report.

VIVUS, Inc. recognizes the value of disseminating research results and expects that publication of all results from this study will be undertaken by a collaborative group of study investigators who made significant contributions to the study design, the treatment of study subjects, and evaluation of study data. However, after 1) submission of the multicenter results for publication, 2) notification ***.

Investigators shall furnish the *** with a written copy of any proposed publication or other disclosure of study results (including disclosures at research seminars, lectures and professional meetings) *** prior to submission for publication or disclosure so that *** may have a reasonable opportunity to protect its proprietary rights to information, inventions, or products developed under this study and to insure that reported data are factually correct. Upon the ***, the investigator shall not publish or disclose information related to this study. Further, if the *** believes that such publication or disclosure contains confidential information, the investigator agrees to remove such confidential information from the proposed publication or disclosure.

VIVUS, Inc. agrees that before it publishes any results of this study in a refereed journal, it will provide the investigator, for review, a prepublication manuscript *** prior to the submission of the manuscript to the publisher.

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APPENDIX 1: SCHEDULE OF STUDY ACTIVITIES

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APPENDIX 2: ***

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APPENDIX 3: ***

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APPENDIX 4: ***

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APPENDIX 5: PROTOCOL AMENDMENTS

Amendment Tracking

Protocol Title: **A Phase III Randomized, Double-Blind, Placebo controlled Multicenter Study to Determine the Safety and Efficacy of VI-0521 in the Treatment of Obesity in Adults with Obesity-Related Co-Morbid Conditions**

Protocol Number: **OB-303**

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Amendment Number 3
Date of Amendment: ***
(19 items)

Rationale: This protocol amendment is being implemented at the request of the FDA to incorporate assessments of *** and *** using the ***, and assessments of *** using the *** in all study subjects at ***. Previously, follow-up *** evaluations were done only if other *** assessments revealed a ***. This amendment also provides for body composition assessments at selected sites using ***. These changes are not anticipated to have any impact on the safety of study subjects.

Section and/or Item	Protocol Date	Amendment 3, *** Change Effected
Protocol Synopsis: Efficacy Endpoints — Secondary efficacy endpoints are:	***	Added: "**Effect on body composition as indicated by ***. *** assessments will be performed at only at a ***.**"
Protocol Synopsis: Safety Endpoints	***	Change: "***" To: "**Follow-up assessments will be done at *** after ***."**

List of Abbreviations	***	Added: "*******"
Rationale	***	Change: "VI-0521 is an exploratory weight loss therapy that is a new combination of two currently approved drugs, phentermine and topiramate." To: "VI-0521 is an **investigational** weight loss therapy that is **a combination** of two currently approved drugs, phentermine and topiramate."
Trial Design: Additional	***	Added: "**Change from *** to *** and *** in body composition [assessed by**

efficacy endpoints will include the following:		***** at ***].**" Change: "Safety evaluations will include assessment of adverse events, including eye symptoms, ***" To: "Safety evaluations will include assessment of adverse events, including eye symptoms, *****"**
Trial Period: Randomization (Visit 2)	***	Added: "**Obtain written informed consent for *** procedures and perform *** scan ***. *** scans may be performed between Visits 1 and 2, after results from Visit 1 indicate subject may be eligible to participate;**" Change: "Assess adverse events (including eye symptoms and ***), if any;" To: "Assess adverse events (including **eye symptoms**), if any;"
Trial Period: Titration (Visit 3)	***	Added: "**Administer *** and *****;" Change: "Assess adverse events (including eye symptoms and ***), if any;" To: "Assess adverse events (including **eye symptoms**), if any;"
Trial Period: Treatment (Visits 4 through 16)	***	Added: "**Administer *** and *****;" Delete: "Administer *** *(Visits 7, 10, and 13 only);"* Change: "Assess adverse events (including eye symptoms and ***), if any;" To: "Assess adverse events (including **eye symptoms**), if any;" Added: **"Perform *** scan *** *(Visit 10 only);"***
End of Treatment (Visit 17 or Withdrawal from Study)	***	Added: "**Administer *****;" Change: "Assess adverse events (including eye symptoms and ***), if any;" To: "Assess adverse events (including **eye symptoms**), if any;" Added: "**Perform *** scan ***;"**
Subject Withdrawal	***	Change: "At about the 56 week time point, withdrawn subjects who have not continued site visits should be asked to return to the site to obtain weight and waist circumference measurements at a minimum and, if possible, the following additional information: adverse events, vital signs, laboratory tests (chemistry, hematology, urinalysis), concomitant medications, questionnaires ***." To: "At about the 56 week time point, withdrawn subjects who have not continued site visits should be asked to return to the site to obtain weight and waist circumference measurements at a minimum and, if possible, the following additional information: adverse events, vital signs, laboratory tests (chemistry, hematology, urinalysis), concomitant medications, questionnaires ***."
***	***	Change: "The *** is being used to ***. This questionnaire will be completed at

		*** and at ***." To: "The *** is being used to ***. This questionnaire will be completed at ***, **and at *** after the ***.**"
***	***	Change: "Subsequent *** evaluations will be done only in *** who demonstrate a ***." To: "Subsequent *** evaluations will be done **at *** after ***. All *** assessments must be administered by a trained interviewer. If any assessments reveal ***, then the results must be reviewed by a physician investigator prior to ***.**"
Body Composition	***	Added New Section: **"At a selected subset of study sites, body composition assessments will be made at baseline (Visit 2), week 28 (Visit 10) and week 56 (Visit 17) using ***. Scans will be collected at a sufficient number of study sites to provide body composition data on approximately *** subjects from this study combined with protocol OB-302. Equipment and procedures used to obtain *** data will be standardized as described in a separate document. All sites will be trained on these procedures prior to performing scans on study subjects. Scans will be read at a central facility and the reader will be blinded to the identity of the subjects, the treatment assignment, and the visit number."**
***	***	Change: "All subjects will be screened for the presence and *** at *** and subsequently at regular intervals throughout the study: ***, and *** using a validated survey instrument *** designed for assessment of *** in a primary care setting." To: "All subjects will be screened for the presence and *** at *** and subsequently at ***** after the *** using a validated survey instrument *** designed for assessment of *** in a primary care setting**." Change: "The *** is a *** module based directly on the diagnostic criteria for ***. At study visits where *** assessments are not included, subjects will be asked the following question to assess ***." To: "The *** is a *** module based directly on the diagnostic criteria for ***. ***** will also be assessed at *** and at *** following the *** using the *****." Change: **"**Any *** must be ***. Investigators are encouraged to administer the *** on an ad-hoc basis as part of the clinical assessment of ***. These ad-hoc questionnaires will be maintained as source documentation, but will not be analyzed as a separate ***." To: "**Any *** must be ***."**
Other Efficacy Endpoints	***	Added: "**In the *** of subjects treated at ***, changes from *** to ***and *** in percent lean body mass and percent *** will be evaluated. Differences between treatment groups will be evaluated using methods similar to those used to evaluate other continuous variables. For these**

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		evaluations, data will be pooled from protocols OB-302 and OB-303."
Appendix 1: Schedule of Study Activities	***	Added: "*******" and only marked at ***
Appendix 1: Schedule of Study Activities — ***	***	Added at ***
Appendix 1: Schedule of Study Activities — ***	***	Added at ***
Appendix 1: Schedule of Study	***	Change: "***"

Activities — ***	To: “***”

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Protocol Title: **A Phase III Randomized, Double-Blind, Placebo controlled Multicenter Study to Determine the Safety and Efficacy of VI-0521 in the Treatment of Obesity in Adults with Obesity-Related Co-Morbid Conditions**

Protocol Number: **OB-303**

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Amendment Number 2
Date of Amendment: ***
(12 items)

Rationale: This amendment is being implemented to address inconsistencies in the description of various study exclusions and analyses, and to specify that an ***. Various typographical errors in the previous version of the protocol have also been corrected. None of the changes implemented with this amendment are anticipated to have any impact on safety risks to the study subjects.

