

NUPATHE INC.
Form 424B3
November 16, 2012

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**Filed Pursuant to Rule 424(b)(3)
Registration No. 333-184738**

PROSPECTUS

40,778,856 Shares of Common Stock

This prospectus relates to the resale or other disposition by the Selling Stockholders identified in this prospectus, or their donees, pledgees, transferees or other successors in interest, of up to an aggregate of 40,778,856 shares of common stock, representing:

5,694,427 outstanding shares of common stock that we sold to certain Selling Stockholders in a series of financings conducted from 2006 to 2010,

84,429 shares of common stock issuable upon the exercise of warrants that we sold to certain Selling Stockholders in 2009, and

35,000,000 shares of common stock issuable to the Selling Stockholders upon the conversion of shares of Series A Preferred Stock and the exercise of warrants that we sold to the Selling Stockholders on October 23, 2012 pursuant to a Securities Purchase Agreement, dated as of September 25, 2012, by and among NuPathe Inc. and the Selling Stockholders.

The Selling Stockholders may, from time to time, sell, transfer or otherwise dispose of any or all of their shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices. See "Plan of Distribution" for additional information.

We are not offering any shares of common stock for sale under this prospectus, and we will not receive any of the proceeds from the sale or other disposition of the shares of common stock covered hereby.

Our common stock is traded on the NASDAQ Global Market under the symbol "PATH." On October 31, 2012, the last reported sale price for our common stock on the NASDAQ Global Market was \$3.64 per share.

We will pay the expenses related to the registration of the shares of common stock covered by this prospectus. The Selling Stockholders will pay any commissions and selling expenses they may incur.

Our business and an investment in our securities involve significant risks. You should read the section entitled "*Risk Factors*" on page 8 of this prospectus and the risk factors incorporated by reference into this prospectus as described in that section before investing in our securities.

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. Any representation to the contrary is a criminal offense.

The date of this prospectus is November 15, 2012

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission (referred to in this prospectus as, the "SEC") using a "shelf" registration or continuous offering process.

You should read this prospectus and the information and documents incorporated by reference carefully because these documents contain important information you should consider when making your investment decision. See "Where You Can Find More Information" and "Information Incorporated by Reference."

You should rely only on the information provided in this prospectus and the information and documents incorporated by reference into this prospectus. We have not, and the Selling Stockholders have not, authorized anyone to provide you with different information. This prospectus is not an offer to sell these securities, and the Selling Stockholders are not soliciting offers to buy these securities, in any state where the offer or sale of these securities is not permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of shares of common stock. You should not assume that the information contained in this prospectus is accurate as of any date other than the date on the front cover of this prospectus, or that the information contained in any document incorporated by reference is accurate as of any date other than the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any sale of a security.

In this prospectus, unless otherwise indicated or the context otherwise requires, references to "NuPathe," "we," "Company," "us," or "our" refer to NuPathe Inc., and references to "Selling Stockholders" refer to those stockholders listed herein under "Selling Stockholders," and their donees, pledgees, transferees or other successors in interest.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC as required by the Securities Exchange Act of 1934, as amended (referred to in this prospectus as, the "Exchange Act"). You can find, copy and inspect information we file with the SEC (including exhibits to such documents) at the SEC's Public Reference Room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You may obtain additional information about the Public Reference Room by calling the SEC at 1-800-SEC-0330. In addition, the SEC maintains a site on the Internet at www.sec.gov which contains reports, proxy statements and other information that we file electronically with the SEC. You may also review such reports, proxy statements and other documents we file with the SEC on our website at www.nupathe.com. The information contained on our website, or accessible thereby, is not a part of this prospectus.

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INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

We are "incorporating by reference" information into this prospectus. This means that we are disclosing important information to you by referring you to other documents that have been filed separately with the SEC. The information incorporated by reference is considered to be part of this prospectus, and information that we file later with the SEC will automatically update and supersede the information contained in documents filed earlier with the SEC or contained in this prospectus. We incorporate by reference into this prospectus the documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act after the initial filing date of the registration statement of which this prospectus forms a part and prior to the termination of this offering (except in each case the information contained in such documents to the extent "furnished" and not "filed"):

our Annual Report on Form 10-K for our fiscal year ended December 31, 2011, filed with the SEC on March 20, 2012;

our Quarterly Report on Form 10-Q for our fiscal quarter ended March 31, 2012, filed with the SEC on May 10, 2012, our Quarterly Report on Form 10-Q for our fiscal quarter ended June 30, 2012, filed with the SEC on August 14, 2012 and our Quarterly Report on Form 10-Q for our fiscal quarter ended September 30, 2012, filed with the SEC on November 9, 2012;

our Current Reports on Form 8-K, filed with the SEC on April 26, 2012, June 1, 2012, June 12, 2012, July 25, 2012, July 30, 2012, September 26, 2012, October 9, 2012, October 12, 2012 and October 23, 2012; and

the description of our common stock in our registration statement on Form 8-A, registering our common stock under the Exchange Act, filed with the SEC on July 29, 2010 pursuant to Section 12 of the Exchange Act, including any amendment or report filed for the purpose of updating such description.

