PERNIX THERAPEUTICS HOLDINGS, INC. Form S-3 November 07, 2014

As filed with the Securities and Exchange Commission on November 7, 2014 Registration No. 333-

> UNITED STATES SECURITIES AND EXCHANGE COMMISSION Washington, D.C. 20549

FORM S-3 REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

PERNIX THERAPEUTICS HOLDINGS, INC. (Exact name of registrant as specified in its charter)

Maryland (State or other jurisdiction of incorporation or organization) 33-0724736 (I.R.S. Employer Identification Number)

10 North Park Place, Suite 201 Morristown, New Jersey 07960 (800) 793-2145 (Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Douglas L. Drysdale President and Chief Executive Officer 10 North Park Place, Suite 201 Morristown, New Jersey 07960 (800) 793-2145 (Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Thomas S. Levato, Esq. Goodwin Procter LLP The New York Times Building 620 Eighth Avenue New York, New York 10018 (212) 813-8800 Approximate date of commencement of proposed sale to the public: From time to time after this Registration Statement becomes effective. If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box: o

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box: x

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

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

Large accelerated filer	0		Accelerated filer	Х
Non-accelerated filer	0	(Do	Smaller reporting company	•
not check if a smaller reporting company)			Sinanei reporting company o	

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Amount to be registered (1)(2)	Proposed maximum offering price per share (3)	Proposed maximum aggregate offering price (3)	Amount of registration fee
Common Stock, \$0.01 par value	17,611,112 shares	\$9.79	\$172,412,787	\$20,035

(1) This amount represents shares to be offered by the Selling Stockholders from time to time after the effective date of this Registration Statement at prevailing market prices at time of sale. Pursuant to Rule 416 under the Securities Act, the shares being registered hereunder include such indeterminate number of shares of common stock as may be issuable with respect to the shares being registered hereunder as a result of stock splits, stock dividends or similar transactions.

The number of shares of common stock includes 3,500,000 issued shares of common stock, 13,611,112 shares of common stock issuable upon exercise of certain of the Company's outstanding convertible notes and 500,000 shares of common stock issuable upon exercise of certain of the Company's outstanding warrants to purchase common stock.

(3) Estimated solely for the purpose of calculating the registration fee in accordance with Rule 457 under the Securities Act. The price per share and aggregate offering price are based on the average of the high and low sales prices of the registrant's common stock on November 3, 2014, as reported on The NASDAQ Global Market.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

The information in this prospectus is not complete and may be changed. The Selling Stockholders may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion, Dated November 7, 2014

PROSPECTUS

17,611,112 Shares

Common Stock

This prospectus relates to the resale from time to time of up to an aggregate of 17,611,112 shares of our common stock by the Selling Stockholders named in this prospectus, as follows:

Up to 3,500,000 shares of our outstanding common stock acquired by one of the Selling Stockholders in a privately negotiated transaction;

Up to 13,611,112 shares of our common stock which may be acquired by certain of the Selling Stockholders upon conversion of 8.00% Convertible Senior Notes due 2019 that we issued to these Selling Stockholders in a private placement on February 21, 2014; and

Up to 500,000 shares of our common stock which may be acquired by one of the Selling Stockholders upon exercise of warrants that we issued to this Selling Stockholder in a private placement on May 13, 2014.

The prices at which these Selling Stockholders may sell these shares will be determined by the prevailing market price for shares of our common stock or in negotiated transactions. We cannot predict when or in what amounts a Selling Stockholder may sell any of the shares offered by this prospectus. We will not receive any of the proceeds from the sale of these shares. All expenses of registration incurred in connection with this offering are being borne by us, but all selling and other expenses incurred by the Selling Stockholders will be borne by the Selling Stockholders. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus.

Our common stock is listed on the NASDAQ Global Market under the symbol "PTX." On November 5, 2014, the last reported sale price of our common stock on the NASDAQ Global Market was \$9.31 per share.

Investing in our securities involves risks. You should review carefully the risks and uncertainties described under the heading "Risk Factors" beginning on page 4 and under similar headings in the other documents that are incorporated by reference herein.

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

The date of this prospectus is , 2014.