Section and/or Item	Protocol Date	Amendment 2, *** Change Effected
Protocol Synopsis: Safety Endpoints	***	Change: “Safety will be assessed by an evaluation of adverse events, including eye symptoms (collected each study visit); ***;” To: “Safety will be assessed by an evaluation of adverse events, including eye symptoms (collected **at** each study visit); ***;”
Protocol Synopsis: Statistical Methods	***	Change: “All subjects who are randomized, take one or more doses of test material and have at least one post treatment efficacy measurement will be included in the analysis. Comparisons between treatments will be assessed using an *** with factors of ***, ***and *** and with ***. A step-down multiple comparison procedure will be used to compare each dose group with ***. That is, comparison with *** will start at the ***. If the statistical test is significant at ***, then the test will proceed to the *** also at the ***.” To: “All subjects who are randomized, take one or more doses of test material and have at least one post treatment efficacy measurement will be included in the analysis. Comparisons between treatments will be assessed using an *** with factors of ***, *** and *** and with *** **for percent weight loss, and *** for percentage of subjects with at least 5% weight loss**. A step-down multiple comparison procedure will be used to compare each dose group with ***. That is, comparison with *** will start at the ***. If the statistical test is significant at *** **for both co-primary endpoints**, then the test will proceed to the *** also at the ***.”
Background	***	Change: “Obesity is associated with numerous co-morbidities including dyslipidemia, coronary artery disease (CAD), hypertension, stroke and type 2 diabetes.(7), (9) Epidemiological data indicate that obesity is associated with

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		increased mortality,(10) and a recent study of over 500,000 individuals concluded that excess body weight during midlife, including overweight, was associated with an increased risk of death. (11)” To: “Obesity is associated with numerous co-morbidities including dyslipidemia, coronary artery disease (CAD), hypertension, stroke and type 2 diabetes.(7), (9) Epidemiological data indicate that obesity is associated with increased mortality,(10) and a recent study of over 500,000 individuals concluded that excess body weight during **midlife, was associated** with an increased risk of death.(11)”
Background	***	Change: “Topiramate, a sulfamate-substituted monosaccharide, is an anticonvulsant agent indicated as adjunctive therapy for partial onset seizures, primary generalized tonic-clonic

		seizures, seizures associated with Lennox-Gastaut syndrome and for migraine headache prophylaxis.(5) The recommended total daily dose of topiramate for treatment of seizures in adults is *** administered in two divided doses; ***. Topiramate is known to ***.(5) Recent clinical studies have shown that topiramate can promote weight loss in ***.(16),(17),(18) However, the exact mechanism by which topiramate exerts its anorectic effect is unknown although it is postulated to ***." To: "Topiramate, a sulfamate-substituted monosaccharide, is an anticonvulsant agent indicated as adjunctive therapy for partial onset seizures, primary generalized tonic-clonic seizures, seizures associated with Lennox-Gastaut syndrome and for migraine headache prophylaxis.(5) The recommended total daily dose of topiramate for treatment of seizures in adults is ***administered in two divided doses; ***. Topiramate is known to ***.(5) Recent clinical studies have shown that topiramate can promote weight loss in ***.(16),(17),(18) However, the exact mechanism by which topiramate exerts its anorectic effect is unknown although it is postulated to ***."
Exclusion Criteria #13	***	Change: "Diagnosis of type 1 diabetes or history of use of any antidiabetic medication other than metformin;" To: "Diagnosis of type 1 **diabetes or use of** any antidiabetic medication other than metformin **within the past month**;"
Titration (Visit 3)	***	Change: "Review the study medication used since Visit 2; assess treatment compliance and perform drug accountability. Re-dispense the card to the subject for use during weeks 3 and 4;" To: "Review the study medication used since Visit 2; assess treatment compliance and perform drug accountability. Re-dispense the **titration** card to the subject for use during weeks 3 and 4;"
Oral Glucose Tolerance Test	***	Change: "An oral glucose tolerance test (OGTT) will be obtained at Visit 1a (after results from Visit 1 indicate the subject may be eligible for participation), at Visit 4 (week 4) and at end of treatment (Visit 17 or study withdrawal)." To: "An oral glucose tolerance test (OGTT) will be obtained at Visit 1a (after results from Visit 1 indicate the subject may be eligible for participation), at Visit 4 (week 4) and at end of treatment (Visit 17 or study withdrawal) **for all subjects**."
Analysis of Primary Endpoints	***	Change: The primary calculated endpoints for the trial are based on the percent weight loss at week 56 calculated as *** and the percentage of subjects achieving at least 5% weight loss at week 56. The intent to treat (ITT) population (Section 9.2.1.3) is the primary subject population. For subjects who discontinue treatment prior to trial completion, every attempt will be made to have them return to the clinic at week 56 for a final weight assessment, regardless of when they discontinued treatment. For subjects

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		who ***. Comparisons between treatments will be assessed using an *** with factors of ***, *** and ***, and with ***. A step-down multiple comparison procedure will be used to compare each dose group with ***. That is, comparison with *** will start at the ***. If the statistical test is significant for the primary end point at ***, then the test will proceed to the *** also at ***." To: "The primary calculated endpoints for the **trial are the percent** weight loss at week 56 calculated as *** and the percentage of subjects achieving at least 5% weight loss at week 56. The intent to treat (ITT) population (Section 9.2.1.3) is the **primary analysis** population. For subjects who discontinue treatment prior to trial completion, every attempt will be made to have them return to the clinic at week 56 for a final weight assessment, regardless of when they discontinued treatment. For subjects who ***. Comparisons between treatments for percent weight loss will be assessed using an *** with factors of ***. **Comparisons between treatments for the percentage of subjects achieving at least 5% weight loss will be assessed by *** with ***, ***, and *** and ***.** A step-down multiple comparison procedure will be used to compare each dose group with ***. That is, comparison with *** will start at the ***. If the statistical test is significant for **both co-primary** end points at ***, then the test will proceed to the *** also at ***."
Analysis of Secondary Endpoints	***	Change: "The difference in absolute weight reduction and the difference in waist reduction at

		week 56 from baseline will also be compared using the same *** as the primary end point. *** with ***, *** and *** and ***, will be used to compare the probability to reach 5% and 10% body weight reduction between baseline and at week 56 between treatment groups." To: "The difference in absolute weight reduction and the difference in waist reduction at week 56 from baseline will also be compared using the same *** as the primary end point. *** with ***, *** and *** and ***, will be used to compare the probability **of reaching** 5% and 10% body weight reduction **from baseline to** week 56 between treatment groups."
Adverse Events	***	Change: "Adverse events will be coded using a MedDRA coding dictionary. The number and percentage of subjects who reported at least one adverse event in each organ class and preferred term category, and the total number and percentage of subjects with any AE over all organ system will be summarized by treatment group. Subsets of AEs that are considered serious or required discontinuation of the study medication will be listed by subject and present separately." To: "Adverse events will be coded using a MedDRA coding dictionary. The number and percentage of subjects who reported at least one adverse event in each **system** organ class and preferred term category, and the total number and percentage of subjects with any AE overall **system organ classes** will be summarized by treatment group. Subsets of AEs that are considered serious or required discontinuation of the study medication will be listed by subject and present**ed** separately."
Interim Analysis	***	Change: "An interim analysis may be conducted once approximately half of the study subjects have completed the intended course of treatment to provide

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		information for the planning of future clinical trials that may be designed or commenced prior to the completion of this trial. No changes will be made to the conduct of the present study, including premature termination or increased sample size, based on the results of this interim analysis and no statistical adjustments for this interim analysis, if conducted." To: "An interim analysis may be conducted once approximately half of the study subjects have completed the intended course of treatment to provide information for the planning of future clinical trials that may be designed or commenced prior to the completion of this trial. No changes will be made to the conduct of the present study, including premature termination or increased sample size, based on the results of this interim analysis and no **adjustments to the significance level for the primary hypothesis will be made if this interim analysis is conducted**."
***	***	Change: "No *** will be employed for this study." To: "*******"

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Protocol Number: **OB-303**

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Amendment Number 1
Date of Amendment: ***
(22 items)

This protocol amendment is being implemented to add a co-primary endpoint to the study analysis section, to add specific guidance for the implementation or adjustment of concomitant antidiabetic therapies based on blood glucose values observed during the course of the study, and to add additional laboratory tests to the schedule of evaluations. The definition of child-bearing potential has also been clarified, and miscellaneous typographical errors have been corrected. These changes are being made at the request of the FDA, and are not anticipated to significantly affect the risk to study subjects.