You may obtain copies, without charge, of documents incorporated by reference into this prospectus, by requesting them in writing or by telephone from us as follows:

NuPathe Inc.
227 Washington Street, Suite 200
Conshohocken Pennsylvania 19428
Attention: General Counsel
(484) 567-0130

Exhibits to the filings will not be sent unless those exhibits have been specifically incorporated by reference into this prospectus. You may also obtain copies of documents incorporated by reference into this prospectus at the SEC's public reference room in Washington D.C., as well as through the SEC's website and our website. See "Where You Can Find More Information."

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

The information included in, or incorporated by reference into, this prospectus contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (referred to in this prospectus as, the "Securities Act"), and Section 21E of the Exchange Act, the attainment of which involves various risks and uncertainties. All statements other than statements of historical fact included in, or incorporated by reference into, this prospectus are forward-looking statements. Forward-looking statements may be identified by the use of forward-looking terminology, such as "may," "will," "could," "would," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "predict," "project," "potential," "scheduled," "continue," "ongoing" or similar terms, variations of those terms or the negative of those terms, although not all forward-looking statements contain these identifying words.

Forward-looking statements are based on assumptions that we have made in light of our experience in the industry in which we operate, as well as our perceptions of historical trends, current conditions, expected future developments and other factors we believe are appropriate under the circumstances. As you read and consider this prospectus and the information incorporated by reference into this prospectus, you should understand that these statements are not guarantees of performance or results. They involve risks, uncertainties (some of which are beyond our control) and assumptions. Although we believe that these forward-looking statements are based on reasonable assumptions, you should be aware that many factors could affect our actual financial condition or results of operations and cause actual results to differ materially from those in the forward-looking statements. These factors include, among other things:

our ability to obtain additional capital on a timely basis and on agreeable terms to meet our debt service and interest obligations and fund operations;

our ability to address the issues raised by the U.S. Food and Drug Administration (referred to in this prospectus as, the "FDA") in its complete response letter regarding our new drug application for Zecuity (previously referred to as, Zelrix and NP101);

additional information, trials, studies or redesign of Zecuity that may be required by the FDA, which could delay, limit or preclude marketing approval of Zecuity;

our ability to obtain marketing approval for Zecuity and our other product candidates;

our ability to obtain commercial and development partners for Zecuity and our other product candidates;

our reliance on third parties to manufacture Zecuity and our other product candidates;

our ability to establish and effectively manage our supply chain;

our ability to establish effective marketing and sales capabilities or enter into agreements with third parties to perform these functions;

market acceptance among physicians and patients and the availability of adequate reimbursement from third party payors for Zecuity and any other product candidates for which we obtain marketing approval;

adverse event profiles discovered after marketing approval and use of a product in a larger number of subjects for longer periods of time than in clinical trials, that could limit such product's usefulness or require its withdrawal;

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serious adverse events or other safety risks that could require us to abandon or delay development of, or preclude or limit approval of, our product candidates;

varying interpretation of trial, study and market data;

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our ability to obtain and maintain intellectual property protection and the scope of such protection;

the performance of our partners and other third parties; and

compliance with legal and regulatory requirements.

Additional factors that could cause actual results to differ materially from those reflected in forward-looking statements are discussed under the heading "Risk Factors" in this prospectus and in the documents incorporated by reference into this prospectus. You are cautioned not to place undue reliance on forward-looking statements.

Forward-looking statements reflect our analysis, judgment, belief or expectation only as of the date of this prospectus or, in the case of forward-looking statements contained in documents incorporated by reference into this prospectus, the date of the applicable document (or any earlier date indicated in the statement). We undertake no obligation to update or revise forward-looking statements whether as a result of new information, future developments or otherwise. We qualify all of our forward-looking statements by these cautionary statements.

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PROSPECTUS SUMMARY

The following is only a summary and therefore does not contain all of the information you should consider before investing in our securities. We urge you to read this entire prospectus, including the matters discussed under "Risk Factors" and the risk factors incorporated by reference into this prospectus as described in that section, and the financial statements, notes to financial statements and other information incorporated by reference from our other filings with the SEC.

