

Pharmasset Inc
 Form 424B5
 January 21, 2011
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Filed Pursuant to Rule 424(b)(5)
 Registration No. 333-171750

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Amount to be Registered	Proposed	Proposed	Amount of Registration Fee(1)
		Maximum Offering Price Per Share	Maximum Aggregate Offering Price	
Common Stock, \$0.001 Par Value	3,795,000	\$46.33	\$175,822,350	\$20,412.97

(1) Calculated in accordance with Rule 457(r) under the Securities Act of 1933, as amended (Securities Act). Payment of the registration fee at the time of filing of the registrant's registration statement on Form S-3, filed with the Securities and Exchange Commission on January 18, 2011 (File No. 333-171750), was deferred pursuant to Rules 456(b) and 457(r) under the Securities Act, and is paid herewith. Of such 3,795,000 shares, an aggregate of 1,000,000 shares may be sold by the selling stockholders, and the balance of such shares may be sold by the registrant.

PROSPECTUS SUPPLEMENT

(To Prospectus Dated January 18, 2011)

3,300,000 Shares

Pharmasset, Inc.

Common Stock

\$46.33 per share

We are offering 2,300,000 shares of our common stock and the selling stockholders identified in this prospectus supplement, including affiliates of the former Chairman of our board of directors, are offering 1,000,000 shares of our common stock. We will not receive any proceeds from the sale of shares held by the selling stockholders.

We have granted the underwriters an option to purchase up to 495,000 additional shares of our common stock. The underwriters may exercise this option at any time within 30 days after the date of this prospectus supplement.

Our common stock is listed on the Global Market of The NASDAQ Stock Market LLC (NASDAQ) under the symbol VRUS. The last reported sale price of our common stock on the NASDAQ Global Market on January 20, 2011 was \$46.43 per share.

Investing in our common stock involves a high degree of risk. See Risk Factors, beginning on page S-5 of this prospectus supplement to read about factors you should consider before buying shares of our common stock.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	<u>Per Share</u>	<u>Total</u>
Public Offering Price	\$ 46.33	\$ 152,889,000
Underwriting Discount	\$ 2.08485	\$ 6,880,005
Proceeds, before expenses, to us	\$ 44.24515	\$ 101,763,845
Proceeds, before expenses, to the selling stockholders	\$ 44.24515	\$ 44,245,150

You should carefully read this prospectus supplement and the accompanying prospectus, together with the documents incorporated by reference herein and therein, before you invest in our common stock.

The underwriters expect to deliver the shares to purchasers on or about January 26, 2011 through the book-entry facilities of The Depository Trust Company.

Citi

Morgan Stanley

BofA Merrill Lynch

Leerink Swann

Wedbush PacGrow Life Sciences

January 20, 2011

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You should rely only on the information contained in or incorporated by reference in this prospectus supplement and the accompanying prospectus and any free writing prospectus we may authorize to be delivered to you. We have not authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. Offers to sell, and solicitations of offers to buy, shares of our common stock are being made only in jurisdictions where offers and sales are permitted. You should not assume that the information contained, or incorporated by reference, in this prospectus supplement or the accompanying prospectus is accurate as of any date other than the date thereof.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the terms of the offering of common stock and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined together with all documents incorporated by reference. To the extent there is a conflict between the information contained in this prospectus supplement or any free writing prospectus we may authorize to be delivered to you, on the one hand, and the information contained in the accompanying prospectus or any document incorporated by reference therein, on the other hand, you should rely on the information in this prospectus supplement or such free writing prospectus, as the case may be, provided that, if any statement in one of these documents is inconsistent with a statement in another document that is filed with the Securities and Exchange Commission, or SEC, at a later time—for example, a document incorporated by reference in the accompanying prospectus—the statement in the document that is filed with the SEC at the later time modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Unless the context otherwise requires, in this prospectus supplement, Pharmasset, the Company, we, us, our and similar names refer to Pharmasset, Inc. Pharmasset and our logo are our trademarks. Other trademarks mentioned in this prospectus supplement are the property of their respective owners.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information about us and this offering. This information is not complete and does not contain all the information you should consider before investing in our common stock. You should carefully read this entire prospectus supplement and the entire accompanying prospectus, including the Risk Factors section beginning on page S-5 of this prospectus supplement and the financial statements and the other information incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision.

Our Business

We are a clinical-stage pharmaceutical company committed to discovering, developing, and commercializing novel drugs to treat viral infections. Our primary focus is on the development of nucleoside/tide analogs as oral therapeutics for the treatment of chronic hepatitis C virus (HCV) infection. Nucleoside/tide analogs are a class of compounds which act as alternative substrates for the viral polymerase, thus inhibiting viral replication. We currently have three clinical-stage product candidates, two of which we are developing ourselves and one of which we are developing with a strategic partner. We are also advancing a series of preclinical candidates in preparation for clinical development. Our three clinical stage product candidates are:

RG7128, an HCV cytosine nucleoside polymerase inhibitor we are developing through a strategic collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (collectively, Roche). In October 2010, Roche presented data from a 12-week interim analysis from the Phase 2b PROPEL study of RG7128 in combination with Pegasys® (pegylated interferon) plus Copegus® (ribavirin), the standard of care for treating HCV (SOC) in patients with HCV genotypes 1 or 4. In addition, RG7128 is in a 24-week Phase 2b JUMP-C study in combination with SOC in patients with HCV genotypes 1 or 4. Roche is planning to conduct the next study of RG7128 in combination with ritonavir-boosted danoprevir. This INFORM-SVR study is part of a series of studies designed to investigate the combination of two oral, direct acting antivirals (DAAs) in the absence of pegylated interferon. Roche is also planning to conduct a Phase 2b study in patients with HCV genotypes 2 or 3. All of these studies are being, or are expected to be, conducted by Roche;

PSI-7977, an HCV uracil nucleotide analog polymerase inhibitor that is in a 12-week Phase 2b study in combination with SOC in patients with HCV genotypes 1, 2 or 3. In January 2011, we announced preliminary data from a 12-week interim analysis from the HCV genotype 2 or 3 arm of the Phase 2b study. In addition, PSI-7977 recently began dosing in an exploratory Phase 2 study in combination with ribavirin, administered with or without pegylated interferon, in patients with HCV genotypes 2 or 3. We expect to initiate a 24-week Phase 2b study of PSI-7977 in combination with SOC during the second quarter of 2011; and

PSI-938, an HCV guanine nucleotide analog polymerase inhibitor that is in Part 2 of a Phase 1 study with PSI-7977 in patients with HCV genotype 1. In January 2011, we announced preliminary data from a 14-day interim analysis from the monotherapy cohort of the Phase 1 combination study. We plan to initiate a Phase 2 study of PSI-938 in combination with PSI-7977 during mid-2011.

In addition, we are developing PSI-661, an HCV guanine nucleotide analog polymerase inhibitor we nominated as a development candidate in October 2009. PSI-661 is in preclinical studies required for submission of an Investigational New Drug (IND) application with the U.S. Food and Drug Administration or equivalent foreign regulatory application. We plan to file an IND for PSI-661 during the first quarter of 2011.

PSI-938 or PSI-661 could potentially be used in combination with our current nucleoside/tide analogs, RG7128 or PSI-7977, as well as other classes of DAAs. Given the similarities of PSI-938 and PSI-661, our plan is to select one of these product candidates for later-stage clinical

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development based upon a review of the early human clinical trial results of both PSI-938 and PSI-661.

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You can obtain more information regarding our business and industry by reading our Annual Report on Form 10-K for the year ended September 30, 2010 filed with the SEC on November 23, 2010, and the other reports we file with the SEC.

Corporate Information

We were incorporated as Pharmasset, Inc. under the laws of Delaware on June 8, 2004. Our corporate headquarters is located at 303-A College Road East, Princeton, New Jersey 08540. Our general telephone number at that address is (609) 613-4100.