Section and/or Item	Protocol Date	Amendment 1, *** Change Effected
Protocol Synopsis: Study Subjects	***	Change: "The study population will consist of *** (BMI ≥ ***and ≤ ***) adults ≤ 70 years of age with *** and at least *** of the following obesity-related comorbid conditions:" To: "The study population will consist of *** (BMI ≥ *** and ≤ ***) adults ≤ 70 years of age **with at least ***** of the following obesity-related comorbid conditions:"
Protocol Synopsis: Efficacy Endpoints	***	Change: "The primary endpoint is the difference between *** and *** groups in mean percent loss of baseline body weight, determined by weight at randomization (baseline) and weight at end of treatment (week 56). Percent weight loss will be calculated as ***." To: "The primary **endpoints are** the differences between *** and *** groups in mean percent loss of baseline body weight, determined by weight at randomization (baseline) and weight at end of treatment (week 56**), and percent of subjects with weight loss of 5% or more at end of treatment (week 56)**. Percent weight loss will be calculated as ***.
Protocol Synopsis: Efficacy Endpoints	***	Change: "The difference in percent of subjects who achieve a reduction in total body weight of at least 5% and at least 10% between randomization (baseline) and end of treatment (week 56) for *** and *** groups; and To: "The difference in percent of subjects who achieve a reduction in total body **weight of at least 10%** between randomization (baseline) and end of treatment (week 56) for *** and *** groups; and

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List of Abbreviations	***	Added: "I-CAM: Intercellular Cell Adhesion Molecule", "PAI-1: Platelet Activator Inhibitor 1", "RBP-4: Retinol Binding Protein 4" and "V-CAM: Vascular Cell Adhesion Molecule"
Introduction	***	Change: "The present study is being conducted to evaluate the combined use of phentermine and topiramate at doses of 7.5 mg phentermine/46 mg topiramate and 15 mg phentermine/92 mg topiramate in the treatment of obesity in adult subjects with body mass index (BMI) greater than or equal to ***." To: "**The present study is being conducted to evaluate the combined use of phentermine and topiramate at doses of 7.5 mg phentermine/46 mg topiramate and 15 mg phentermine/92 mg topiramate in the treatment of obesity in adult subjects."**
Trial Design	***	Change: "The primary endpoint is the difference between *** and *** groups in mean percent loss of baseline body weight, determined by weight at randomization (baseline) and weight at end of treatment (week 56). Percent weight loss will be calculated as ***. Secondary efficacy endpoints are: · The difference in absolute weight loss between randomization (baseline) and end of treatment (week 56) for *** and *** groups. · The difference in percent of subjects who achieve a reduction in total body weight of at least 5% and at least 10% between randomization (baseline) and end of treatment (week 56) for *** and *** groups." To: "The primary **endpoints are** differences between *** and *** groups in mean percent loss of baseline body weight, determined by weight at randomization (baseline) and weight at end of treatment (week 56), **and percent of subjects with weight loss of 5% or more at end of treatment (week 56).** Percent weight loss will be calculated as ***. Secondary efficacy endpoints are: · The difference in absolute weight loss between randomization (baseline) and end of treatment (week 56) for active and placebo groups. · The difference in percent of subjects who achieve a reduction in total body **weight of at least 10% between** randomization (baseline) and end of treatment (week 56) for ***

		and *** groups."
Inclusion Criteria	***	Change: "Have a BMI ≥*** and ≤***;" To: "Have a BMI ≥*** and ≤*** **(for diabetic subjects, there is no lower limit on BMI for study inclusion);**"
Inclusion Criteria	***	Change: "If females of child-bearing potential, be using adequate contraception, defined as double barrier methods, stable hormonal contraception plus single barrier method or tubal ligation. Females are considered to be of child-bearing potential unless they have undergone a hysterectomy or bilateral oophorectomy, have a documented follicle stimulating hormone level ≥40 IU/L or are 55 years of age or greater and have experienced cessation of menses for at least 1 year; To: "If females of child-bearing potential, be using adequate contraception, defined as double barrier methods, stable hormonal contraception plus single barrier method or tubal ligation. Females are considered to be of child-bearing potential unless they have undergone a hysterectomy or bilateral oophorectomy, **are 55 years of age or greater and have experienced spontaneous cessation of**

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		menses for at least 1 year, or have a documented follicle stimulating hormone level ≥40 IU/L;"
***	***	Change: "When *** is not appropriate or when *** may be required due to events unrelated to subject treatment, subjects may ***. If dosing has been ***, a new titration kit should be ordered through *** to ***." To: "When *** is not appropriate or when *** may be required due to events unrelated to subject treatment, subjects may ***. ***** are possible with agreement from the medical monitor. All subjects undergoing *** for *** may be *** based on discretion of the PI.** If dosing has been ***, a new titration kit should be ordered through *** to ***."
Treatment of Diabetes	***	Change: "Subjects with consistently elevated fasting blood glucose values should ***. Subjects whose fasting blood glucose ***, or whose blood glucose cannot be adequately controlled with the concomitant treatments allowed in this trial should be discontinued from study treatment and referred back to their primary healthcare provider for additional glycemic management. Subjects may continue attending study visits ***." To: "Subjects with consistently elevated fasting blood glucose values should ***. **For this study, actionable levels for glucose values are ***. Subjects who note *** fasting glucose values that exceed these thresholds in daily glucose monitoring logs during the week prior to a study visit would be considered appropriate for concomitant medication adjustment**. Subjects whose fasting blood glucose ***, or whose blood glucose cannot be adequately controlled with the concomitant treatments allowed in this trial should be discontinued from study treatment and referred back to their primary healthcare provider for additional glycemic management."
Randomization (Visit 2)	***	Change: "Assess adverse events (including eye symptoms), if any;" To: "Assess adverse events (including eye symptoms **and *****), if any;"
Titration (Visit 3)	***	Change: "Assess adverse events (including eye symptoms), if any;" To: "Assess adverse events (including eye symptoms **and *****), if any;"
Treatment (Visits 4 through 16)	***	Change: "Assess adverse events (including eye symptoms), if any;" To: "Assess adverse events (including eye symptoms **and *****), if any;"
End of Treatment (Visit 17 or Withdrawal from Study)	***	Change: "Assess adverse events (including eye symptoms), if any;" To: "Assess adverse events (including eye symptoms **and *****), if any;"
Biomarkers	***	Change: "Appropriate blood and urine biomarkers [C-reactive protein, microalbumin (urine) and creatinine (urine)] will be evaluated at screening (visit 1a), visit 10 (week 28) and end of treatment (visit 17 or study withdrawal)."

		To: “Appropriate blood and urine biomarkers [C-reactive protein, microalbumin (urine) and creatinine (urine)] will be evaluated at screening (visit 1a), visit 10 (week 28) and end of treatment (visit 17 or study withdrawal). **Additionally, adiponectin, intercellular cell adhesion molecule (I-CAM), vascular cell adhesion molecule (V-CAM), retinal binding protein 4 (RBP-4), platelet activator inhibitor 1 (PAI-1) and fibrinogen will be evaluated at screening (visit 1a) and end of treatment (visit 17 or study withdrawal). With the exception of urine microalbumin and creatinine, all post-screening biomarker results will be blinded to investigators and sponsor.**”
Eliciting Adverse Event Information	***	Change: “The following sections describe additional requirements to ensure ***.”