Our Company

NuPathe Inc. is a specialty pharmaceutical company focused on innovative neuroscience solutions for diseases of the central nervous system including neurological and psychiatric disorders. NuPathe's lead product candidate, Zecuity (previously referred to as Zelrix and NP101) is an active, single-use, transdermal patch being developed for the treatment of migraine. The active ingredient in Zecuity, sumatriptan, is the most prescribed treatment for migraine in the U.S. Sumatriptan is available in oral, nasal and injectable formulations but it is not currently available in a transdermal formulation because sumatriptan is not passively absorbed by the skin.

Utilizing our SmartRelief™ technology, Zecuity is able to deliver sumatriptan through the skin by applying a mild battery power. The proprietary software in Zecuity's microprocessor manages fast, sustained and controlled drug delivery and adjusts current flow for optimal drug delivery during use without any user input or adjustment. If approved, Zecuity will be the first and only transdermal patch for the treatment of migraine.

Migraine is a debilitating neurological disease that affects approximately 31 million people in the U.S., half of whom are diagnosed and treated. During their migraines, many patients suffer from one or more significant gastrointestinal problems, which include nausea, vomiting and a compromised ability to digest, known as decreased gastric motility. Research suggests that approximately half of the diagnosed and treated migraine patients frequently experience migraine-related nausea (> 50% of their attacks). The presence of nausea or vomiting can impede the use of oral medications, while reduced gastric motility can result in low and inconsistent absorption of oral medications which may cause some patients to fail to respond consistently to such medications. Patients who frequently experience migraine-related nausea (also referred to in this prospectus as "MRN") also report significantly more disease burden and indicate significantly less satisfaction with their current migraine medications, report more medication side effects, and report more medication-related interference in work, family, and social life.

The American Academy of Neurology guidelines recommend a non-oral route of administration for migraine patients who experience nausea or vomiting as significant migraine symptoms. Despite this recommendation and the prevalence of nausea and vomiting, IMS Health, Incorporated, a pharmaceuticals market research firm, reported that non-oral formulations comprised only 4% of triptan units sold in the U.S. in 2010. We believe the route of administration and adverse events associated with current non-oral migraine treatments, such as nasal and injectable formulations, contribute to the low adoption rate of these medications.

In its pivotal Phase 3 clinical trial, Zecuity achieved significance at relieving both headache pain and eliminating nausea within one hour while also providing sustained headache pain relief for 24 hours. Zecuity rapidly delivered therapeutic plasma levels of sumatriptan without reaching levels that are commonly associated with triptan sensations (pressure in chest and throat, tingling, and numbness). As a result, the incidence of triptan sensations was low without compromising the ability to address key efficacy parameters. In Zecuity's Phase 3 clinical trials, the incidence of triptan sensations was 1.5%. These compare favorably to oral (> 8%) and injectable (> 42%) sumatriptan as presented in the U.S. prescribing information for these products.

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Based on its route of administration and clinical data, we believe Zecuity is uniquely positioned to meet the needs of the underserved population of patients who frequently experience MRN and for those who experience inconsistent relief or triptan sensation adverse events from their current treatment.

We also have two proprietary product candidates in pre-clinical development that utilize our LAD , or Long-Acting Delivery, biodegradable implant technology that allows delivery of therapeutic levels of medication over a period of months with a single dose. NP201, for the continuous symptomatic treatment of Parkinson's disease, utilizes a leading FDA-approved dopamine agonist, ropinirole, and is being developed to provide up to two months of continuous delivery. NP202, for the long-term treatment of schizophrenia and bipolar disorder, is being developed to address the long-standing problem of patient noncompliance by providing three months of continuous delivery of risperidone, an FDA-approved atypical antipsychotic.

Corporate Information

We were organized as a corporation under the laws of the State of Delaware in January 2005. Our principal executive offices are located at 227 Washington Street, Suite 200, Conshohocken, Pennsylvania 19428 and our telephone number is (484) 567-0130. Our website address is www.nupathe.com. The information contained on our website, or accessible thereby, is not a part of this prospectus.

Financing Transaction

On October 23, 2012, we sold 14,000,000 units of our securities to the Selling Stockholders at a per unit purchase price of \$2.00, pursuant to a Securities Purchase Agreement, dated September 25, 2012, by and among us and the Selling Stockholders (such agreement is referred to in this prospectus as, the "Purchase Agreement," and the sale of securities to the Selling Stockholders pursuant to the Purchase Agreement is referred to in this prospectus as, the "Financing"). The units were sold to the Selling Stockholders pursuant to an exemption from registration afforded by Section 4(2) of the Securities Act and Rule 506 of Regulation D promulgated thereunder. Each unit consisted of one one-thousandth (1/1,000th) of a share of our newly-designated Series A Preferred Stock, which is initially convertible into one share of our common stock, and a warrant to purchase one share of our common stock from April 23, 2013 through October 23, 2017 at an initial exercise price of \$2.00.