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THE OFFERING

Common Stock Offered by Us	2,300,000 shares
Common Stock Offered by Selling Stockholders	1,000,000 shares
Common Stock to be Outstanding after this Offering	36,520,379 shares
Overallotment Option	495,000 shares
Use of Proceeds	We intend to use the net proceeds from the shares sold by us in this offering for general corporate purposes, which may include but not be limited to, the funding of clinical trials, the funding of in-licensing agreements for product candidates, additional technologies or other forms of intellectual property and the acquisition of assets or businesses that are complementary to our existing business. We will not receive any proceeds from the sale of shares by the selling stockholders in this offering.
Risk Factors	See Risk Factors beginning on page S-5 and in our Annual Report on Form 10-K for the year ended September 30, 2010 for a discussion of factors you should consider carefully before deciding to invest in our common stock.
NASDAQ Global Market symbol	VRUS

The number of shares of our common stock to be outstanding after this offering is based on 34,220,379 shares of common stock outstanding as of December 31, 2010. Unless specifically stated otherwise, the information in this prospectus supplement excludes:

3,167,192 shares of our common stock issuable upon the exercise of stock options outstanding as of December 31, 2010, at a weighted average exercise price of \$15.83 per share, of which options to purchase 1,923,047 shares of our common stock were then exercisable;

209,826 shares of our common stock reserved for future grants of stock options (or other similar equity instruments) under our 2007 Equity Incentive Plan, as amended, as of December 31, 2010; and

warrants to purchase 63,623 shares of our common stock for \$12.05 per share, all of which are currently exercisable.

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise by the underwriters of their option to purchase additional shares of our common stock.

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RISK FACTORS

Investing in our securities involves risk. Please see the risk factors under the heading "Risk Factors" in our Annual Report on Form 10-K for the year ended September 30, 2010 as filed with the SEC on November 23, 2010. Before making an investment decision, you should carefully consider these risks as well as other information we include or incorporate by reference in this prospectus supplement and the accompanying prospectus. The risks and uncertainties we have described are not the only ones facing our company. Additional risks and uncertainties not presently known to us or that we currently deem to be immaterial may also affect our business operations.

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FORWARD-LOOKING STATEMENTS

This prospectus supplement contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, or the Exchange Act. Those statements are therefore entitled to the protection of the safe harbor provisions of these laws. These forward-looking statements, which are usually accompanied by words such as may, might, will, should, could, intends, estimates, predicts, potential, continue, believes, anticipates, plans, expect, involve risks and uncertainties, and relate to, without limitation, statements about our product candidates, our market opportunities, our strategy, our competition, our projected revenue and expense levels and the adequacy of our available cash resources. This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein also contain forward-looking statements attributed to third parties relating to their estimates regarding our industry. These statements are only predictions based on current expectations and projections about future events. There are important factors that could cause our actual results, level of activity, performance or achievements to differ materially from those expressed or forecasted in, or implied by, such forward-looking statements, including those factors to which we refer you in Risk Factors above.

Our business, financial condition, results of operations and prospects may change. Although we believe that the expectations reflected in these forward-looking statements are based upon reasonable assumptions, no assurance can be given that such expectations will be attained or that any deviations will not be material. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. We disclaim any obligation or undertaking to disseminate any updates or revision to any forward-looking statement contained in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference herein and therein to reflect any change in our expectations with regard thereto or any change in events, conditions or circumstances on which any such statement is based.

You should read this prospectus supplement, the accompanying prospectus and the documents that we incorporate by reference herein and therein completely and with the understanding that our actual future results may be materially different from what we expect. You should assume that the information appearing in this prospectus supplement and the accompanying prospectus is accurate as of the date on the front cover of this prospectus supplement and the accompanying prospectus, respectively, only. We qualify all of the information presented in this prospectus supplement and the accompanying prospectus, and particularly our forward-looking statements, by these cautionary statements.

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USE OF PROCEEDS

We estimate that our net proceeds from our sale of our common stock in this offering will be approximately \$101.5 million, or approximately \$123.4 million if the underwriters exercise in full their option to purchase from us 495,000 additional shares of our common stock, based upon the public offering price of \$46.33 and after deducting the underwriting discount and estimated offering expenses that are payable by us. We intend to use the net proceeds from our sale of our common stock in this offering for general corporate purposes, which may include, but not be limited to:

the funding of clinical trials;

the funding of in-licensing agreements for product candidates, additional technologies or other forms of intellectual property; and

the acquisition of assets or businesses that are complementary to our existing business.

We may also invest our net proceeds temporarily in mutual and money market funds, bank certificates of deposit and investment-grade commercial paper, corporate notes, and government securities until we use them for their stated purpose.

We will not receive any proceeds from the sale of shares of our common stock by the selling stockholders in this offering.

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Purchasers of our common stock offered by this prospectus supplement and the accompanying prospectus will experience an immediate dilution in the net tangible book value of their common stock from the public offering price. The net tangible book value of our common stock as of September 30, 2010 was \$104.1 million or \$3.06 per share. Net tangible book value per share of our common stock is equal to our net tangible assets (tangible assets less total liabilities) divided by the number of shares of our common stock issued and outstanding as of September 30, 2010.

Dilution per share represents the difference between the public offering price per share of our common stock and the adjusted net tangible book value per share of our common stock after giving effect to this offering. After reflecting the sale by us of 2,300,000 shares of our common stock at the public offering price of \$46.33 per share, less the underwriting discount and estimated offering expenses, our adjusted net tangible book value per share of our common stock as of September 30, 2010 would have been \$205.7 million or \$5.66 per share. The change represents an immediate increase in net tangible book value per share of our common stock of \$2.60 per share to existing stockholders and an immediate dilution of \$40.67 per share to new investors purchasing from us the shares of our common stock in this offering. The following table illustrates this per share dilution:

Public offering price per share		\$ 46.33
Net tangible book value per share as of September 30, 2010	\$ 3.06	
Increase per share attributable to new investors	2.60	
		5.66
Adjusted net tangible book value per share as of September 30, 2010		5.66
Dilution per share to new investors		\$ 40.67

If the underwriters exercise in full their option to purchase from us 495,000 additional shares of our common stock at the public offering price of \$46.33 per share, the adjusted net tangible book value after this offering would be \$6.18 per share, representing an increase in net tangible book value of \$3.12 per share to existing stockholders and immediate dilution in net tangible book value of \$40.15 per share to new investors purchasing from us our common stock in this offering at the public offering price.

Table of Contents**SELLING STOCKHOLDERS**

The following table, which was prepared based on information supplied to us by the selling stockholders, sets forth the name of each selling stockholder, including affiliates of the former Chairman of our board of directors (our Board), the number of shares of our common stock beneficially owned by each selling stockholder and the maximum number of shares of our common stock being offered by each selling stockholder pursuant to this prospectus supplement. The table also provides information regarding the beneficial ownership of our common stock by each selling stockholder as adjusted to reflect the assumed sale of all of the shares of our common stock offered by such selling stockholder under this prospectus supplement.

Beneficial ownership and percentage ownership are determined in accordance with the rules and regulations of the SEC and include voting or investment power with respect to shares of our common stock. This information does not necessarily indicate beneficial ownership for any other purpose. In computing the number of shares of our common stock beneficially owned by a person and the percentage ownership of that person, shares of our common stock subject to options held by that person that are currently exercisable or exercisable within 60 days of January 14, 2011 are deemed outstanding. Such shares, however, are not deemed outstanding for the purposes of computing the percentage ownership of any other person. The percentage of beneficial ownership is based on 34,220,379 shares of our common stock outstanding on January 14, 2011.

Name of Selling Stockholder	Number of Shares of Common Stock Beneficially Owned Prior to the Offering	Maximum Number of Shares of Common Stock Being Offered	Number of Shares of Common Stock Beneficially Owned After Offering	Percentage of Shares of Common Stock Beneficially Owned Before Offering	Percentage of Shares of Common Stock Beneficially Owned After Offering(2)
Burrill Life Sciences Capital Fund, L.P.	1,959,183(1)	818,183	959,183	5.7%	2.6%
Burrill Indiana Life Sciences Capital Fund, L.P.	1,959,183(1)	181,817	959,183	5.7%	2.6%

- (1) Represents 1,959,183 shares of our common stock, including (i) 51,250 shares of our common stock that are subject to immediately exercisable stock options and 5,000 shares of our common stock that are owned solely by G. Steven Burrill; (ii) 1,556,947 shares of our common stock held by Burrill Life Sciences Capital Fund, L.P. and (iii) 345,986 shares of our common stock held by Burrill Indiana Life Sciences Capital Fund, L.P. Does not include 1,000 shares of restricted stock held by Mr. Burrill which were forfeited by Mr. Burrill upon his resignation as a member of our Board on January 18, 2011. Mr. Burrill served as a member of our Board and as Chairman of our Board from August 2004 and November 2004 respectively, until January 18, 2011. Mr. Burrill also served as a member of the Audit Committee and the Compensation Committee of our Board until January 18, 2011. Mr. Burrill is the chief executive officer of Burrill & Company LLC, the general partner of Burrill Life Sciences Capital Fund, L.P. and Burrill Indiana Life Sciences Capital Fund, L.P. (collectively, the Funds), and he shares investment and voting power over the shares owned by the Funds. The Funds and Mr. Burrill are affiliates of a registered broker-dealer and, accordingly, may be deemed to be an underwriter.
- (2) Based upon 36,520,379 shares of our common stock to be outstanding after the offering (not including the exercise by the underwriters of the option to purchase an additional 495,000 shares of our common stock).