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		To: “The following sections describe additional requirements to ensure ***.”
***	***	Change: “Should this additional assessment indicate the presence ***” To: “Should this additional assessment indicate the presence **of** ***”
Hypoglycemia	***	New Section added and new Table: “**Guidelines for the reporting of adverse events based on results obtained in *** maintained by *** are summarized in Table 2.** **Table 3. Guidelines for adverse event reports based on ***”**
Analysis of Primary Endpoints	***	Change: “*** The primary calculated endpoint for the trial is based on the percent weight loss at week 56 calculated as ***.” To: “*** The primary calculated endpoints for the trial are based on the percent weight loss at week 56 calculated as *** **and the percentage of subjects achieving at least 5% weight loss at week 56.”**
Analysis of Secondary Endpoint	***	Change: “The difference in percent of subjects who achieve a reduction in total body weight of at least 5% and at least 10% between randomization (baseline) and end of treatment (week 56) for *** and *** groups.” To: “The difference in percent of subjects who achieve a reduction in total body **weight of at least 10%** between randomization (baseline) and end of treatment (week 56) for *** and *** groups.”
Interim Analysis	***	Change: “No changes will be made to the conduct of the present study, including premature termination or” To: “No changes will be made to the conduct of the present study, including premature termination **or increased sample size, based on the results of this interim analysis and no statistical adjustments for this interim analysis, if conducted**.”
Appendix 1	***	Change: “***” To: “***”

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PROJECT OVERVIEW

OB-303

The OB-303 trial is a phase III randomized, double blind, placebo controlled multicenter study to determine the safety and efficacy of VI-0521 in the treatment of obesity in adults with obesity-related comorbid conditions.

PROJECT TEAM

Study Management

The overall management of the study will be the responsibility of the Senior Clinical Trial Manager (CTM). The Senior CTM will oversee and coordinate the management of the study as well as oversee the study specific CTM. This oversight will ensure consistency and allow VIVUS Study Management to have one primary contact for the Qnexa program. The Medpace CTM assigned to OB-303 will work closely with the VIVUS Clinical Leader and Medpace Medical Expert to address protocol questions and interpretations while maintaining close oversight of study-related processes and documents. The OB-303 CTM will supervise all Clinical Research Associates (CRAs) and Project Coordinators assigned to the project.

The Project Coordinators will be responsible for day-to-day study management functions, including the generation of status reports, organization of supplies, generation and compilation of newsletters, and input of all study information into the ClinTrak® Study Management System, a web-based, proprietary research management system designed by Medpace. The Project Coordinators will organize teleconferences and team meetings, including the compilation of agendas and meeting minutes.

The Study Start-Up Manager and Study Start-Up Coordinators will work closely with the CTM and Project Coordinators to ensure sites become active in the most time effective manner.

The Medpace Contracts Attorney will be responsible for the execution of Investigator contracts (upon VIVUS defined process). The Contracts Attorney will work closely with the Start-Up Manager and Medpace CTM to ensure contracts are executed in a timely manner.

The Medpace Medical Expert assigned to this project will work closely with the VIVUS Clinical Leader . The Medpace Medical Expert will assist with protocol design and medical interpretation of entry criteria and adverse events (AEs). The Medical Expert will also be involved in the training of CRAs and other staff members participating in the

project. The Medical Expert will review and approve the coding of concomitant medications, medical histories, AEs, and will provide the medical context for the statistical analysis and medical writing.

The Medical Expert will assist in the review of the protocol, train Medpace personnel internally as to the background of the study compound and design of the study, participate in the project teleconferences and meetings, work hand-in-hand with the OB-303 CTM, and have heavy involvement in the clinical study report. The Medical Expert's role and decision making rights are dictated by VIVUS (e.g. inclusion/exclusion of patients, discussions with Investigators about withdrawing a patient, etc.). This decision making power often times reduces the oversight needed by the sponsor. For questions the OB-303 CTM is not comfortable answering, she will contact the Medical Expert for guidance. Obviously, VIVUS will be involved in study oversight based on pre-defined terms with the VIVUS Clinical Development Team. The Medpace Medical Expert is available 24 hours a day, 7 days a week via the Medpace Project Helpline.

Clinical Monitoring

Medpace operates in North America with a primarily centralized monitoring team of over 140 CRAs to promote greater standardization, cohesiveness, support, and stability. Each of the Medpace CRAs assigned to this project have monitoring experience and strong clinical backgrounds.

Clinical Safety

The Clinical Safety will be managed by VIVUS or its designee. VIVUS Clinical Leader to be involved with casualty assignment for all Serious Adverse Events (SAEs).

Data Management

A Data Manager will serve as the primary contact for the Data Management team. Data Coordinators will be involved in the day-to-day operations and report issues to the Data Manager. Data Entry Specialists and Database Programmers will also be utilized.

Biometrics

Key members of our Biometrics team include Biostatisticians and Statistical Analysts. The Biostatistician assigned to this project will develop the analysis plan and coordinate biometrics activities. The Lead Statistical Analyst will work closely with the Biostatistician to ensure a clear understanding of the

analysis plan and communicate any programming issues that may arise.

Medical Writing

The Medical Writing team works in collaboration with the Medical Experts to prepare research reports meeting International Conference on Harmonisation (ICH) and Sponsor guidelines. All Medpace Medical Writers have extensive experience in regulatory

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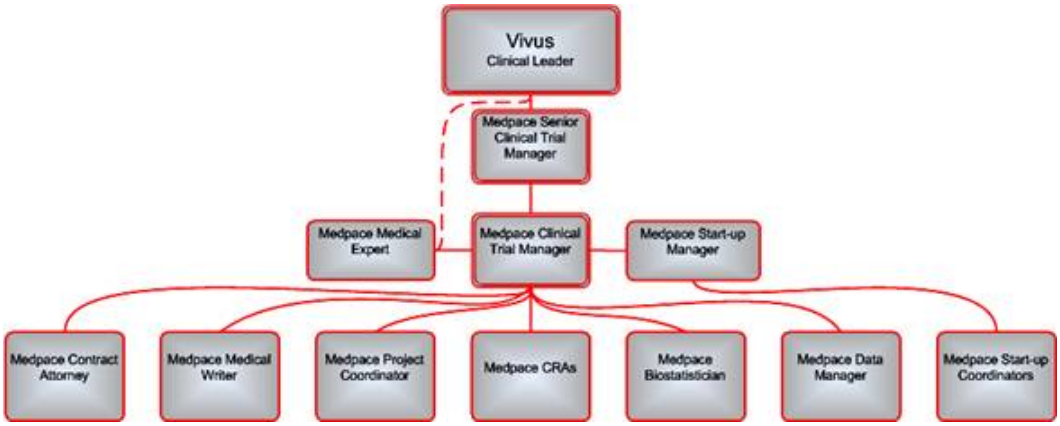
submission preparation. The Medical Writing team is actively involved throughout the conduct of the trial.

Team Organization Chart



PROJECT START-UP

Protocol

VIVUS will prepare the protocol. Medpace will review the protocol and provide comments before it is finalized.

Case Report Forms

Medpace will design the electronic case report forms (eCRFs) for the trial, including completion instructions, according to the final protocols and the Medpace template. VIVUS must review and approve the eCRFs before they are finalized.

Project Initiation

Prior to the study site initiation visits, a project kickoff meeting will be held at Medpace involving Medpace and VIVUS personnel to review the study protocol, eCRFs, and overall project coordination. Medpace project team members and VIVUS personnel will participate in this meeting.

Interactive Voice Response System

Medpace will provide a customized (study-specific) interactive voice response system (IVRS) to provide patient randomization, and drug management. The Medpace IVRS is a proprietary in-house developed system. The system provides both voice and web access and has been developed in conjunction with our web based Clintrak® system providing

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seamless functionality throughout the conduct of the study. The VIVUS Team (no limit applied to number of team members) will have access to review reports within the IVRS. Medpace will perform the User Acceptance Testing (UAT) for each site.

The IVRS will include:

- Subject Screens/Screen Failures;
- Subject randomization;

- Patient visit tracking;
- Inventory management (site supply set-up, initial bulk supply, and resupply of one additional shipment per patient);
- Notifications of site shipments;
- Confirmation of receipt of shipments; and
- Customized reports.

VIVUS will review IVRS and approve system prior to finalization.

Study Medication Supply and Storage

VIVUS will be responsible for the supply, packaging, labeling, storage, and destruction of study medication. Distribution of the study medication will be tracked and initiated via the Medpace IVRS. Study medication accountability procedures will follow Medpace standard operating procedures (SOPs) and utilize a study medication accountability log that has been approved by VIVUS.

Recruitment Oversight Plan

The Medpace CTM, in collaboration with VIVUS, will develop a recruitment oversight plan. Medpace understands the importance of rapid recruitment and the necessity to keep patients in the trial until completion. Medpace will develop processes prior to study initiation to ensure recruitment is efficient and retention of patients in the study is maximized. The plan will include details on:

- Initial collection of essential documents;
- Patient recruitment (including tools, site-specific plans, contingencies, etc.); and
- Patient recruitment tracking reports.