A summary description of the Financing and the terms, rights and privileges of the Series A Preferred Stock and the warrants issued in the Financing is contained in our Current Report on Form 8-K filed with the SEC on September 26, 2012, and copies of the Purchase Agreement, Certificate of Powers, Designations, Preferences Rights and Qualifications, Limitations or Restrictions of Series A Preferred Stock and the form of warrant were filed as Exhibits 99.1, 99.2 and 99.3, respectively, to such Current Report on Form 8-K, and are incorporated herein by reference.

Pursuant to the Purchase Agreement, we are required to prepare and file with the SEC a registration statement covering the resale or other disposition by the Selling Stockholders or their donees, pledgees, transferees or other successors in interest of an aggregate of 40,778,856 shares of common stock representing:

5,694,427 outstanding shares of common stock that we sold to certain Selling Stockholders in a series of financings conducted from 2006 to 2010,

84,429 shares of common stock issuable upon the exercise of warrants that we sold to certain Selling Stockholders in 2009, and

35,000,000 shares of common stock issuable upon the conversion of the shares of Series A Preferred Stock and the exercise of the warrants we sold to the Selling Stockholders in the

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Financing, which amount represents 125% of the number of shares of common stock currently issuable upon conversion and exercise of such securities, as required by the terms of the Purchase Agreement.

If we breach our obligations under the Purchase Agreement to have the registration statement declared effective or remain effective for the periods specified in the Purchase Agreement, then we will be obligated to pay liquidated damages in certain circumstances.

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RISK FACTORS

An investment in our securities involves a high degree of risk. In addition to the risk factors set forth below, you should carefully consider each of the risk factors set forth under the heading "Risk Factors" in our most recent Annual Report on Form 10-K and in our subsequent Quarterly Reports on Form 10-Q, which are incorporated by reference into this prospectus. Before making an investment decision, you should carefully consider these risks as well as other information contained in, incorporated by reference into, this prospectus. The occurrence of any one or more of these risks could materially harm our business, operating results, financial condition and prospects. In these circumstances, the market price of our common stock could decline, and you may lose all or part of our investment.

Certain rights granted to the holders of our Series A Preferred Stock may make it more difficult for other stockholders to influence significant corporate decisions and may hinder a change of control.

Certain terms of our Series A Preferred Stock may make it more difficult for other stockholders to influence significant corporate decisions. For example, the holders of our Series A Preferred Stock:

are entitled to elect three directors to our Board of Directors;

can prevent our issuance of securities with equal or superior rights, preferences or privileges to those of the Series A Preferred Stock;

can prevent the payment of dividends;

can prevent the sale or other divestiture of material assets; and

can prevent a change in control of our company.

These rights (and all other rights and privileges relating to the Series A Preferred Stock) may adversely affect the value (or perceived value) of our shares of common stock.

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USE OF PROCEEDS

We will not receive any of the proceeds from the sale or other disposition of the shares of common stock offered hereby.

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SELLING STOCKHOLDERS

We have prepared this prospectus to allow the Selling Stockholders or their donees, pledgees, transferees or other successors-in-interest to sell or otherwise dispose of, from time to time, up to an aggregate of 40,778,856 shares of common stock representing:

5,694,427 outstanding shares of common stock that we sold to certain Selling Stockholders in a series of financings conducted from 2006 to 2010,

84,429 shares of common stock issuable upon the exercise of warrants that we sold to certain Selling Stockholders in 2009, and

35,000,000 shares of common stock that may be issuable upon conversion of the Series A Preferred Stock and exercise of the warrants purchased by the Selling Stockholders in the Financing.

The table below presents information regarding the Selling Stockholders, the shares of common stock beneficially owned prior to this offering and the shares of common stock that they may sell or otherwise dispose of from time to time under this prospectus. The shares of common stock covered by this prospectus may be offered or disposed of by the Selling Stockholders, from time to time, in the manner contemplated under the "Plan of Distribution." We do not know when or in what amounts the Selling Stockholders may sell or otherwise dispose of the shares of common stock covered hereby. The Selling Stockholders might not sell any or all of the shares covered by this prospectus or may sell or dispose of some or all of the shares other than pursuant to this prospectus. Because the Selling Stockholders may not sell or otherwise dispose of some or all of the shares covered by this prospectus and because there are currently no agreements, arrangements or understandings with respect to the sale or other disposition of any of the shares, we cannot estimate the number of the shares that will be held by the Selling Stockholders after completion of the offering. However, for purposes of this table, we have assumed that all of the shares of common stock covered by this prospectus will be sold by the Selling Stockholders.