TABLE OF CONTENTS

	Page
About This Prospectus	1
Cautionary Note Regarding Forward-Looking Statements	2
Our Company	3
Risk Factors	4
Use of Proceeds	4
Selling Stockholders	5
Description of Our Capital Stock	6
Description of Certain Provisions of Maryland Law and Our Certificate Of	9
Incorporation and By-Laws	
Plan of Distribution	13
Legal Matters	15
Experts	16
Documents Incorporated by Reference	16
Where You Can Find More Information	17

i

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC. The prospectus relates to up to 17,611,112 shares of our common stock which the Selling Stockholders named in this prospectus may sell from time to time. We will not receive any of the proceeds from these sales. We have agreed to pay the expenses incurred in registering these shares, including legal and accounting fees.

You should rely only on the information contained or incorporated by reference in this prospectus. We have not, and the Selling Stockholders have not, authorized anyone to provide you with information different from that contained in this prospectus. The Selling Stockholders are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where it is lawful to do so. The Selling Stockholders should not make an offer of these shares in any jurisdiction where the offer is not permitted. Brokers or dealers should confirm the existence of an exemption from registration or effect a registration in connection with any offer and sale of these shares.

The information in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of our common stock.

You should read this prospectus together with the additional information described under the heading "Where You Can Find More Information."

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents that we incorporate by reference herein, includes 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, as amended, or the "Exchange Act." For this purpose, any statements contained herein, other than statements of historical fact, including statements regarding the progress and timing of our product development programs and related trials; our future opportunities; our strategy, future operations, anticipated financial position, future revenues and projected costs; our management's prospects, plans and objectives; and any other statements about management's future expectations, beliefs, goals, plans or prospects constitute forward-looking statements. We may, in some cases, use words such as "anticipate," "believe," "could," "estimate," "expect," "intend," "may," "plan," "project," "should," "target," "will," "would" or other words that convey uncertainty of futu or outcomes to identify these forward-looking statements. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including the risks described under the heading "Risk Factors" in our most recent annual report on Form 10-K and our quarterly reports on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC. If one or more of these factors materialize, or if any underlying assumptions prove incorrect, our actual results, performance or achievements may vary materially from any future results, performance or achievements expressed or implied by these forward-looking statements. Our forward-looking statements do not reflect the potential impact of any acquisitions, mergers, dispositions, business development transactions, joint ventures or investments we may enter into or make in the future.

You should rely only on information contained, or incorporated by reference, in this prospectus, the registration statement of which this prospectus is a part, the documents incorporated by reference in this prospectus, and any applicable prospectus supplement or free writing prospectus and understand that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements. Although we believe that the expectations reflected in our forward-looking statements are reasonable, we cannot guarantee future results, events, levels of activity, performance or achievement. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We undertake no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, unless required by law. Before deciding to purchase our securities, you should carefully consider the risk factors incorporated herein by reference, in addition to the other information set forth in this prospectus, any accompanying prospectus supplement, any free writing prospectus and in the documents incorporated by reference.

OUR COMPANY

This business overview highlights information contained in certain documents incorporated by reference into this prospectus. This business overview does not contain all of the information that you should consider before investing in our securities. You should read the entire prospectus carefully, including the "Risk Factors" section and the financial statements and the notes to those statements incorporated herein by reference, before making an investment decision.

References in this prospectus to the terms "Pernix," "company," "we," "our" or "us" or other similar terms means Pernix Therapeutics Holdings, Inc. and its subsidiaries.

Overview

We are a specialty pharmaceutical company focused on the acquisition, development and commercialization of prescription drugs, primarily for the U.S. market. The Company targets underserved therapeutic areas, such as central nervous system (CNS), including neurology and psychiatry, and has an interest in expanding into additional specialty segments. The Company promotes its branded products to physicians through its Pernix sales force, uses contracted sales organizations to market its non-core cough and cold products, and markets its generic portfolio through its wholly owned subsidiaries, Macoven Pharmaceuticals, LLC ("Macoven") and Cypress Pharmaceuticals, Inc. ("Cypress").