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Citigroup Global Markets Inc. (Citi) is acting as sole book-running manager of this offering and as representative of the underwriters named below. Subject to the terms and conditions stated in the underwriting agreement dated the date of this prospectus supplement, each underwriter named below has severally agreed to purchase from us and the selling stockholders, and we and the selling stockholders have agreed to sell to that underwriter, the number of shares of our common stock set forth opposite the underwriter's name.

Underwriter	Number of Shares
Citigroup Global Markets Inc.	1,650,000
Morgan Stanley & Co. Incorporated	726,000
Merrill Lynch, Pierce, Fenner & Smith Incorporated	396,000
Leerink Swann LLC	264,000
Wedbush Securities Inc.	264,000
Total	3,300,000

The underwriting agreement provides that the obligations of the underwriters to purchase the shares included in this offering are subject to approval of legal matters by counsel and to other conditions. The underwriters are obligated to purchase all the shares (other than those covered by the over-allotment option described below) if they purchase any of the shares.

Shares sold by the underwriters to the public will initially be offered at the public offering price set forth on the cover of this prospectus supplement. Any shares sold by the underwriters to securities dealers may be sold at a discount from the initial public offering price not to exceed \$1.25091 per share. If all the shares are not sold at the initial offering price, the underwriters may change the offering price and the other selling terms.

If the underwriters sell more shares than the total number set forth in the table above, we have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus supplement, to purchase up to 495,000 additional shares at the public offering price less the underwriting discount. The underwriters may exercise the option solely for the purpose of covering over-allotments, if any, in connection with this offering. To the extent the option is exercised, each underwriter must purchase a number of additional shares approximately proportionate to that underwriter's initial purchase commitment. Any shares issued or sold under the option will be issued and sold on the same terms and conditions as the other shares that are the subject of this offering.

We, our directors, certain of our officers, the former Chairman of our Board and the selling stockholders have agreed that, without the prior written consent of Citi, we and they will not, during the period ending 60 days after the date of this prospectus supplement:

offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities

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convertible into or exercisable or exchangeable for our common stock; or

enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of our common stock;

whether any such transaction described above is to be settled by delivery of our common stock or such other securities, in cash or otherwise.

In addition, during such 60-day restricted period, we will not file any registration statement with the SEC relating to the offering of any shares of our common stock or any securities convertible into or exchangeable for our common stock.

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The restrictions described above do not apply to:

with respect to us:

the shares of our common stock to be sold by us in this offering;

the issuance by us of shares of our common stock or options to purchase shares of our common stock, or common stock upon exercise of options, pursuant to our 1998 Stock Plan or our 2007 Equity Incentive Plan, as amended; or

the issuance by us of shares of our common stock upon the exercise of warrants to purchase our common stock that are currently outstanding (as described above under the heading "The Offering" on page S-4); or

with respect to our directors and certain of our officers:

transactions relating to shares of our common stock or other securities acquired in open market transactions after the completion of this offering, provided that no filing under Section 16(a) of the Exchange Act shall be required or shall be voluntarily made in connection with subsequent sales of our common stock or other securities acquired in such open market transactions;

transfers of shares of our common stock or any security convertible into our common stock as a bona fide gift; or

transfers of shares of our common stock or any security convertible into our common stock either during the respective director's or officer's lifetime or upon death by will or intestate succession to the immediate family of the director or officer or to a trust the beneficiaries of which are exclusively the respective director or officer and/or a member or members of his or her immediate family;

provided that in the case of any transfer or distribution described in the two preceding bullets (i) each donee or distributee agrees in writing to the same restrictions as set forth above and (ii) no filing under Section 16(a) of the Exchange Act, reporting a reduction in beneficial ownership of shares of our common stock, shall be required or shall be voluntarily made during the 60-day restricted period; or

with respect to the selling stockholders and G. Steven Burrill, the former Chairman of our Board:

transactions relating to shares of our common stock or other securities acquired in open market transactions after the completion of this offering, provided that no filing under Section 16(a) of the Exchange Act shall be required or shall be voluntarily made in connection with subsequent sales of our common stock or other securities acquired in such open market transactions;

the shares of our common stock to be sold by the selling stockholders in this offering;

the sale by Mr. Burrill in open market transactions after the completion of this offering of an aggregate of 56,250 shares of our common stock, provided that no filing under Section 16(a) of the Exchange Act shall be required or shall be voluntarily made in connection with such sales;

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transfers of shares of our common stock or any security convertible into our common stock as a bona fide gift;

transfers of shares of our common stock or any security convertible into our common stock either during the selling stockholder's lifetime or upon death by will or intestate succession to the immediate family of such selling stockholder or to a trust the beneficiaries of which are exclusively the selling stockholder and/or a member or members of such selling stockholder's immediate family; or

distributions of shares of our common stock or any security convertible into our common stock to general or limited partners of a selling stockholder;

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provided that in the case of any transfer or distribution described in the preceding three bullets (i) each donee or distributee agrees in writing to the same restrictions as the selling stockholders and (ii) no filing under Section 16(a) of the Exchange Act, reporting a reduction in beneficial ownership of shares of our common stock, shall be required or shall be voluntarily made during the 60-day restricted period.

The shares are listed on the NASDAQ Global Market under the symbol VRUS. The transfer agent for our common stock to be issued in this offering is Computershare Trust Company, N.A. located at 250 Royall Street, Canton, MA 02021.

The following table shows the underwriting discount that we are to pay to the underwriters in connection with this offering. This amount is shown assuming both no exercise and full exercise of the underwriters' over-allotment option.

	Paid by Pharmasset	
	No Exercise	Full Exercise
Per share	\$ 2.08485	\$ 2.08485
Total	\$ 4,795,155	\$ 5,827,156

The following table summarizes the underwriting discount that the selling stockholders are to pay to the underwriters in connection with this offering. This amount is shown assuming both no exercise and full exercise of the underwriters' over-allotment option.

	Paid by Selling Stockholders	
	No Exercise	Full Exercise
Per share	\$ 2.08485	\$ 2.08485
Total	\$ 2,084,850	\$ 2,084,850

We estimate that the total expenses of the offering that are payable by us, not including the underwriting discount, will be \$250,000.

In connection with the offering, the underwriters may purchase and sell shares in the open market. Purchases and sales in the open market may include short sales, purchases to cover short positions, which may include purchases pursuant to the over-allotment option, and stabilizing purchases.

Short sales involve secondary market sales by the underwriters of a greater number of shares than they are required to purchase in this offering.

Covered short sales are sales of shares in an amount up to the number of shares represented by the underwriters' over-allotment option.

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Naked short sales are sales of shares in an amount in excess of the number of shares represented by the underwriters over-allotment option.

Covering transactions involve purchases of shares either pursuant to the over-allotment option or in the open market after the distribution has been completed in order to cover short positions.

To close a naked short position, the underwriters must purchase shares in the open market after the distribution has been completed. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in this offering.

To close a covered short position, the underwriters must purchase shares in the open market after the distribution has been completed or must exercise the over-allotment option. In determining the source of

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shares to close the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the over-allotment option.

Stabilizing transactions involve bids to purchase shares so long as the stabilizing bids do not exceed a specified maximum.

Purchases to cover short positions and stabilizing purchases, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the shares. They may also cause the price of the shares to be higher than the price that would otherwise exist in the open market in the absence of these transactions. The underwriters may conduct these transactions on the NASDAQ Global Market, in the over-the-counter market or otherwise. If the underwriters commence any of these transactions, they may discontinue them at any time.

The underwriters may, from time to time, engage in transactions with and perform services for us in the ordinary course of their business for which they may receive customary fees and reimbursement of expenses.

We and the selling stockholders have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make because of any of those liabilities.