Except as noted in the footnotes below, none of the Selling Stockholders has held any position or office with us or any of our predecessors or affiliates within the last three years or has had a material

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relationship with us or any of our predecessors or affiliates within the past three years other than as a result of the ownership of our shares or other securities.

Name of Selling Stockholder(2)	Number of Shares Beneficially Owned Prior to the Offering(2)	Beneficial Ownership(1)		Percent of Class Beneficially Owned After the Offering(1)(3)
		Number of Shares Offered Hereby	Number of Shares Beneficially Owned After the Offering(3)	
Battelle Ventures LP(4)	3,074,823	1,808,443	1,266,380	8.6%
Innovation Valley Partners, LP(5)	367,987	200,938	167,049	1.1%
Rosalind Capital Partners L.P.(6)	300,000	300,000	0	0%
Rosalind Master Fund L.P.(7)	200,000	200,000	0	0%
David B. Musket(8)	200,000	200,000	0	0%
ProMed Partners, L.P.(9)	100,000	100,000	0	0%
Auriga Global Investors SV, SA(10)	2,750,000	2,750,000	0	0%
Auriga Investors Montserrat Global Fund(11)	750,000	750,000	0	0%
Aspire Capital Fund, LLC(12)	655,587	500,000	155,587	1.1%
Sabby Volatility Warrant Master Fund, Ltd.(13)	1,000,000	1,000,000	0	0%
Sabby Healthcare Volatility Master Fund, Ltd.(14)	4,000,000	4,000,000	0	0%
Capital Ventures International(15)	450,000	450,000	0	0%
S.R. One, Limited(16)	4,166,846	3,000,000	1,151,211	7.8%
Quaker Partners(17)	8,102,712	8,102,712	0	0%
Safeguard Delaware, Inc.(18)	7,651,128	7,651,128	0	0%
Midsummer Small Cap Master, Ltd(19)	400,000	400,000	0	0%
Joann Mostovoy(20)	300,000	300,000	0	0%
Cummings Bay Healthcare Fund, L.P.(21)	420,000	420,000	0	0%
Pyxis Long/Short Healthcare Fund(22)	1,380,000	1,380,000	0	0%
Prosight Fund, LP(23)	250,000	250,000	0	0%

(1) Beneficial ownership is determined in accordance with Section 13(d) of the Exchange Act and generally includes voting and investment power with respect to securities and includes any securities that grant the Selling Stockholder the right to acquire shares of common stock within 60 days of October 23, 2012. For presentation purposes, we have also included in the "Number of Shares Beneficially Owned Prior to the Offering" the number of shares of common stock that may be acquired upon the exercise of warrants issued in the Financing, even though such warrants are not exercisable until April 23, 2013. Percentage ownership is calculated for each Selling Stockholder separately based on 14,763,801 shares of common stock issued and outstanding as of October 23, 2012 plus the number of shares of common stock which the Selling Stockholder may acquire within 60 days of October 23, 2012, which shares are considered outstanding and beneficially owned by such Selling Stockholder but not for the purpose of calculating the percentage of ownership of any other Selling Stockholder. As a result, "Percent of Class Beneficially Owned After the Offering" for each Selling Stockholder is calculated by dividing (x) the number of shares beneficially owned by the Selling Stockholder after the offering by (y) 14,763,801 shares of common stock issued and outstanding as of October 23, 2012, plus the number of shares of common stock that such Selling Stockholder has the right to acquire beneficial ownership of within 60 days of October 23, 2012.

(2) Unless otherwise indicated, this table is based on information supplied to us by the Selling Stockholders and certain of our records.

(3) This column assumes the sale of all shares of common stock offered pursuant to this prospectus.