The tools noted above include:

- Inclusion/exclusion cards;

- Patient emergency cards;
- Enrollment tracking forms;
- Laminated patient visit schedule;
- Pocket protocol; and
- Advertising tools (e.g., posters, table tents, language for newspaper/radio advertisements, etc.).

Medpace understands each site has a different experience and approach to patient recruitment. The Medpace CTM and Medpace CRAs will work with personnel from each site to help maximize their efforts. The project team maintains frequent contact during the active recruitment phase to assess each site's activity and offer assistance when needed. Medpace acknowledges the importance of site recognition and offers various incentives throughout the recruitment period. Examples of site incentives are "Site of the Month" awards and weekly faxes displaying each site's activity (often included in the newsletter as well). The time associated with these types of incentives are inclusive of the budget. However, often times, monetary incentives are built into the Investigator's grant to encourage rapid essential document collection and/or timely recruitment.

Patient retention is vital to the success of a trial. The Medpace CTM and the Medpace CRAs will work with the sites to understand the needs and motivations for patients to remain in the study. They will help educate the sites on the importance of "customer service" and "patient satisfaction" as elements that ensure continued patient participation. Examples of patient retention methods include quarterly patient newsletters, ideas for site customer service, and tokens of appreciation for patients.

Site Selection and Pre-study Visits

VIVUS, in conjunction with Medpace, will identify qualified Investigators. VIVUS and Medpace will also work together to provide and negotiate Confidentiality Disclosure Agreements (CDAs) as well as create and evaluate site questionnaires. In not knowing the number of pre-study visits Medpace will be required to conduct, a unit price for a pre-study visit has been provided in the budget.

Pre-study visits will be conducted consistent with Medpace SOPs. Medpace will provide a pre-study visit report to VIVUS within 10 business days of each visit.

These visits will include, but are not limited to:

- Determining whether or not the site has clinical staff of appropriate education, training, and experience to manage the study and have sufficient capacity to perform the required tasks;

- Determining whether or not the site has appropriate facilities to conduct the study;
- Determining there are no competing studies that will conflict with patient enrollment and that the site has sufficient patients and processes to enroll patients in the time identified for patient recruitment; and
- Determining whether or not the site has appropriate resources and procedures to maintain appropriate records according to FDA requirements.

Study Start-up Team

The efficient start-up of the *** study sites for OB-303 will have a significant effect on patient recruitment time. Medpace will utilize its Study Start-up team for additional support during the initial phase of the trials to expedite the overall study start-up for each site.

The Study Start-up team works directly with the CTM and the Project Coordinators. The team is comprised of a Study Start-up Manager and several experienced Study Start-up Coordinators. The team is responsible for many of the key start-up activities, including:

- Submission to the central IRB;
- Coordination and tracking of essential documents packages for each site;
- Investigator meeting presentations and binders; and
- Site tools.

Central Laboratory Selection

Medpace Reference Laboratories (MRL) will be utilized for processing the clinical laboratory samples. MRL is committed to providing comprehensive laboratory services of the highest quality to the pharmaceutical and biotechnology industries.

Investigators' Meeting

An Investigators' Meeting will be held for the OB-303 study. VIVUS will arrange the meeting (including contracting with a third-party vendor) and Medpace will prepare the meeting materials, including preparation and distribution of binders. The Medpace OB-303 Team will attend the meeting. VIVUS will open the meeting and Medpace will present on the topics delegated by VIVUS. The meeting minutes will be prepared by Medpace, reviewed and approved by VIVUS, and distributed to the study sites by Medpace. The preparation of the meeting minutes is optional; however, is included in the budget. Medpace assumes the Investigators' Meeting will serve as the initiation visit for the Investigators. Therefore, the budget reflects 20% of the sites will require an initiation visit (for those unable to attend the Investigators' Meeting).

Clinical Trial Agreements for Sites, Central Laboratory, and EDC Vendor

Medpace will prepare and provide sample clinical trial agreements (including budgets) for the study sites. VIVUS will review and approve the final draft versions of the clinical trial agreements. The agreements will be distributed and negotiated with each site by Medpace (with final approval by VIVUS). Medpace will make payments to the clinical sites according to the VIVUS-approved schedule. All payments for sites, Medpace Reference Laboratories, and Phase Forward will be made electronically to Medpace within seven days of invoice receipt. If electronic payment exceeds or falls below actual costs, VIVUS will adjust payment based on the prior month's payment reconciliation. Investigator payment invoices will include the following detail:

- Clinical study number;
- PI or Site #;
- Patient ID;
- Amounts paid per visit;
- Total amount earned to date;
- Prior payments; and
- Current payment amount.

Institutional Review Board and Initial Essential Documents Packages

Medpace will select a central Institutional Review Board (IRB) and coordinate the initial submissions to the IRB. VIVUS must approve the central IRB selected. Medpace will be responsible for payments to the central IRB utilizing funds provided in the same manner as described above.

A study-specific, prototype informed consent form (ICF) will be designed by Medpace. The ICFs will be reviewed and approved by VIVUS. Medpace will distribute the ICFs to the Central IRB. Medpace will be responsible for negotiating changes to the informed consents with the central IRB.

Deviations from the VIVUS template must be brought to the attention of the VIVUS Clinical Leader who will facilitate VIVUS legal review and approval, if required.

All components of the Initial Essential Documents Package will be collected, tracked, and maintained by Medpace according to Medpace SOPs. The Medpace Study Start-up team will review all documents, negotiate any changes with study site personnel, and correct any errors. The Initial Essential Document Package includes the following:

- Signed protocol signature pages;
- Financial disclosure questionnaires (FDQs) (template to be provided by VIVUS, Medpace to collect the forms);
- Clinical study agreement (includes study budget);

- FDA Form 1572;
- Laboratory certifications and reference values;
- Curricula vitae for all Investigators;
- IRB approval of the protocol (and any amendments), the informed consent and sponsor approved advertisements; and
- Qualification of IRB members.

The FDQs shall apply throughout the entire term of the study and for one year following last patient last visit (LPLV). If there is any change in the accuracy of a particular site's FDQ during that time period, that site will be responsible for notifying Medpace of the change. Medpace will send a fax to all sites once the study has ended reminding them of their responsibilities (one of which includes notifying Medpace of any FDQ changes). If a site notifies Medpace of a change in staff from LPLV to one year after LPLV, Medpace will collect an updated FDQ and forward on to VIVUS. Costs associated with this task are included in the budget.

Site Initiation Visits

Site initiation visits will be conducted by the Medpace CRAs consistent with Medpace SOPs. For purposes of this proposal, it is assumed that the Investigators' Meeting will serve as the initiation visit and only 20% of the sites for each study will require separate initiation visits. Typically, if the Investigator Meeting is considered the initiation visit, the CRA will contact the site via phone to review study procedures and the CRA's first routine monitoring visit will occur shortly (can be defined as 1 or 2 weeks) after a patient is screened for the trial. During this visit, the CRA will review bullets 2-5 below. A site initiation visit report will be completed and forwarded to VIVUS within 10 business days of the visit. These visits will include, but are not limited to, the following tasks:

- Train site and applicable study personnel on the protocol and study procedures;
- Ensure the site has received all study supplies required for the conduct of the study, including study medication and access to eCRFs;
- Provide and review the Trial Master File binder. Medpace CRAs will provide instruction to the site personnel on the organization and maintenance of the documents in the binder;
- Review study medication accountability procedures;
- Provide eCRF completion instructions; and
- Explain the serious adverse event (SAE) reporting procedures.

CLINICAL OPERATIONS

Monitoring Data Review Guidelines

The Medpace Lead CRA in collaboration with the project team members will develop a project-specific Monitoring Plan for the study. This plan will include detailed interpretations of study expectations for the CRAs assigned to the study. Issues are discussed and updated on an ongoing basis throughout the project. Medpace will request that VIVUS approve the initial document and then re-approve the document on a quarterly basis.