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MATERIAL U.S. FEDERAL TAX CONSIDERATIONS FOR NON-U.S. HOLDERS

The following discussion is a general summary of the material U.S. federal income and estate tax consequences of the ownership and disposition of our common stock applicable to Non-U.S. Holders. As used herein, a Non-U.S. Holder means a beneficial owner of our common stock that is *not* a U.S. person for U.S. federal income tax purposes, and that will hold shares of our common stock as capital assets (*i.e.*, generally, for investment). For U.S. federal income tax purposes, a U.S. person includes:

an individual who is a citizen or resident of the United States;

a corporation (or other entity treated as a corporation for U.S. federal income tax purposes) created or organized in the United States or under the laws of the United States, any state thereof or the District of Columbia;

an estate the income of which is includible in gross income regardless of source; or

a trust that (A) is subject to the primary supervision of a court within the United States and the control of one or more U.S. persons, or (B) otherwise has validly elected to be treated as a U.S. domestic trust.

If a partnership holds shares of our common stock, the U.S. federal income tax treatment of a partner in the partnership will generally depend on the status of the partner and the activities of the partnership. This discussion does not address the tax treatment of partnerships or persons who hold their common stock through partnerships or other pass-through entities for U.S. federal income tax purposes. A partner in a partnership or other pass-through entity that will hold shares of our common stock should consult with its own tax advisor regarding the tax consequences of the holding and disposing of shares of our common stock through a partnership or other pass-through entity, as applicable.

This summary does not consider specific facts and circumstances that may be relevant to a particular Non-U.S. Holder's tax position and does not consider U.S. state and local or non-U.S. tax consequences. It also does not consider Non-U.S. Holders subject to special tax treatment under the U.S. federal income tax laws (including banks and insurance companies, dealers in securities, holders of our common stock held as part of a straddle, hedge, conversion transaction or other risk-reduction transaction, controlled foreign corporations, passive foreign investment companies, companies that accumulate earnings to avoid U.S. federal income tax, foreign tax-exempt organizations, former U.S. citizens or residents and persons who hold or receive common stock as compensation or pursuant to the exercise of compensatory options). This summary is based on provisions of the U.S. Internal Revenue Code of 1986, as amended, or the Code, applicable Treasury regulations, administrative pronouncements of the U.S. Internal Revenue Service, or the IRS, and judicial decisions, all as in effect on the date hereof, and all of which are subject to change, possibly on a retroactive basis, and different interpretations.

This summary is included herein as general information only. Accordingly, each prospective Non-U.S. Holder is urged to consult its tax advisor with respect to the U.S. federal, state, local and non-U.S. income, estate and other tax consequences of holding and disposing of our common stock.

U.S. Trade or Business Income

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For purposes of this discussion, dividend income and gain on the sale or other taxable disposition of our common stock will be considered to be U.S. trade or business income if such income or gain is (i) effectively connected with the conduct by a Non-U.S. Holder of a trade or business within the United States and (ii) in the case of a Non-U.S. Holder that is eligible for the benefits of an income tax treaty with the United States, attributable to a permanent establishment (or, for an individual, a fixed base) maintained by the Non-U.S. Holder in the United States. Generally, U.S. trade or business income is not subject to U.S. federal withholding tax (provided the Non-U.S. Holder complies with applicable certification and disclosure requirements). Instead, a Non-U.S. Holder is subject to U.S. federal income tax on U.S. trade or business income on a net income basis at

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regular U.S. federal income tax rates in the same manner as a U.S. person. Any U.S. trade or business income received by a Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a 30% rate, or at a lower rate prescribed by an applicable income tax treaty, under specific circumstances.

Distributions

Distributions of cash or property that we pay will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). A Non-U.S. Holder generally will be subject to U.S. federal withholding tax at a 30% rate, or at a reduced rate prescribed by an applicable income tax treaty, on any dividends received in respect of our common stock. If the amount of a distribution exceeds our current and accumulated earnings and profits, such excess first will be treated as a tax-free return of capital to the extent of the Non-U.S. Holder's tax basis in our common stock, and thereafter will be treated as capital gain. In order to obtain a reduced rate of U.S. federal withholding tax under an applicable income tax treaty, a Non-U.S. Holder will be required to provide a properly executed IRS Form W-8BEN certifying its entitlement to benefits under the treaty. A Non-U.S. Holder of our common stock that is eligible for a reduced rate of U.S. federal withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by filing an appropriate claim for a refund with the IRS. A Non-U.S. Holder should consult its own tax advisor regarding its possible entitlement to benefits under an income tax treaty.

The U.S. federal withholding tax does not apply to dividends that are U.S. trade or business income, as defined above, of a Non-U.S. Holder who provides a properly executed IRS Form W-8ECI, certifying that the dividends are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States.

Dispositions of Our Common Stock

A Non-U.S. Holder generally will not be subject to U.S. federal income or withholding tax in respect of any gain on a sale or other disposition of our common stock unless:

the gain is U.S. trade or business income, as discussed above;

the Non-U.S. Holder is an individual who is present in the United States for 183 or more days in the taxable year of the disposition and meets other conditions; or

we are or have been a United States real property holding corporation, or a USRPHC, under Section 897 of the Code at any time during the shorter of the five-year period ending on the date of disposition and the Non-U.S. Holder's holding period for our common stock.

In general, a corporation is a USRPHC if the fair market value of its United States real property interests, as defined in the Code and applicable Treasury regulations, equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests and its other assets used or held for use in a trade or business. If we are determined to be a USRPHC, the U.S. federal income and withholding taxes relating to interests in USRPHCs nevertheless will not apply to gains derived from the sale or other disposition of the common stock by a Non-U.S. Holder whose shareholdings, actual and constructive, at all times during the applicable period, amount to 5% or less of our common stock, provided that our common stock is regularly traded on an established securities market. We do not believe that we currently are a USRPHC, and we do not anticipate becoming a USRPHC in the future. However, no assurance can be given that we will not be a USRPHC, or that our common stock

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will be considered regularly traded, when a Non-U.S. Holder sells its shares of our common stock.

U.S. Federal Estate Taxes

Shares of our common stock owned or treated as owned by an individual who is a Non-U.S. Holder at the time of death will be included in the individual's gross estate for U.S. federal estate tax purposes, and may be subject to U.S. federal estate tax, unless an applicable estate tax treaty provides otherwise.

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Information Reporting and Backup Withholding Requirements

We must annually report to the IRS and to each Non-U.S. Holder any dividend income that is subject to U.S. federal withholding tax, or that is exempt from such withholding tax pursuant to an income tax treaty. Copies of these information returns also may be made available under the provisions of a specific treaty or agreement to the tax authorities of the country in which the Non-U.S. Holder resides. Under certain circumstances, the Code imposes a backup withholding obligation (currently at a rate of 28%) on certain reportable payments. Dividends paid to a Non-U.S. Holder of our common stock generally will be exempt from backup withholding if the Non-U.S. Holder provides a properly executed applicable IRS Form W-8 or otherwise establishes an exemption.

The payment of the proceeds from the disposition of common stock to or through the U.S. office of any broker, U.S. or foreign, will be subject to information reporting and possible backup withholding unless the holder certifies as to its non-U.S. status under penalties of perjury or otherwise establishes an exemption, provided that the broker does not have actual knowledge or reason to know that the holder is a U.S. person or that the conditions of any other exemption are not, in fact, satisfied. The payment of the proceeds from the disposition of common stock to or through a non-U.S. office of a non-U.S. broker will not be subject to information reporting or backup withholding unless the non-U.S. broker has certain types of relationships with the United States (a U.S. related person). In the case of the payment of the proceeds from the disposition of our common stock to or through a non-U.S. office of a broker that is either a U.S. person or a U.S. related person, the Treasury regulations require information reporting (but not the backup withholding) on the payment unless the broker has documentary evidence in its files that the holder is a Non-U.S. Holder and the broker has no knowledge to the contrary. Non-U.S. Holders should consult their own tax advisors on the application of information reporting and backup withholding to them in their particular circumstances (including upon their disposition of our common stock).

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a Non-U.S. Holder will be refunded or credited against the Non-U.S. Holder's U.S. federal income tax liability, if any, if the Non-U.S. Holder provides the required information to the IRS.