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- (4) Includes (i) 1,266,380 shares of common stock, (ii) 8,443 shares of common stock issuable upon the exercise of a warrant within 60 days of October 23, 2012, (iii) 900,000 shares of common stock that may be acquired upon conversion of 900 shares of Series A Preferred Stock, and (iv) 900,000 shares of common stock that may be acquired upon the exercise of Warrants that become exercisable on April 23, 2013. The 1,266,380 shares of common stock currently held by this Selling Stockholder are not included in the number of shares offered hereby.
- Battelle Ventures, LP has indicated to us that Morton Collins, Rakefet Kasdin, Ralph Taylor-Smith and Tracy S. Warren, as the members of BVP GP, LLC, its general partner, have voting and investment power over the shares held by it.
- (5) Includes (i) 167,049 shares of common stock, (ii) 938 shares of common stock issuable upon the exercise of a warrant within 60 days of October 23, 2012, (iii) 100,000 shares of common stock that may be acquired upon conversion of 100 shares of Series A Preferred Stock, and (iv) 100,000 shares of common stock that may be acquired upon the exercise of Warrants that become exercisable on April 23, 2013. The 167,049 shares of common stock currently held by this Selling Stockholder are not included in the number of shares offered hereby.
- Innovation Valley Partners, LP has indicated to us that Glenn Kline, Morton Collins, Rakefet Kasdin, Ralph Taylor-Smith and Tracy S. Warren, as the members of IVP GP, LLC, its general partner, have voting and investment power over the shares held by it.
- (6) Includes (i) 150,000 shares of common stock that may be acquired upon conversion of 150 shares of Series A Preferred Stock, and (ii) 150,000 shares of common stock that may be acquired upon the exercise of Warrants that become exercisable on April 23, 2013.
- Rosalind Capital Partners L.P. has indicated to us that Steven A. J. Salamon has voting and investment power over the shares held by it.
- (7) Includes (i) 100,000 shares of common stock that may be acquired upon conversion of 100 shares of Series A Preferred Stock, and (ii) 100,000 shares of common stock that may be acquired upon the exercise of Warrants that become exercisable on April 23, 2013.
- Rosalind Master Fund L.P. has indicated to us that Steven A. J. Salamon has voting and investment power over the shares held by it.
- (8) Includes (i) 100,000 shares of common stock that may be acquired upon conversion of 100 shares of Series A Preferred Stock, and (ii) 100,000 shares of common stock that may be acquired upon the exercise of Warrants that become exercisable on April 23, 2013.
- (9) Includes (i) 50,000 shares of common stock that may be acquired upon conversion of 50 shares of Series A Preferred Stock, and (ii) 50,000 shares of common stock that may be acquired upon the exercise of Warrants that become exercisable on April 23, 2013.
- ProMed Partners, L.P. has indicated to us that David B. Musket, its general partner, has voting and investment power over the shares held by it.
- (10) Includes (i) 1,375,000 shares of common stock that may be acquired upon conversion of 1,375 shares of Series A Preferred Stock, and (ii) 1,375,000 shares of common stock that may be acquired upon the exercise of Warrants that become exercisable on April 23, 2013.
- Auriga Global Investors SV, SA has indicated to us that Dr. Raj Mehra has voting and investment power over the shares held by it.
- (11) Includes (i) 375,000 shares of common stock that may be acquired upon conversion of 375 shares of Series A Preferred Stock, and (ii) 375,000 shares of common stock that may be acquired upon the exercise of Warrants that become exercisable on April 23, 2013.

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Auriga Investors Montserrat Global Fund has indicated to us that Dr. Raj Mehra has voting and investment power over the shares held by it.

- (12) Includes (i) 155,857 shares of common stock, (ii) 250,000 shares of common stock that may be acquired upon conversion of 250 shares of Series A Preferred Stock, and (iii) 250,000 shares of common stock that may be acquired upon the exercise of Warrants that become exercisable on April 23, 2013. The 155,857 shares of common stock currently held by this Selling Stockholder are not included in the number of shares offered hereby.

Aspire Capital Fund, LLC has indicated to us that Steven G. Martin, Erik J. Brown and Christos Komissopoulos have voting and investment power over the shares held by it.

- (13) Includes (i) 500,000 shares of common stock that may be acquired upon conversion of 500 shares of Series A Preferred Stock, and (ii) 500,000 shares of common stock that may be acquired upon the exercise of Warrants that become exercisable on April 23, 2013.

Each of Sabby Healthcare Volatility Master Fund, Ltd. and Sabby Volatility Warrant Master Fund, Ltd. (collectively, the "Sabby Funds") has indicated to us that Hal Mintz has voting and investment power over the shares held by it. Each of the Sabby Funds has also indicated to us that Sabby Management, LLC serves as its investment manager, that Hal Mintz is the manager of Sabby Management, LLC and that each of Sabby Management, LLC and Hal Mintz disclaim beneficial ownership over these shares except to the extent of any pecuniary interest therein.

- (14) Includes (i) 2,000,000 shares of common stock that may be acquired upon conversion of 2,000 shares of Series A Preferred Stock, and (ii) 2,000,000 shares of common stock that may be acquired upon the exercise of Warrants that become exercisable on April 23, 2013.