The Company's branded products include TREXIMET®, a medication indicated for the acute treatment of migraine pain and inflammation, SILENOR®, a non-controlled substance and approved medication for the treatment of insomnia characterized by difficulty with sleep, CEDAX®, an antibiotic for middle ear infections, and a family of prescription products for cough and cold (ZUTRIPRO®, REZIRA®, and VITUZ®). The Company recently entered into an agreement with a third party to promote the Company's prescription treatments for cough and cold (ZUTRIPRO, REZIRA, and VITUZ). The Company also has an Exclusive License Agreement with Osmotica Pharmaceutical Corp. to promote KHEDEZLATM, Extended-Release Tablets, 50 and 100 mg for major depressive disorder. As described below, the Company completed the acquisition of the United States ("U.S.") intellectual property rights to the migraine product, TREXIMET on August 20, 2014.

The Company promotes its branded products through its sales and marketing organization that covers approximately 100 sales territories. The Company will also supplement its sales effort from time to time by contracting with other third party marketing organizations to assist in promoting certain of its products.

The Company sells its generic products in the areas of cough and cold, pain, vitamins, dermatology, antibiotics and gastroenterology through its wholly-owned subsidiaries, Macoven and Cypress.

Recent Developments

On August 20, 2014 we announced the closing of our acquisition of the U.S. rights to Treximet® (sumatriptan / naproxen sodium) for the acute treatment of migraine attacks with or without aura in adults from GlaxoSmithKline plc, or GSK, for an upfront purchase price of \$250,000,000, plus up to an additional \$17,000,000 if the U.S. Food & Drug Administration authorizes the filing of a sNDA for the purpose of pediatric exclusivity, subject to certain deductions based on delays in supplying the commercial product to the company. Subsequently, the deductions resulting from delays in supplying the commercial product reduced the \$17,000,000 payable amount to approximately \$1,950,000. As a condition to closing, GSK will continue to manufacture Treximet® under a long-term Supply Agreement with us. In addition, GSK assigned to us GSK's rights under the Product Development and Commercialization Agreement, or the PDC Agreement, between GSK and POZEN, Inc., and the amended the PDC Agreement to facilitate further development of Treximet®. Under the amendment, we will complete the filing with

the U.S. Food & Drug Administration for exclusivity for the pediatric indication for Treximet® and undertake certain new activities to extend the product's life. In addition, we released certain restrictions on POZEN's right to develop and commercialize additional dosage forms of sumatriptan/naproxen combinations outside of the United States.

Treximet[®] is covered by three patents in the U.S. which expire August 14, 2017. In addition, we will be seeking pediatric exclusivity and other potential FDA exclusivity options which may provide an additional six months to three years of exclusivity.

In connection with the Treximet® acquisition, we issued \$220,000,000 aggregate principal amount of 12% Senior Secured Notes due 2020 pursuant to an indenture with U.S. Bank National Association as trustee and collateral agent. We received aggregate gross proceeds of \$220,000,000, which were used to fund a portion of the \$250,000,000 cash consideration of the purchase price for Treximet®. The balance of the purchase price was funded by cash on hand.

Company Information

Our common stock trades on the NASDAQ Global Market, or NASDAQ, under the trading symbol "PTX."

Our principal executive office is at 10 North Park Place, Suite 201, Morristown, New Jersey 07960, and our telephone number is (800) 793-2145. Our website address is www.pernixtx.com. Information found on, or accessible through, our website is not a part of, and is not incorporated into, this prospectus, and you should not consider it part of this prospectus or part of any prospectus supplement. Our website address is included in this document as an inactive textual reference only.

RISK FACTORS

An investment in our securities involves a high degree of risk. In addition to the other information included in, or incorporated by reference into, this prospectus, the applicable prospectus supplement and any related free writing prospectus, you should carefully consider the risk factors incorporated by reference to our Annual Report on Form 10-K for the year ended December 31, 2013, as the same may be updated from time to time by our future filings under the Exchange Act, when determining whether or not to purchase the securities offered under this prospectus and the prospectus supplement.

USE OF PROCEEDS

We are registering these shares of common stock for resale by the Selling Stockholders. We are not selling any securities under this prospectus and will not receive any proceeds from sales of the shares of common stock sold from time to time under this prospectus by the Selling Stockholders.

We have agreed to pay all costs, expenses and fees relating to registering the shares of our common stock referenced in this prospectus. The Selling Stockholders will pay any brokerage commissions and/or similar charges incurred for the sale of such shares of our common stock.