New Legislation Relating to Foreign Accounts

Newly enacted legislation may impose withholding taxes on certain types of payments made to foreign financial institutions and non-financial foreign entities (each as defined under these rules). The legislation imposes a 30% withholding tax on dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a foreign financial institution or to a non-financial foreign entity, unless (i) the foreign financial institution undertakes certain diligence and reporting obligations with respect to certain U.S. account holders or (ii) the non-financial foreign entity either certifies it does not have any substantial U.S. owners or furnishes identifying information regarding each substantial U.S. owner. If the payee is a foreign financial institution, it must enter into an agreement with the United States Treasury requiring, among other things, that it undertake to identify accounts held by certain U.S. persons or U.S.-owned foreign entities, annually report certain information about such accounts, and withhold 30% on payments to account holders whose actions prevent it from complying with these reporting and other requirements. The legislation would apply to payments made after December 31, 2012. Prospective investors should consult their tax advisors regarding the possible implications of this legislation on their investment in our common stock.

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LEGAL MATTERS

The validity of the shares of common stock we are offering will be passed upon by Pepper Hamilton LLP, Philadelphia, Pennsylvania. Wilmer Cutler Pickering Hale and Dorr LLP, Boston, Massachusetts, is counsel for the underwriters.

EXPERTS

The financial statements and management's assessment of the effectiveness of internal control over financial reporting incorporated by reference in this prospectus supplement and elsewhere in this registration statement have been so incorporated by reference in reliance upon the reports of Grant Thornton LLP, independent registered public accountants, upon the authority of said firm as experts in accounting and auditing in giving said reports.

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PROSPECTUS

Pharmasset, Inc.

COMMON STOCK

This prospectus relates to common stock that we or certain selling stockholders may sell from time to time in one or more offerings in amounts, at prices and on terms to be determined at the time of any such offering. This prospectus describes the general manner in which our common stock will be offered. Each time any common stock is offered pursuant to this prospectus, we will provide a prospectus supplement to this prospectus. The prospectus supplement will contain specific information about the offering, including the number of shares of our common stock to be sold by us or any selling stockholders. The prospectus supplement may also add, update or change information contained in this prospectus. You should read this prospectus and any applicable accompanying prospectus supplement carefully before you make your investment decision.

Our common stock is listed on The NASDAQ Stock Market LLC under the symbol VRUS.

Our common stock may be sold directly by us or any selling stockholders, through dealers or agents designated from time to time, to or through underwriters or through a combination of these methods. See Plan of Distribution in this prospectus. We may also describe the plan of distribution for any particular offering of common stock in any applicable prospectus supplement. If any agents, underwriters or dealers are involved in the sale of shares of common stock in respect of which this prospectus is being delivered, we will disclose their names and the nature of any arrangements with them in a prospectus supplement. The net proceeds expected to be received by us or any selling stockholders from any such sale will also be included in a prospectus supplement.

Investing in our common stock involves risks. See Risk Factors on page 5 of this prospectus. We may include specific risk factors in an applicable prospectus supplement under the heading Risk Factors. You should review that section of the prospectus supplement for a discussion of matters that investors in our common stock should consider.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is January 18, 2011

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ABOUT THIS PROSPECTUS

This prospectus is part of an automatic registration statement on Form S-3, or Registration Statement, that we filed with the Securities and Exchange Commission, or SEC, using a shelf registration process as a well-known seasoned issuer as defined in Rule 405 under the Securities Act of 1933, as amended, which we refer to as the Securities Act. Under the automatic shelf registration process, we or any selling stockholders to be named in a prospectus supplement may offer and sell, from time to time, shares of our common stock in one or more offerings or resales. This prospectus provides you with a general description of our common stock. Each time we or any selling stockholders use this prospectus to sell our common stock, we will provide a prospectus supplement that will contain specific information about us or such selling stockholders and the terms on which our common stock is being offered and sold. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and any prospectus supplement and the documents incorporated by reference into this prospectus, together with the additional information described below under Where You Can Find More Information, carefully before making an investment decision.

Any statement made in this prospectus or in a document incorporated by reference in this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in any prospectus supplement or in any other subsequently filed document that is also incorporated by reference in this prospectus modifies or supersedes that statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus. See Incorporation of Certain Documents by Reference in this prospectus.

Unless the context otherwise requires, in this prospectus, Pharmasset, the Company, we, us, our and similar names refer to Pharmasset, Inc.

Pharmasset and our logo are our trademarks. Other trademarks mentioned in this prospectus are the property of their respective owners.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and we file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy the reports, proxy statements and other information that we file at the SEC's Public Reference Room at 100 F Street NE, Washington, D.C. 20549 at prescribed rates. Information on the operation of the Public Reference Room may be obtained by calling the SEC at 1-800-SEC-0330. Our filings are also available free of charge at the SEC's website at <http://www.sec.gov> and through The NASDAQ Stock Market LLC, or NASDAQ, on which our common stock is listed. Information about obtaining copies of our public filings with NASDAQ is available at its website at <http://www.nasdaq.com>.

This prospectus is part of the Registration Statement that we filed with the SEC under the Securities Act. This prospectus does not contain all of the information set forth in the Registration Statement. For more information about us and our securities, you should read the Registration Statement and its exhibits and schedules. Copies of the Registration Statement, including its exhibits, may be inspected free of charge at the offices of the SEC or obtained at prescribed rates from the SEC's Public Reference Room at 100 F Street NE, Washington, D.C. 20549. Copies of the Registration Statement may also be obtained free of charge at the SEC's website at <http://www.sec.gov>.

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INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference the information we file with the SEC, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus, and information that we file with the SEC after the time the Registration Statement of which this prospectus forms a part is filed with the SEC will automatically update and may supersede this information. We are incorporating by reference into this prospectus the documents listed below:

the description of our common stock contained in our Form 8-A filed with the SEC on April 24, 2007, including any amendments or reports filed for the purpose of updating the description;

our Annual Report on Form 10-K for the fiscal year ended September 30, 2010 filed with the SEC on November 23, 2010;

our Current Reports on Form 8-K filed with the SEC on November 18, 2010 and December 13, 2010; and

all documents that we file with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act after the time the Registration Statement of which this prospectus forms a part is filed with the SEC and before the termination of the final offering of securities under this prospectus.

We do not incorporate by reference any information furnished to the SEC pursuant to Items 2.02 or 7.01 of Form 8-K unless specifically stated otherwise in such documents. Any statement contained in a prospectus or in a document incorporated by reference in this prospectus as of the time the Registration Statement of which this prospectus forms a part is filed with the SEC shall be modified or superseded for purposes of this prospectus to the extent that a statement contained in an amendment to this prospectus, any prospectus supplement or in any other subsequently filed document which is incorporated by reference modifies or supersedes such statement.

You can obtain copies of any of the documents incorporated by reference in this prospectus from us or, as described above, through the SEC or the SEC's website at <http://www.sec.gov>. Documents incorporated by reference are available from us, without charge, excluding all exhibits unless specifically incorporated by reference in the documents. You may obtain documents incorporated by reference in this prospectus by writing to us at the following address or by calling us at the telephone number listed below:

Pharmasset, Inc.

303-A College Road East

Princeton, New Jersey 08540

Attention: Investor Relations

Telephone: (609) 613-4100

We also maintain a web site at <http://www.pharmasset.com> (which is not intended to be an active hyperlink in this prospectus) through which you can obtain copies of documents that we have filed with the SEC. The contents of that site are not incorporated by reference in or otherwise a part of this prospectus.

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FORWARD-LOOKING STATEMENTS

This prospectus, any prospectus supplement, and the documents incorporated by reference herein and therein contain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. Those statements are therefore entitled to the protection of the safe harbor provisions of these laws. These forward-looking statements, which are usually accompanied by words such as may, might, will, should, could, intends, estimates, predicts, potential, continue, believes, anticipates, plans, expects and similar risks and uncertainties, and relate to, without limitation, statements about our research and development plans and programs, market opportunities, our strategy, our competition, our projected revenue and expense levels and the adequacy of our available cash resources. This prospectus, any prospectus supplement, and the documents incorporated by reference herein and therein also contain forward-looking statements attributed to third parties relating to their estimates regarding our industry. These statements are only predictions based on current expectations and projections about future events. There are important factors that could cause our actual results, level of activity, performance or achievements to differ materially from those expressed or forecasted in, or implied by, such forward-looking statements, including those factors discussed in Risk Factors below.

Although we believe that the expectations reflected in these forward-looking statements are based upon reasonable assumptions, no assurance can be given that such expectations will be attained or that any deviations will not be material. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this prospectus, any prospectus supplement, and the documents incorporated by reference herein and therein may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. We disclaim any obligation or undertaking to disseminate any updates or revision to any forward-looking statement contained herein or therein to reflect any change in our expectations with regard thereto or any change in events, conditions or circumstances on which any such statement is based.