Each of the Sabby Funds has indicated to us that Hal Mintz has voting and investment power over the shares held by it. Each of the Sabby Funds has also indicated to us that Sabby Management, LLC serves as its investment manager, that Hal Mintz is the manager of Sabby Management, LLC and that each of Sabby Management, LLC and Hal Mintz disclaim beneficial ownership over these shares except to the extent of any pecuniary interest therein.

- (15) Includes (i) 225,000 shares of common stock that may be acquired upon conversion of 225 shares of Series A Preferred Stock, and (ii) 225,000 shares of common stock that may be acquired upon the exercise of Warrants that become exercisable on April 23, 2013.

Heights Capital Management, Inc., the authorized agent of Capital Ventures International ("CVI"), has discretionary authority to vote and dispose of the shares held by CVI and may be deemed to be the beneficial owner of these shares. Martin Kobinger, in his capacity as Investment Manager of Heights Capital Management, Inc., may also be deemed to have investment discretion and voting power over the shares held by CVI. Mr. Kobinger disclaims any such beneficial ownership of the shares.

- (16) Includes (i) 1,151,211 shares of common stock, (ii) 15,635 shares of common stock issuable upon exercise of a warrant within 60 days of October 23, 2012, (iii) 1,500,000 shares of common stock that may be acquired upon conversion of 1,500 shares of Series A Preferred Stock, and (iv) 1,500,000 shares of common stock that may be acquired upon the exercise of Warrants that become exercisable on April 23, 2013. The 1,151,211 shares of common stock currently held by this Selling Stockholder are not included in the number of shares offered hereby.

- (17) Includes (i) 2,793,182 shares of common stock, (ii) 37,524 shares of common stock issuable upon the exercise of a warrant within 60 days of October 23, 2012, (iii) 2,500,000 shares of common stock that may be acquired upon conversion of 2,500 shares of Series A Preferred Stock, and (iv) 2,500,000 shares of common stock that may be acquired upon the exercise of Warrants that become exercisable on April 23, 2013, over which Quaker BioVentures II, L.P. shares investment

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and dispositive control with Quaker BioVentures Capital II, L.P. (its general partner) and Quaker BioVentures Capital II, LLC (its general partner's general partner). Also includes (i) 268,879 shares of common stock and (ii) 3,127 shares of common stock issuable upon exercise of a warrant within 60 days of October 23, 2012, over which BioAdvance Ventures, L.P. shares investment and dispositive control with BioAdvance GP I, L.P. (its general partner) and BioAdvance GP II, Inc. (its general partner's general partner). Richard Kollender, Ira Lubert, Adele Oliva and P. Sherrill Neff are members of the investment committee of Quaker Partners that controls the voting and disposition of these shares. The address of Quaker Partners is 2929 Arch Street, Philadelphia, PA 19104.

Richard Kollender, a Partner of Quaker Partners, was appointed to our Board of Directors as a "Series A Director" in connection with, and as a condition to, the closing of the Financing. Mr. Kollender previously served as a member of our Board of Directors from 2007 to 2011.

- (18) Ownership consists of 2,632,366 shares of common stock, 2,500,000 shares of common stock that may be acquired upon conversion of 2,500 shares of Series A Preferred Stock, 18,762 shares of common stock issuable upon the exercise of a warrant within 60 days of October 23, 2012, and 2,500,000 shares of common stock that may be acquired upon the exercise of warrants that become exercisable on April 23, 2013, held of record by Safeguard Delaware, Inc., a wholly owned subsidiary of Safeguard Scientifics, Inc. The address of Safeguard Delaware, Inc. is 1105 North Market Street, Suite 1300, Wilmington, DE 19801.

James A. Datin, Executive Vice President and Managing Director at Safeguard, and Brian J. Sisko, Senior Vice President and General Counsel at Safeguard, were appointed to our Board of Directors as "Series A Directors" in connection with, and as a condition to, the closing of the Financing. Dr. Gary Kurtzman, Senior Vice President and Managing Director at Safeguard, served as a member of our Board of Directors from 2006 to 2012.

- (19) Includes (i) 200,000 shares of common stock that may be acquired upon conversion of 200 shares of Series A Preferred Stock, and (ii) 200,000 shares of common stock that may be acquired upon the exercise of Warrants that become exercisable on April 23, 2013.

Midsummer Small Cap Master, Ltd has indicated to us that Michael Amsalem and Joshua Thomas have voting and investment power over the shares held by it.

