

Manhattan Pharmaceuticals, Inc.

33,928,571 Shares
Common Stock

This prospectus supplement supplements the prospectus dated October 15, 2008, which relates to the shares of our common stock that may be sold by the selling securityholders named therein.

This prospectus supplement should be read in connection with, and may not be delivered or utilized without, the prospectus dated October 15, 2008 and the prospectus supplements dated November 21, 2008 and November 26, 2008. This prospectus supplement is qualified by reference to the prospectus and the prospectus supplements, except to the extent that the information in this prospectus supplement updates or supersedes the information contained in the prospectus dated October 15, 2008 or the prospectus supplements dated November 21, 2008 and November 26, 2008.

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

The date of this prospectus supplement is January 21, 2009

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

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

Date of Report (Date of earliest event reported): December 23, 2008

Manhattan Pharmaceuticals, Inc.

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction
of incorporation)

001-32639

(Commission File Number)

36-3898269

(IRS Employer
Identification No.)

**48 Wall Street, Suite 1110
New York, New York 10005**

(Address of principal executive offices) (Zip Code)

(212) 582-3950

(Registrant's telephone number, including area code)

Not applicable

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
 - Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
 - Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
 - Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
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Item 3.02 Unregistered Sales of Equity Securities

As previously disclosed on a Current Report on Form 8-K filed on November 25, 2008, Manhattan Pharmaceuticals, Inc. (the "Company") entered into a Securities Purchase Agreement (the "Securities Purchase Agreement"), dated November 19, 2008 with the investors set forth on Exhibit A-1 and Exhibit A-2 thereto, as amended from time to time (the "Investors"), pursuant to which it sold 207 units (each a "Unit" and collectively, the "Units") with each Unit consisting of (i) a 12% Senior Secured Note Promissory Note in the principal amount of \$5,000 (each a "Note", and collectively, the "Notes") and (ii) a warrant to purchase up to 166,667 shares of the Company's common stock ("Common Stock") at an exercise price of \$.09 per share which expire on December 31, 2013 (each a "Warrant" and collectively, the "Warrants").

On December 23, 2008, the Company completed a second closing (the "Second Closing") under the terms of the Securities Purchase Agreement. At the Second Closing the Company sold an additional 56 Units. The Company may sell up to an additional 237 Units (437 Units if the Overallotment is exercised) through January 31, 2009 in subsequent closings.

All of the Investors represented that they were "accredited investors," as that term is defined in Rule 501(a) of Regulation D under the Securities Act, and the sale of the Units was made in reliance on exemptions provided by Regulation D and Section 4(2) of the Securities Act of 1933, as amended.

In connection with the Second Closing, the Company issued a warrant to purchase 1,400,003 shares of Common Stock at an exercise price of \$.09 per share to its placement agent (the "Placement Agent Warrant") as additional compensation for its services.

The Company did not use any form of advertising or general solicitation in connection with the sale of the Units. The Notes, the Warrants and shares of Common Stock issuable upon exercise of the Warrants are non-transferable in the absence of an effective registration statement under the Act, or an available exemption therefrom, and all certificates are imprinted with a restrictive legend to that effect.

Forward Looking Statements

This Current Report on Form 8-K contains forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements typically are identified by use of terms such as "may," "will," "should," "plan," "expect," "anticipate," "estimate" and similar words, although some forward-looking statements are expressed differently. Forward-looking statements represent our management's judgment regarding future events. Although the Company believes that the expectations reflected in such forward-looking statements are reasonable, the Company can give no assurance that such expectations will prove to be correct. All statements other than statements of historical fact included in this Current Report on Form 8-K are forward-looking statements. The Company cannot guarantee the accuracy of the forward-looking statements, and you should be aware that the Company's actual results could differ materially from those contained in the forward-looking statements due to a number of factors, including the statements under "Risk Factors" contained in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2007 filed with the Securities and Exchange Commission.

SIGNATURE

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

MANHATTAN PHARMACEUTICALS, INC.

Date: December 30, 2008

By: /s/ Michael G. McGuinness

Michael G. McGuinness
Chief Financial Officer