You should read this prospectus, any prospectus supplement, and the documents incorporated by reference herein and therein, as well as the exhibits filed with or incorporated by reference into the Registration Statement, completely and with the understanding that our actual future results may be materially different from what we expect. You should assume that the information appearing in this prospectus and any prospectus supplement is accurate as of the date on the front cover of this prospectus or such prospectus supplement only. You should assume that the information incorporated by reference herein is accurate only as of the date of the document from which such information is incorporated. Our business, financial condition, results of operations and prospects may change. We may not update these forward-looking statements, even though our situation may change in the future, unless we have obligations under the federal securities laws to update and disclose material developments related to previously disclosed information. We qualify all of the information presented in this prospectus and any prospectus supplement, and particularly our forward-looking statements, by these cautionary statements.

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ABOUT PHARMASSET, INC.

We are a clinical-stage pharmaceutical company committed to discovering, developing, and commercializing novel drugs to treat viral infections. Our primary focus is on the development of nucleoside/tide analogs as oral therapeutics for the treatment of chronic hepatitis C virus (HCV) infection. Nucleoside/tide analogs are a class of compounds which act as alternative substrates for the viral polymerase, thus inhibiting viral replication. We currently have three clinical-stage product candidates, two of which we are developing ourselves and one of which we are developing with a strategic partner. We are also advancing a series of preclinical candidates in preparation for clinical development. Our three clinical stage product candidates are:

RG7128, an HCV cytosine nucleoside polymerase inhibitor we are developing through a strategic collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (collectively, Roche). In October 2010, Roche presented data from a 12-week interim analysis from the Phase 2b PROPEL study of RG7128 in combination with Pegasys® (pegylated interferon) plus Copegus® (ribavirin), the standard of care for treating HCV (SOC) in patients with HCV genotypes 1 or 4. In addition, RG7128 is in a 24-week Phase 2b JUMP-C study in combination with SOC in patients with HCV genotypes 1 or 4. Roche is planning to conduct the next study of RG7128 in combination with ritonavir-boosted danoprevir. This INFORM-SVR study is part of a series of studies designed to investigate the combination of two oral, direct acting antivirals (DAAs) in the absence of pegylated interferon. Roche is also planning to conduct a Phase 2b study in patients with HCV genotypes 2 or 3. All of these studies are being, or are expected to be, conducted by Roche;

PSI-7977, an HCV uracil nucleotide analog polymerase inhibitor that is in a 12-week Phase 2b study in combination with SOC in patients with HCV genotypes 1, 2 or 3. In January 2011, we announced preliminary data from a 12-week interim analysis from the HCV genotype 2 or 3 arm of the Phase 2b study. In addition, PSI-7977 recently began dosing in an exploratory Phase 2 study in combination with ribavirin, administered with or without pegylated interferon, in patients with HCV genotypes 2 or 3. We expect to initiate a 24-week Phase 2b study of PSI-7977 in combination with SOC during the second quarter of 2011; and

PSI-938, an HCV guanine nucleotide analog polymerase inhibitor that is in Part 2 of a Phase 1 study with PSI-7977 in patients with HCV genotype 1. In January 2011, we announced preliminary data from a 14-day interim analysis from the monotherapy cohort of the Phase 1 combination study. We plan to initiate a Phase 2 study of PSI-938 in combination with PSI-7977 during mid-2011. In addition, we are developing PSI-661, an HCV guanine nucleotide analog polymerase inhibitor we nominated as a development candidate in October 2009. PSI-661 is in preclinical studies required for submission of an Investigational New Drug application with the U.S. Food and Drug Administration or equivalent foreign regulatory application. We plan to file an IND for PSI-661 during the first quarter of 2011. PSI-938 or PSI-661 could potentially be used in combination with our current nucleoside/tide analogs, RG7128 or PSI-7977, as well as other classes of DAAs. Given the similarities of PSI-938 and PSI-661, our plan is to select one of these product candidates for later-stage clinical development based upon a review of the early human clinical trial results of both PSI-938 and PSI-661.

You can get more information regarding our business and industry by reading our most recent Annual Report on Form 10-K and the other reports we file with the SEC. See [Where You Can Find More Information](#) and [Incorporation of Certain Documents by Reference](#).

CORPORATE INFORMATION

We were incorporated as Pharmasset, Inc. under the laws of Delaware on June 8, 2004. Our corporate headquarters is located at 303-A College Road East, Princeton, New Jersey 08540. Our general telephone number at that address is (609) 613-4100.

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RISK FACTORS

Investing in our securities involves risk. Please see the risk factors under the heading "Risk Factors" in our most recent Annual Report on Form 10-K, which is on file with the SEC and is incorporated herein by reference. Before making an investment decision, you should carefully consider these risks as well as other information we include or incorporate by reference in this prospectus and any prospectus supplement. The risks and uncertainties we have described are not the only ones facing our company. Additional risks and uncertainties not presently known to us or that we currently deem to be immaterial may also affect our business operations.

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USE OF PROCEEDS

Unless we indicate otherwise in the prospectus supplement for a particular offering by us, we intend to use the net proceeds from our sale of shares of our common stock offered by this prospectus for general corporate purposes, which may include, but not be limited to, the funding of clinical trials, the funding of in-licensing agreements for product candidates, additional technologies or other forms of intellectual property, the repayment of our debt and the acquisition of assets or businesses that are complementary to our existing business. We will set forth in the prospectus supplement for a particular offering our intended use for the net proceeds received from our sale of shares of our common stock in such offering. We may also invest the net proceeds temporarily in mutual and money market funds, bank certificates of deposit and investment-grade commercial paper, corporate notes, and government securities until we use them for their stated purpose.

We will not receive any proceeds from the resale of shares of our common stock by selling stockholders under this prospectus or any prospectus supplement.

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DESCRIPTION OF OUR COMMON STOCK

We or any selling stockholders may offer shares of our common stock from time to time in one or more offerings under this prospectus at prices and on terms to be determined by market conditions at the time of the offering. This prospectus provides you with a general description of our common stock that we or any selling stockholders may offer. In connection with each offering, we or any selling stockholders will provide a prospectus supplement that will describe the specific amounts, prices and terms of the common stock being offered.

The prospectus supplement may also add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement will offer a security other than our common stock described in this prospectus.

This prospectus may not be used to consummate a sale of shares of our common stock unless it is accompanied by a prospectus supplement.

General

Our certificate of incorporation authorizes the issuance of up to 100,000,000 shares of common stock, par value \$0.001 per share and 10,000,000 shares of undesignated preferred stock, par value \$0.001 per share, the rights and preferences of which may be established from time to time by our board of directors. As of December 31, 2010, we had outstanding 34,220,379 shares of common stock and zero shares of preferred stock.

The following is qualified in its entirety by reference to our certificate of incorporation and our bylaws, and by the provisions of applicable law. Our certificate of incorporation and bylaws, in effect as of the date of this prospectus, are included as exhibits to our Annual Report on Form 10-K filed with the SEC on December 31, 2007 and our Current Report on Form 8-K filed with the SEC on March 22, 2010, respectively.

Holders of our common stock are entitled to one vote for each share for the election of directors and on all other matters submitted to a vote of stockholders, and do not have cumulative voting rights. Generally, in matters other than the election of directors, the affirmative vote of a majority of the shares present in person or represented by proxy and entitled to vote on the matter shall be the action of the stockholders. For the election of directors, directors are elected by a plurality of the votes of the shares present in person or represented by proxy and entitled to vote. Holders of our common stock are entitled to receive, as, when and if declared by our board of directors from time to time, such dividends and other distributions in cash, stock or property from our assets or funds legally available for such purposes, subject to any preferential dividend or other rights of any then outstanding preferred stock.

No preemptive, conversion, subscription or liquidation rights or sinking fund provisions apply to our common stock. All outstanding shares of our common stock are fully paid and non-assessable. In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in the assets available for distribution, subject to any preferential or other rights of any then outstanding preferred stock.

Our board of directors has the authority, without action by our stockholders, to designate and issue preferred stock in one or more classes or one or more series of stock within any class and to designate the rights, preferences and privileges of each class or series, which may be greater than the rights of our common stock. It is not possible to state the actual effect of the issuance of any shares of preferred stock upon the rights of holders of our common stock until our board of directors determines the specific rights of the holders of such preferred stock. However, the effects might include, among other things:

restricting dividends on the common stock;

diluting the voting power of the common stock;

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impairing the liquidation rights of the common stock; or

delaying or preventing a change in our control without further action by the stockholders.