- (20) Includes (i) 150,000 shares of common stock that may be acquired upon conversion of 150 shares of Series A Preferred Stock, and (ii) 150,000 shares of common stock that may be acquired upon the exercise of Warrants that become exercisable on April 23, 2013.

- (21) Includes (i) 210,000 shares of common stock that may be acquired upon conversion of 210 shares of Series A Preferred Stock, and (ii) 210,000 shares of common stock that may be acquired upon the exercise of Warrants that become exercisable on April 23, 2013.

- (22) Includes (i) 690,000 shares of common stock that may be acquired upon conversion of 690 shares of Series A Preferred Stock, and (ii) 690,000 shares of common stock that may be acquired upon the exercise of Warrants that become exercisable on April 23, 2013.

- (23) Includes (i) 125,000 shares of common stock that may be acquired upon conversion of 125 shares of Series A Preferred Stock, and (ii) 125,000 shares of common stock that may be acquired upon the exercise of Warrants that become exercisable on April 23, 2013.

Prosight Fund, LP has indicated to us that Lawrence Hawkins has voting and investment power over the shares held by it.

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PLAN OF DISTRIBUTION

The Selling Stockholders may, from time to time, sell any or all of their shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These sales may be at fixed or negotiated prices. The Selling Stockholders may use any one or more of the following methods when selling shares:

ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;

block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;

purchases by a broker-dealer as principal and resale by the broker-dealer for its account;

an exchange distribution in accordance with the rules of the applicable exchange;

privately negotiated transactions;

short sales;

broker-dealers may agree with the Selling Stockholders to sell a specified number of such shares at a stipulated price per share;

a combination of any such methods of sale; and

any other method permitted pursuant to applicable law.

The Selling Stockholders may also sell shares under Rule 144 under the Securities Act, if available, rather than under this prospectus.

Broker-dealers engaged by the Selling Stockholders may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the Selling Stockholders (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated. The Selling Stockholders do not expect these commissions and discounts to exceed what is customary in the types of transactions involved. Any profits on the resale of shares of common stock by a broker-dealer acting as principal might be deemed to be underwriting discounts or commissions under the Securities Act. Discounts, concessions, commissions and similar selling expenses, if any, attributable to the sale of shares will be borne by a Selling Stockholder. The Selling Stockholders may agree to indemnify any agent, dealer or broker-dealer that participates in transactions involving sales of the shares if liabilities are imposed on that person under the Securities Act.

The Selling Stockholders may from time to time pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time under this prospectus after we have filed a supplement to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act supplementing or amending the list of Selling Stockholders to include the pledgee, transferee or other successors in interest as Selling Stockholders under this prospectus.

The Selling Stockholders also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus and may sell the shares of common stock from time to time under this prospectus after we have filed a supplement to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act supplementing or amending the list of Selling Stockholders to include the pledgee, transferee or other successors in interest as Selling Stockholders under this prospectus.

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The Selling Stockholders and any broker-dealers or agents that are involved in selling the shares of common stock may be deemed to be "underwriters" within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares of common stock purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act.

We are required to pay all fees and expenses incident to the registration of the shares of common stock. We have agreed to indemnify the Selling Stockholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

The Selling Stockholders have advised us that they have not entered into any agreements, understandings or arrangements with any underwriters or broker-dealers regarding the sale of their shares of common stock, nor is there an underwriter or coordinating broker acting in connection with a proposed sale of shares of common stock by any Selling Stockholder. If we are notified by any Selling Stockholder that any material arrangement has been entered into with a broker-dealer for the sale of shares of common stock, if required, we will file a supplement to this prospectus. If the Selling Stockholders use this prospectus for any sale of the shares of common stock, they will be subject to the prospectus delivery requirements of the Securities Act.

The anti-manipulation rules of Regulation M under the Securities Exchange Act of 1934 may apply to sales of our common stock and activities of the Selling Stockholders.

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LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Morgan, Lewis & Bockius LLP, Philadelphia, Pennsylvania.

EXPERTS

The financial statements of NuPathe Inc. as of December 31, 2011 and 2010, and for each of the years in the three-year period ended December 31, 2011 and the period from January 7, 2005 (inception) through December 31, 2011, have been incorporated by reference herein and in the registration statement in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon authority of said firm as experts in accounting and auditing.

KPMG's report dated March 20, 2012 contains an explanatory paragraph that states that NuPathe Inc.'s recurring losses and negative cash flows from operations since its inception raise substantial doubt about its ability to continue as a going concern. The financial statements do not include any adjustment that might result from the outcome of that uncertainty.

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40,778,856 Shares of Common Stock