Routine Clinical Monitoring Visits

Medpace will conduct routine monitoring visits at each site consistent with Medpace SOPs. The frequency of the visits will be determined by the site's activity, but will be conducted on average every four to six weeks. Visits at the beginning and end of the study may be more frequent based on the needs of the study, including, but not limited to, recruitment, quality data and study close-out activities. Based on recruitment being very rapid, the first routine visit will be performed within 2 weeks after the first two patients are screened at the site. The CRA will perform 100% source documentation. In addition, data queries will be resolved during the visits, eCRF changes will be verified, and supporting documentation for SAEs will be obtained. The Medpace CRA will verify all laboratory samples have been obtained according to guidelines and the results are available in the patient's source documents. A monitoring visit report will be forwarded to VIVUS within 10 business days of the visit. VIVUS will be notified of any significant issues by phone within one business day.

The following tasks will also be performed:

- Train any new site personnel and review study issues with applicable site personnel;
- Ensure the site has sufficient study supplies (including study medication);
- Ensure the site is entering eligible patients into the study in a timely manner, and notify the Medpace Study Manager immediately of any problems;
- Detect any significant compliance or other issues and notify the Medpace Study Manager by phone, within one business day of the monitoring visit;
- Confirm the Trial Master File is complete and current, and the site is complying with applicable regulations and the protocol. VIVUS will be notified immediately of any significant deviations;
- Ensure the site is completing eCRFs in a timely manner;

- Ensure all completed eCRFs are reviewed, verified, corrected, and transmitted to Medpace;
- Review eCRFs for accuracy and protocol adherence;
- Verify study medication dispensing, compliance, and accountability for each patient; and
- Ensure the Investigator reported all SAEs to Medpace and the applicable IRB.

Medpace will provide a follow-up letter to the study site after each visit. The letter will include, but will not be limited to, the following:

- Important findings during the visit;
- Recommendations of corrective actions to be taken by the site; and
- Follow-up information regarding questions asked during the visit.

The Monitoring Visit Reports with all attachments including follow-up letters, will be available for view through the Medpace web based Clintrak® Study Management system within 10 days of the monitoring visit.

In-house Clinical Monitoring Activities

Investigators will be contacted on a regular basis (every week during the active recruitment period and between monitoring visits) to ensure progress at the study site. The CRA will take the opportunity to review enrollment, answer protocol-related questions, discuss eCRF completion issues, obtain information regarding AEs, and ensure the site continues to be committed to the completion of the study in a timely manner and according to the protocol.

Telephone contacts will be entered in the Medpace ClinTrak Study Management system. Contacts requiring urgent attention will be relayed to VIVUS immediately and will be resolved in collaboration with the Medpace CTM and the VIVUS Clinical Leader.

Withdrawals Due to Adverse Events

Withdrawals due to AEs will be tracked and reconciled with the eCRF database on an ongoing basis by Medpace. The CRA will be responsible for reporting withdrawals due to AEs to VIVUS using the monitoring visit report.

Medpace will write narratives for all withdrawals due to AEs, for use in the clinical trial study report.

Status Reporting

The Medpace Senior CTM will serve as the central channel for communication between Medpace and VIVUS. The OB-303 CTM will work in conjunction with the clinical monitoring group to track study progress and report to VIVUS on a weekly basis. In addition, the OB-303 CTM will be responsible for overall management of site information, overseeing the status of Investigator contracts, direct supervision of CRAs, tracking of enrollment information, and distribution of study supplies. The Medpace OB-303 CTM will be the primary contact for the sites to address protocol interpretations and inclusion/exclusion criteria. All protocol-related issues will be recorded in an ongoing document to ensure consistency. The CTM is available 24 hours a day, 7 days a week via the Medpace Project Helpline.

Medpace will develop a communication plan at the start-up of the study. The Senior CTM will work with the VIVUS project team to define details regarding study communication, including status reporting and team conference calls. Medpace typically delivers status reports on a predetermined day (and time) of the week, which is established around the weekly team calls so that the information can be discussed. Utilization of IVRS will also allow the project team to review patient status on a real time basis.

The Medpace CTM will collaborate with the Medpace Medical Expert and the VIVUS Clinical Leader to address any questions that may arise. The ClinTrak Study Management databases will serve as the primary source of project status information and will allow the Medpace CTM to report on any aspect of the study. The databases are updated on a real-time basis, providing accurate and up-to-date information.

Elements of ClinTrak include:

- Phone contacts;
- Monitoring visit reports;
- Patient status including details on withdrawals during the treatment phase;
- Study supplies; and
- Protocol deviations.

Medpace will provide weekly status reports via a secure project website, to include the following status by site:

- Number of patients screened;
- Number of screen failures;
- Number of patients randomized;

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- Number of patients dropped with drop rates; and
- Number of patients completed.

In addition, monthly reports will be provided, to include the following:

- Monitoring visits scheduled; and
- Monitoring visits completed.

Data Management status reports will be provided monthly via a secure website. These reports will include the following:

- Cumulative and interval eCRF status by site (including number of eCRFs transmitted and cleaned);
- Cumulative and interval patient status by site (including number of patients ongoing, completed, and early terminations) based on eCRF data in-house; and

- Cumulative and interval query status by site (including number of queries issued and days outstanding).

Project Website

Medpace will develop a secure OB-303 website that will be available to all project team members and site personnel. The website will include information and tools relevant to the study, such as status reports, meeting agendas and minutes, newsletters, monitor visit status, and the project timeline. Access is controlled by the type of user. Access to the tabs (sections) on the websites are controlled by the user type so that sites can have access to the section specifically designed for site access. Medpace can set up an automatic notification process of updates to the user email accounts. Clinical sites will have access only to parts of the website that pertain to their function. They will have the ability to receive study information and download study-related forms.

Team Meetings

VIVUS and Medpace

Medpace assumes that one face-to-face meeting, other than the Investigators' meeting and kickoff meeting will take place for the OB-303 study at VIVUS.

Weekly teleconferences will be held during the study. The teleconferences will be held to discuss study progress and review project documents (as necessary). The Medpace Project Coordinators will be responsible for preparing and distributing agendas and minutes for each meeting/teleconference.

Additional meetings/teleconferences will be scheduled throughout the project, as needed.

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Internal Meetings

Medpace will develop a project-specific internal project development/training program for all project team members. Included in this program will be the following:

- Protocol/eCRF review meeting;
- Medical in-services;
- Periodic Monitoring Plan meetings; and
- Periodic project meetings.

Newsletter

Medpace will prepare a 2-4 page full color site monthly newsletter for OB-303 as an additional avenue of communication and training for all site personnel. VIVUS will provide input and approval of the newsletter prior to distribution. Medpace will be responsible for printing and distributing two copies of each newsletter to each site.

Closeout Visits

Medpace will conduct closeout visits at each site consistent with Medpace SOPs after all patients have completed or discontinued from the study at the respective site. This visit may be performed as part of a final routine site monitoring visit. Site closeout visit reports will be forwarded to VIVUS within 10 business days of the visit. The following tasks will be performed:

- Resolve outstanding data queries;
- Ensure all study medication supplies are accounted for and that medication records and unused supplies are returned to VIVUS;
- Ensure the Investigator's copies of data and source documents are properly stored;
- Ensure the Trial Master File is complete, correct, and properly stored;
- Ensure the Investigator is aware of record retention requirements and other obligations, and a final site status report is sent to the IRB and VIVUS; and
- Instruct the site to update the FDQs for one year after the study is completed.

Site Audits

Site audit visits will be conducted, as deemed necessary, by VIVUS.

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Medpace will respond to any audit findings and ensure the proper actions are taken to resolve outstanding issues.

REGULATORY AFFAIRS AND SAFETY REPORTING

Serious Adverse Events

All SAEs will be reported immediately, within 24 hours of discovery or notification of the event, by the clinical study site to VIVUS, or its designee, according to SOPs specified by VIVUS.

VIVUS will be responsible for submitting all immediately reportable SAEs (serious, causally related and unexpected) to the Food and Drug Administration (FDA) in accordance with the current regulations.

If a SAE has occurred at a site, the Medpace CRA will always 100% source document verify the event during the monitoring visit to ensure it has been recorded, documented, and reported appropriately and accurately. In addition, data queries will be resolved during the visits, CRF changes will be verified, and supporting documentation for SAEs will be obtained.