Anti-Takeover Effects of Provisions of Our Certificate of Incorporation, Our Bylaws and Delaware Law

Some provisions of our certificate of incorporation and bylaws, as well as Section 203 of the General Corporation Law of the State of Delaware, may contain various provisions intended to promote stability of our stockholder base and render more difficult certain unsolicited or hostile attempts to take us over, which could disrupt us, divert the attention of our directors, executive officers and employees and adversely affect the independence and integrity of our business. A summary of these provisions of our certificate of incorporation, our bylaws and Delaware law is set forth below.

Classified Board; Removal of Directors. Pursuant to our certificate of incorporation, the size of our board of directors shall not be less than three or greater than 21. Our board of directors determines its specific size at any given time. Our certificate of incorporation provides that the directors will be divided into three classes, with each class consisting as nearly as possible in size of one-third of the directors. Directors elected by our stockholders at an annual meeting of stockholders will be elected by a plurality of the votes of the shares present in person or represented by proxy and entitled to vote at such annual meeting.

Our certificate of incorporation provides that except as otherwise provided for or fixed by or pursuant to an amendment to our certificate of incorporation setting forth the rights of the holders of any class or series of preferred stock, newly created directorships resulting from any increase in the number of directors and any vacancies on our board of directors shall be filled by the affirmative vote of a majority of the remaining directors then in office, even though less than a quorum of the board. Any director elected in accordance with the preceding sentence shall be a director of the same class as the director whose vacancy he or she fills and shall hold office until the next annual meeting of stockholders, and until such director's successor shall have been duly elected and qualified. No decrease in the number of directors constituting our board of directors will shorten the term of any incumbent director. Our bylaws provide that any director may be removed from office for cause at any time by vote of the holders of a majority of the shares then entitled to vote at an election of directors.

These provisions of our certificate of incorporation and bylaws would preclude a third party from removing incumbent directors and simultaneously gaining control of our board of directors by filling the vacancies created by removal with its own nominees. Under the classified board provisions described above, it would take at least two elections of directors for any individual or group to gain control of our board of directors. Accordingly, these provisions could discourage a third party from initiating a proxy contest, making a tender offer or otherwise attempting to gain control of us.

Special Stockholders Meetings and Right to Act by Written Consent. Our bylaws provide that a special meeting of stockholders may be called only by the chairman of our board of directors or our President or upon a resolution adopted by our board of directors. Our stockholders are not permitted to call, or to require that our board of directors call, a special meeting of stockholders. Moreover, the business permitted to be conducted at any special meeting of stockholders is limited to the business brought before the meeting pursuant to the notice of the meeting given by us. Our bylaws provide that any action of stockholders may be taken only at a meeting of the stockholders and may not be taken without a meeting through the execution of a consent or consents thereto by the stockholders.

Procedures for Stockholder Nominations and Proposals. Our bylaws establish an advance notice procedure for stockholders to nominate candidates for election as directors and to propose any new business at any annual meeting. With respect to stockholder nominations and proposals, only persons nominated in accordance with this procedure are eligible to serve as directors, and only business brought before the annual meeting in accordance with this procedure may be conducted at the annual meeting. Under this procedure, notice of stockholder

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nominations and proposals for new business at the annual meeting, regardless of whether a stockholder seeks inclusion of a proposal in our proxy pursuant to Rule 14a-8 under the Exchange Act, must be received at our principal executive offices not less than 120 calendar days prior to the date of our proxy statement made available to stockholders in connection with the previous year's annual meeting of stockholders, except that, if no annual meeting of stockholders was held in the previous year, or if the date of the annual meeting of stockholders has been changed by more than 30 calendar days from the date contemplated at the time of the previous year's proxy statement, the notice must be received at our principal executive offices not less than the later of (i) 150 calendar days prior to the date of the contemplated annual meeting and (ii) the date that is 10 calendar days after the date of the first public announcement or other notification to the stockholders of the date of the contemplated annual meeting. For nominations and proposals for any special meetings, our bylaws require notice not more than 60 days nor less than 10 days before the special meeting. Our bylaws provide that notice to our secretary with respect to any stockholder nomination or proposal must include certain information regarding the nominee, the proposal and the stockholder nominating a director or proposing business.

By requiring advance notice of nominations by our stockholders, our board of directors is given the opportunity to consider the qualifications of the proposed nominees and, to the extent deemed necessary or desirable by our board of directors, to inform stockholders about such qualifications. The advance notice requirement related to other proposed business will provide a more orderly procedure for conducting annual meetings of our stockholders and, to the extent deemed necessary or desirable by our board of directors, will provide our board of directors with an opportunity to inform our stockholders, prior to such meetings, of our board of directors' position regarding action to be taken with respect to such business, so that our stockholders can better decide whether to attend such a meeting or to grant a proxy regarding the disposition of any such business.

Although our bylaws do not give our board of directors any power to approve or disapprove stockholder nominations for the election of directors or proposals for action, the Chairman of our board of directors has the power to determine compliance with the stockholder notice procedure described above. Our bylaws also may have the effect of precluding a contest for the election of directors or the consideration of stockholder proposals if the proper procedures are not followed, and of discouraging or deterring a third party from conducting a solicitation of proxies to elect its own slate of directors or to approve its own proposal, without regard to whether consideration of such nominees or proposals might be harmful or beneficial to us and our stockholders.

Authorized but Unissued Shares. The authorized but unissued shares of our common stock and preferred stock are available for future issuance without stockholder approval, subject to various limitations imposed by NASDAQ. These additional shares may be used for a variety of corporate purposes, including future public offerings to raise additional capital, corporate acquisitions and employee benefit plans. The existence of authorized but unissued shares of common stock and preferred stock could make it more difficult, or discourage an attempt, to obtain control of us by means of a proxy contest, tender offer, merger or otherwise.

Amendment of Our Certificate of Incorporation and Bylaws. Our certificate of incorporation provides that we reserve the right to amend, alter, change or repeal any provisions contained in our certificate of incorporation in the manner now or hereafter prescribed by law, and all the provisions of our certificate of incorporation and all rights conferred on our stockholders, directors and officers in our certificate of incorporation are subject to this reserved power. Pursuant to Section 242 of the General Corporation Law of the State of Delaware, we may amend our certificate of incorporation, from time to time, in any respect, so long as our certificate of incorporation as amended would contain only such provisions as would be lawful to insert in an original certificate of incorporation filed at the time of the filing of the amendment. Upon approval of such amendment by our board of directors, the affirmative vote of a majority of the outstanding stock entitled to vote on such amendment would be required to effect the amendment to our certificate of incorporation.

In addition, our bylaws provide that the amendment or repeal by our stockholders of any bylaw may be made by the affirmative vote of the holders of a majority of the shares then entitled to vote at an election of

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directors, except that bylaws governing (i) special meetings of stockholders, (ii) notice of stockholder meetings, (iii) consents of notice, (iv) validity of notice, (v) stockholder action by written consent, (vi) removal of directors, (vii) election of directors, (viii) board vacancies, board classification and board compensation and (ix) amendments to the bylaws may only be amended by the affirmative vote of the holders of not less than 60% of the shares outstanding and entitled to vote at an election of directors. Our certificate of incorporation and bylaws also provide that, subject to the terms of any series of preferred stock, our bylaws may be amended by our board of directors upon the affirmative vote of a majority of the directors present at any regular or special meeting of the board of directors at which a quorum is present or by a written consent of the directors.

Delaware Anti-Takeover Statute. We are subject to Section 203 of the General Corporation Law of the State of Delaware. This law prohibits a publicly held Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years after the time such stockholder became an interested stockholder unless certain conditions are satisfied. The prohibitions set forth in Section 203 of the General Corporation Law of the State of Delaware do not apply if, among other things:

prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;

upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned by persons who are directors and also officers and by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

on or subsequent to the date of the transaction, the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines "business combination" to include:

any merger or consolidation involving the corporation and the interested stockholder;

any sale, lease, exchange, mortgage, pledge, transfer or other disposition, except proportionately as a stockholder of such corporation, to or with the interested stockholder, of assets of the corporation having an aggregate market value equal to 10% or more of either the aggregate market value of all the assets of the corporation or the aggregate market value of all the outstanding stock of the corporation;

in general, any transaction that results in the issuance or transfer by the corporation of any of its stock to the interested stockholder;

any transaction involving the corporation which has the effect of increasing the proportionate share of the stock of any class or series, or securities convertible into the stock of any class or series, of the corporation which is owned by the interested stockholder, except as a result of immaterial changes due to fractional share adjustments or as a result of any purchase or redemption of any shares of stock not caused, directly or indirectly, by the interested stockholder; or

the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

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In general, Section 203 defines an interested stockholder as:

any person that owns 15% or more of the outstanding voting stock of the corporation;

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any person that is an affiliate or associate of the corporation and was the owner of 15% or more of the outstanding voting stock of the corporation at any time within the three-year period immediately prior to the date on which it is sought to be determined whether or not such person is an interested stockholder; and

the affiliates or associates of either of the preceding two categories.