Medpace will provide VIVUS listings of non-serious adverse events from all sites to support filing of the Annual Safety Reports. Medpace will reconcile SAE listings with the AE database.

DATA MANAGEMENT

Data Management activities performed by Medpace will include eCRF tracking, preparation of a data management manual, eCRF review, coding of adverse events and concomitant medications, medical histories, data cleaning/editing, querying, query tracking, final database quality review, and delivery of the final SAS® database. The data cleaning process will be performed on an ongoing basis following Medpace Data Management SOPs. Two data transfers (SAS transport files) will be performed: a test transfer prior to FPFV and a final transfer. A unit price for additional data transfers has been provided in the budget.

Database Development and Data Management Manual

Medpace will design and validate the data entry systems prior to entry of data. A Data Management Manual will be prepared for each study using the Medpace template, and will include the following data management documents:

- Database specifications, based on VIVUS specifications;

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- Guidelines for the tracking of eCRFs and data queries;
- Data Management Guidelines, which will include guidelines for reviewing the data, and description of the database edit check specifications to be performed for data cleaning; and
- Description of the database quality control (QC) plan.

The manuals will be reviewed and approved by VIVUS.

Data from the Central Laboratory

Medpace will arrange periodic data transfers from MRL. Medpace will track and reconcile discrepancies between the MRL demographic data and the eCRF database, which are generated during the data cleanup process throughout each project.

Data Entry and Data Querying

Medpace assumes no codable forms will be transmitted for screen failure patients. Data is entered by site personnel that have been trained on the eCRF system. Data will be reviewed according to Medpace Data Management Guidelines and edits. A data query will be generated electronically within the eCRF system. The resolutions/corrections are made by site personnel by changing the data. All changes are recorded in an audit trail. All answered queries are verified/closed by Medpace Data Management. All resolutions/corrections will be performed consistent with Medpace SOPs. The Data Coordinators will work directly with the site personnel in resolving queries.

Coding

Medpace will be responsible for coding adverse events, medical histories, and concomitant medications.

- MedDRA will be used to code adverse events and medical histories. Adverse events and medical histories will be coded to the lowest level term, preferred term, and system organ class.

- WHO DRUG will be used to code concomitant medications. Concomitant medications will be coded to the generic name and anatomic therapeutic class 3. It is assumed by Medpace that VIVUS holds a valid agreement with the Uppsala Monitoring Centre (UMC) for the WHO DRUG dictionary.

All coding will be done on a single version of each coding system (versions to be agreed upon by VIVUS). Medpace will provide the coding dictionaries.

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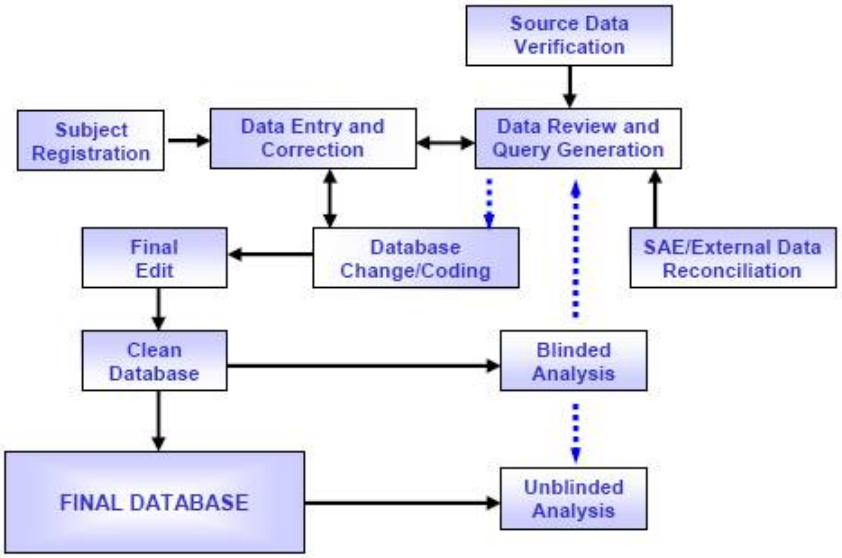
Data Flow Chart



STATISTICAL ANALYSIS

Medpace will develop the data analysis plan (DAP) per the VIVUS/Medpace format and template. VIVUS will review and approve the DAP prior to initiation of programming. Included in the DAP is a detailed statistical methodology and programming specification for all statistical analyses, tables/figures/listings (TFLs), and derived datasets.

Medpace will be responsible for programming and generating all TFLs, according to the Medpace standard analysis validation and quality control procedures. All TFLs will be programmed using SAS (Version 8), according to the VIVUS Programming Standards document. Pre-final TFLs will be generated twice on clean data for format review. Final TFLs will be generated on final data for the clinical study report.

MEDICAL WRITING

The Medpace Medical Writing team works in collaboration with the Medpace Medical Expert to provide a clinical study report according to FDA/ICH guidelines. The preparation of the Integrated Clinical/Statistical Study Report involves three stages of development: (1) the Study Report Shell (SRS), (2) the Pre-Final Study Report (PFSR), and (3) the Final Study Report (FSR).

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The SRS is prepared after sign-off of the Final DAP. The SRS is created using a template and/or style guide provided by VIVUS, or by utilizing the Medpace standard report template, which adheres to the ICH guideline, "Structure and Content of Clinical Study Reports," and follows the *American Medical Association Manual of Style*. The SRS incorporates information from the protocol, amendments, and eCRFs into sections of the report, including but not limited to the study design, study population, treatments administered, and the evaluation schedule. The statistical methods and results sections encompass information derived from the Final DAP. The results sections include mock-up in-text tables and text. The SRS undergoes a complete team review, which includes the Medical Monitor, Statistician, CTM, Data Manager, and other team members, if applicable. After the Medical Writer incorporates all team changes into the SRS, the SRS undergoes Medpace's comprehensive document QC process. Once all changes from the document QC process are implemented into the SRS, the SRS is forwarded to the VIVUS for review.

Preparation of the PFSR occurs after receipt and implementation of VIVUS comments on the SRS, declaration of a clean database, and completion of Pre-Final Analyses. If necessary, a results review meeting is conducted with key members of the Medpace and VIVUS project team as the Medical Writer begins preparing the PFSR. The PFSR is a complete version of the report without the appendices. The PFSR undergoes a complete team review, which includes the Medical Monitor, Statistician, CTM, Data Manager, and other team members, if applicable. After the Medical Writer incorporates all team changes into the

PFSR, the PFSR undergoes Medpace's comprehensive document QC process. Once all changes from the document QC process are implemented into the PFSR, the PFSR is forwarded to VIVUS for review.

The FSR is prepared once VIVUS' comments on the PFSR are returned and all requested changes are agreed upon (including the acceptance of final text for all complicated or sensitive sections, which may require sending non-QC'd drafts of the report to VIVUS), and the Final Analyses are completed. The FSR is a complete version of the report including paginated appendices and/or supplements. The FSR undergoes a complete internal QC review and is forwarded to VIVUS for sign-off. The signed cover sheet is returned by VIVUS to verify their acceptance of the FSR.

STUDY CLOSEOUT

At the conclusion of each study, once all deliverables have been met, Medpace will return the original study files to VIVUS. These will include:

- General project administration files (this file includes items such as: Outside Vendor Correspondence, Multiple Site Correspondence (e.g. faxes to all sites), Central IRB Correspondence, Project Specific SOPs and Procedures, Monitoring Plan, Trial Master File, Project Timelines, Newsletters, and Meeting Minutes)

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- Site files (this file includes site items such as: Essential Documents, Budget, Site Correspondence, Monitoring Visit Reports, Drug shipment documents, Study Supply forms, and Protocol Deviations);
- Final statistical tables and listings with results;
- Data management documentation (this file includes items such as: Database Definition Document, Final eCRFs, External Database Import Specs., Data Management Plan, Coding Reports, Analysis Plan, and Randomization Code); and
- Final clinical study report.

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Assumptions

OB-303	Description
Number of Investigators	***
Number of Screened Patients	***
Number of Randomized Patients	***
Number of Randomized Patients/Site	***
Duration of Enrollment Period	***
Duration of Treatment Period	***
Number of Investigators' Meetings	***
Number of Kickoff Meetings (at Medpace)	***
Number of Sponsor Meetings (at VIVUS)	***
Number of Conference Calls	***
Frequency of Conference Calls	***
Number of Clinical Monitors	***
Number of Pre-study Visits	***
Number of Initiation Visits	***
Number of Routine Monitoring Visits	***
Number of Closeout Visits	***
Monitoring Frequency	***
Number of Newsletters per Site (monthly)	***
Estimated Number of eCRFs per Completed Patient	***
Estimated Number of Unique eCRFs per Completed Patient	***
Total Number of eCRFs	***
Estimated Number of AE Codes Per Patient	***
Estimated Number of Medical History Codes Per Patient	***

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Estimated Number of Concomitant Medications Codes Per Patient	***
Estimated Number of Queries Per Patient	***
External Data Sources	***
Data Transfers from Medpace to VIVUS	***
Number of Raw Listings	***
Number of Unique TFs	***
Number of Version TFs	***

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Task Order #03
Appendix 3 — Project Schedule
VIVUS, Inc.
Qnexa OB-303

Milestones

OB-303	Date
Medpace Begins Work	***
Protocol Finalized	***
First Patient First Visit	***
Last Patient First Visit	***
Last Patient Last Visit	***
Final Database Lock	***
Final TFLs Available	***
Delivery of Final Clinical Study Report	***

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Task Order #03
Appendix 4 — Budget
VIVUS, Inc.
Qnexa OB-303

Medpace Fee Estimate

***

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***

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Task Order #03
Appendix 5 — Payment Schedule
VIVUS, Inc.
Qnexa OB-303

Payment Schedule

As set forth in this Agreement, professional service fees totalling $*** will be paid by VIVUS for professional services rendered by Medpace according to the following schedule.

***

Pass-through expenses will be billed to VIVUS on a monthly basis as incurred. The first Wire-Transfer payment will be invoiced prior to any site becoming active to ensure funds are available for site payments. Medpace will pay sites immediately following receipt of Wire-Transfers. Medpace will invoice VIVUS on a monthly basis and payments will be made by VIVUS within seven days of invoice receipt.

Payment Information and General Conditions

***

Inflation

The fees stipulated in the fee estimate *include* inflation for the duration of the study as specified in this proposal. Any significant shift in timelines will require a revision to the fees.

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Appendix 6 **Transfer of Obligations Form**

CONFIDENTIAL

Directions: Complete a form for each clinical study where Sponsor obligations have been transferred in accordance with 21 CFR Part 312, Subpart D (Responsibilities of Sponsors). Forward the completed form to Sponsor's Regulatory Affairs Department for submission to the applicable regulatory agencies.

Drug: VI-0521 Study ID: OB 303

Study Title: A phase III randomized, double blind, placebo controlled multicenter study to determine the safety and efficacy of VI-0521 in the treatment of obesity in adults with obesity-related comorbid conditions.

CRO Name: Medpace, Inc.

CRO Address: ***

OBLIGATIONS TRANSFERRED TO MEDPACE: x THE APPROPRIATE BOX(ES).

o All obligations in 21 CFR 312, Subpart D (Responsibilities of Sponsors) have been transferred to Medpace.
x The following obligations have been transferred to Medpace:

Sec. 312.32: IND Safety Reports
x Promptly review safety information. *Sponsor will be notified within one (1) business day of discovery of significant new or serious adverse events or risks, or any unusual frequency of reactions with respect to the drug.
o Notify all participating investigators in a written IND safety report of any AE associated with the drug that is both serious and unexpected.
o Notify the FDA in a written IND safety report of any AE associated with the drug that is both serious and unexpected.

Sec. 312.53: Selecting investigators and monitors
x (a) Select qualified investigators
x (b) Control investigational drug shipment
x (c) Obtain information from investigators
  x (1) Signed Form FDA-1572
  x (2) CV or other qualification statement
  x (3) Clinical protocol outline
  x (4) Financial disclosure information
x (d) Select qualified monitors

Sec. 312.54: Emergency research
o (a) Monitor the progress of all studies involving an exception from informed consent.
o (b) Monitor such studies to identify when an IRB determines that it can't approve the research.

Sec. 312.55: Informing investigators

x (a) Provide sites with the current Inv. Brochure.

x (b) Inform investigators of new observations on the drug, particularly with respect to AEs and safe use.

Sec. 312.56: Review of ongoing investigations

o (a) Monitor the progress of all IND studies.

x (b) Secure compliance from noncompliant investigators or discontinue drug shipments and end the investigator's participation in the study.

o (c) Review and evaluate the safety and efficacy results as it is obtained from the investigator.

x (d) Discontinue use of the investigational drug if it is determined to present an unreasonable and significant risk to subjects, notify all IRBs and investigators, and assure the return or alternate disposition of the drug from the investigators.

Sec. 312.57: Record keeping and record retention

x (a) Maintain adequate records showing investigational drug receipt, shipment, or other disposition. *Master Drug Logs will include the name of the Investigator to whom the drug is shipped, the date, and the quantity and batch of each such shipment.

x (b) Maintain complete and accurate records showing any financial interests of the investigator subject to 21 CFR 54.

x (c) Retain the records and reports required by the regulations for 2 years after the marketing application is approved, or if not approved, until 2 years after investigational drug shipment is discontinued and FDA has been notified.

o (d) Retain reserve samples of any test article and reference standard identified and used in bioequivalence or bioavailability studies.

Sec. 312.58: Inspection of sponsor's records and reports

x (a) Permit FDA personnel to have access to and copy and verify any records and reports related to the clinical investigation.

x (b) Permit DEA personnel to have access to and copy records related to the shipment, delivery, receipt and disposition of any investigational controlled substance. Assure adequate storage precautions are taken for investigational new drug substances listed in any schedule of the Controlled Substances Act.

Sec. 312.59: Disposition of unused supply of investigational drug

x Assure the return (or alternate disposition) of all unused supplies of the investigational drug from each discontinued/terminated investigator; maintain written records of any disposition of the investigational drug.

Other

o Please describe any other applicable transfers below:

September 7, 2007

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Exhibit 31.1

CERTIFICATION

I, Leland F. Wilson, certify that:

1. I have reviewed this quarterly report on Form 10-Q of VIVUS, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 8, 2013

By: /s/ LELAND F. WILSON
Leland F. Wilson
Chief Executive Officer

Exhibit 31.2

CERTIFICATION

I, Timothy E. Morris, certify that:

1. I have reviewed this quarterly report on Form 10-Q of VIVUS, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 8, 2013

By: /s/ TIMOTHY E. MORRIS
Timothy E. Morris
Sr. Vice President Finance and Global Corporate Development, Chief Financial Officer

Exhibit 32

CERTIFICATION OF CHIEF EXECUTIVE OFFICER AND CHIEF FINANCIAL OFFICER
PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

I, Leland F. Wilson, Chief Executive Officer of VIVUS, Inc., certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that the Quarterly Report of VIVUS, Inc. on Form 10-Q for the period ended March 31, 2013 fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934 and that information contained in such Quarterly Report on Form 10-Q fairly presents, in all material respects, the financial condition and results of operations of VIVUS, Inc. This written statement is being furnished to the Securities and Exchange Commission as an exhibit to such Quarterly Report on Form 10-Q. A signed original of this statement has been provided to VIVUS, Inc. and will be retained by VIVUS, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.

Date: May 8, 2013

By: /s/ LELAND F. WILSON
Leland F. Wilson

I, Timothy E. Morris, Sr. Vice President Finance and Global Corporate Development, Chief Financial Officer, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that the Quarterly Report of VIVUS, Inc. on Form 10-Q for the period ended March 31, 2013 fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934 and that information contained in such Quarterly Report on Form 10-Q fairly presents, in all material respects, the financial condition and results of operations of VIVUS, Inc. This written statement is being furnished to the Securities and Exchange Commission as an exhibit to such Quarterly Report on Form 10-Q. A signed original of this statement has been provided to VIVUS, Inc. and will be retained by VIVUS, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.

Date: May 8, 2013

By: /s/ TIMOTHY E. MORRIS
Timothy E. Morris