Limitation of Liability

Our certificate of incorporation provides that no director shall be personally liable to us or to our stockholders for monetary damages for breach of fiduciary duty as a director, except that the limitation shall not eliminate or limit liability to the extent that the elimination or limitation of such liability is not permitted by the General Corporation Law of the State of Delaware as the same exists or may hereafter be amended.

NASDAQ National Market Listing

Our common stock is listed on NASDAQ under the symbol VRUS.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A., located at 250 Royall Street, Canton, MA 02021. Its telephone number is (781) 575-2000.

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SELLING STOCKHOLDERS

Information regarding the beneficial ownership of our common stock by any selling stockholders, the number of shares being offered by any selling stockholders and the number of shares beneficially owned by any selling stockholders after the applicable offering, where applicable, will be set forth in a prospectus supplement, in a post-effective amendment, or in filings we make with the SEC that are incorporated herein by reference.

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PLAN OF DISTRIBUTION

We and any selling stockholders may sell shares of our common stock being offered pursuant to this prospectus directly to purchasers, to or through underwriters, through dealers or agents or through a combination of such methods. The prospectus supplement will set forth the terms of the offering of shares of our common stock, including the names of the underwriters, dealers or agents, if any, the purchase price, the net proceeds to us and any selling stockholders, any underwriting discounts and other items constituting underwriters' compensation, the initial public offering price and any discounts or concessions allowed or re-allowed or paid to dealers.

The offer and sale of shares of our common stock described in this prospectus by us, any selling stockholders, the underwriters or the third parties described above may be effected from time to time in one or more transactions, including privately negotiated transactions, either at a fixed price or at prices that may be changed, at market prices prevailing at the time of sale, at prices relating to such prevailing market prices or at negotiated prices.

If underwriters are used in an offering, we and any selling stockholders will execute an underwriting agreement with such underwriters and will specify the name of each underwriter and the terms of the transaction (including any underwriting discounts and other terms constituting compensation of the underwriters and any dealers) in a prospectus supplement. Shares of our common stock may be offered to the public either through underwriting syndicates represented by managing underwriters or directly by one or more investment banking firms or others, as designated. If an underwriting syndicate is used, the managing underwriter(s) will be specified on the cover of the prospectus supplement. If underwriters are used in the sale, the offered shares of our common stock will be acquired by the underwriters for their own accounts and may be resold from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. Any public offering price and any discounts or concessions allowed or re-allowed or paid to dealers may be changed from time to time. Unless otherwise set forth in the prospectus supplement, the obligations of the underwriters to purchase the offered shares of our common stock will be subject to conditions precedent and the underwriters will be obligated to purchase all of the offered shares if any are purchased.

Any selling stockholders may also resell all or a portion of their shares of our common stock in transactions exempt from the registration requirements of the Securities Act in reliance upon Rule 144 under the Securities Act provided they meet the criteria and conform to the requirements thereof.

If dealers are used in an offering, we or any selling stockholders will sell the shares of our common stock to the dealers as principals. The dealers then may resell the shares to the public at varying prices which they determine at the time of resale. The names of the dealers and the terms of the transaction will be specified in a prospectus supplement.

Shares of our common stock may be sold directly by us or any selling stockholders or through agents we or any such selling stockholders designate from time to time at a fixed price or prices, which may be changed, or at varying prices determined at the time of sale. If agents are used in an offering, the names of the agents and the terms of the agency will be specified in a prospectus supplement. Unless otherwise indicated in a prospectus supplement, the agents will act on a best-efforts basis for the period of their appointment.

Any selling stockholders, underwriters, broker-dealers and agents that participate in the distribution of the shares may be deemed to be underwriters as defined in the Securities Act. Any commissions paid or any discounts or concessions allowed to any such persons, and any profits they receive on resale of the shares, may be deemed to be underwriting discounts and commissions under the Securities Act. Additionally, because the selling stockholders may be deemed to be underwriters within the meaning of Section 2(11) of the Securities Act, such selling stockholders may be subject to the prospectus delivery requirements of the Securities Act.

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Agents, underwriters and dealers may be entitled under relevant agreements with us or any selling stockholders to indemnification by us or such selling stockholders against certain liabilities, including liabilities under the Securities Act, or to contribution with respect to payments which such agents, underwriters and dealers may be required to make in respect thereof. The terms and conditions of any indemnification or contribution will be described in the applicable prospectus supplement. We may pay any or all expenses incurred with respect to the registration of the shares of common stock owned by any selling stockholders, other than underwriting fees, discounts or commissions, which will be borne by the selling stockholders.

If so indicated in a prospectus supplement, we or any selling stockholders will authorize underwriters or other persons acting as agents to solicit offers by institutional investors to purchase shares of our common stock pursuant to contracts providing for payment and delivery on a future date. We or any selling stockholders may enter into contracts with commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutional investors. The obligations of any institutional investor will be subject to the condition that its purchase of the offered shares will not be illegal at the time of delivery. The underwriters and other agents will not be responsible for the validity or performance of such contracts.

Underwriters, broker-dealers or agents may receive compensation in the form of commissions, discounts or concessions from us or any selling stockholders. Underwriters, broker-dealers or agents may also receive compensation from the purchasers of shares for whom they act as agents or to whom they sell as principals, or both. Compensation as to a particular underwriter, broker-dealer or agent might be in excess of customary commissions and will be in amounts to be negotiated in connection with transactions involving shares. In effecting sales, broker-dealers engaged by us or any selling stockholder may arrange for other broker-dealers to participate in the resales. Maximum compensation to any underwriters, dealers or agents will not exceed any applicable Financial Industry Regulatory Authority, Inc. limitations.

Certain agents, underwriters and dealers, and their associates and affiliates may be customers of, have borrowing relationships with, engage in other transactions with, and/or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

Underwriters or agents may purchase and sell the shares in the open market. These transactions may include over-allotments, stabilizing transactions, syndicate covering transactions and penalty bids. Over-allotments involve sales of our common stock in excess of the offering size, which creates a short position. Stabilizing transactions consist of bids or purchases for the purpose of preventing or retarding a decline in the market price of shares of our common stock and are permitted so long as the stabilizing bids do not exceed a specified maximum. Syndicate covering transactions involve the placing of any bid on behalf of the underwriting syndicate or the effecting of any purchase to reduce a short position created in connection with an offering of shares of our common stock. The underwriters or agents also may impose a penalty bid, which permits them to reclaim selling concessions allowed to syndicate members or certain dealers if they repurchase shares of our common stock in stabilizing or covering transactions. These activities may stabilize, maintain or otherwise affect the market price of shares of our common stock, which may be higher than the price that might otherwise prevail in the open market. These activities, if begun, may be discontinued at any time. These transactions may be effected on any exchange on which shares of our common stock are traded, in the over-the-counter market or otherwise.

The shares of our common stock sold pursuant to a prospectus supplement will be eligible for trading on NASDAQ, subject, if required, to official notice of issuance, or such other trading market as specified in a prospectus supplement.

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LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, legal matters related to the shares of common stock offered under this prospectus and any offerings made pursuant to this prospectus will be passed upon by Pepper Hamilton LLP, Philadelphia, Pennsylvania. If legal matters in connection with any offering made pursuant to this prospectus are passed upon by counsel other than Pepper Hamilton LLP, such counsel will be named in the prospectus supplement relating to such offering.

EXPERTS

The financial statements and management's assessment of the effectiveness of internal control over financial reporting incorporated by reference in this prospectus and elsewhere in this registration statement have been so incorporated by reference in reliance upon the reports of Grant Thornton LLP, independent registered public accountants, upon the authority of said firm as experts in accounting and auditing in giving said reports.

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3,300,000 Shares

Pharmasset, Inc.

Common Stock

PROSPECTUS SUPPLEMENT

January 20, 2011

Citi

Morgan Stanley

BofA Merrill Lynch

Leerink Swann

Wedbush PacGrow Life Sciences