4

SELLING STOCKHOLDERS

The shares of common stock being offered by the Selling Stockholders were either acquired in privately negotiated transactions or are issuable upon (i) conversion of our 8.00% Convertible Senior Notes due 2019 that we issued in a private placement on February 21, 2014 or (ii) exercise of certain Warrants to Purchase Common Stock that we issued in a privately negotiated transaction on May 13, 2014. For additional information regarding the issuance of such Notes, see "Description of Our Capital Stock - 8.00% Convertible Senior Notes due 2019" and "Description of Our Capital Stock - 8.00% Convertible Senior Notes due 2019" and "Description of Our Stockholders to offer the shares for resale from time to time.

The table below lists the Selling Stockholders and other information regarding the beneficial ownership of the shares of common stock held by each of the Selling Stockholders. The second column lists the number of shares of common stock beneficially owned by each Selling Stockholder, based on its ownership as of September 30, 2014, as such beneficial ownership is determined in accordance with the rules of the SEC.

The third column lists the shares of common stock being offered by this prospectus by each Selling Stockholder.

The fourth column assumes the sale of all of the shares offered by the Selling Stockholders pursuant to this prospectus.

Beneficial ownership is determined in accordance with rules promulgated by the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. This table is based upon information supplied to us by the Selling Stockholders and information filed with the SEC. The percent of beneficial ownership for the Selling Stockholders is based on 38,204,068 shares of our common stock outstanding as of September 30, 2014.

We may amend or supplement this prospectus from time to time in the future to update or change this list and shares which may be resold.

	Number of Shares Beneficially		Number of Shares to be Owned after The	Percent of Outstanding Shares to be Owned after
	Owned Prior to	Number of Shares	Offering	The
Name and Address	Offering	Registered for Sale	(1)	Offering (1)
Cetus Capital II, LLC (2)	2,447,917	2,447,917		
Littlejohn Opportunities Master Fund LP				
(3)	677,083	677,083		
SG Distressed Fund, LP (4)	347,222	347,222		
Broadfin Healthcare Master Fund, Ltd. (5)	3,500,000	3,500,000		
POZEN Inc. (6)	500,000	500,000		
Athyrium Opportunities Fund (A) LP (7)	6,528,668	6,528,668		
Athyrium Opportunities Fund (B) LP (8)	3,610,222	3,610,222		

(1) We do not know when or in what amounts the Selling Stockholders will offer shares for sale, if at all. The Selling Stockholders may sell any or all of the shares included in and offered by this prospectus. Because the Selling Stockholders may offer all or some of the shares pursuant to this offering, we cannot estimate the number of shares that will be held by the Selling Stockholders after completion of the offering. However, for purposes of this table, we have assumed that after completion of the offering, none of the shares included in and covered by

this prospectus will be held by the Selling Stockholders.

- (2) The address of Cetus Capital II, LLC is 8 Sound Shore Drive, Suite 303, Greenwich, CT 06830. Littlejohn Fund IV, L.P. is the sole member of Cetus Capital II, LLC, and Littlejohn Fund IV, L.P. is managed by Littlejohn Managers LLC. Each of Littlejohn Fund IV, L.P. and Littlejohn Managers LLC has voting and investment power over these securities, and each of them disclaim beneficial ownership of the securities reported herein.
- (3) The address of Littlejohn Opportunities Master Fund LP is 8 Sound Shore Drive, Suite 303, Greenwich, CT 06830. Littlejohn Opportunities GP is the general partner of Littlejohn Opportunities Master Fund LP and has voting and investment power over these securities. Littlejohn Opportunities GP disclaims beneficial ownership of the securities reported herein.
- (4) The address of SG Distressed Fund, LP is 8 Sound Shore Drive, Suite 303, Greenwich, CT 06830. Littlejohn Opportunities GP is the general partner of SG Distressed Fund, LP and has voting and investment power over these securities. Littlejohn Opportunities GP disclaims beneficial ownership of the securities reported herein.
- (5) The address of Broadfin Healthcare Master Fund, Ltd. ("Broadfin") is 20 Genesis Close Ansbacher House, Second Floor, P.O. Box 1344, Grand Cayman KY1-1108, Cayman Islands and the business address of each of Broadfin Capital, LLC and Kevin Kotler is 237 Park Avenue, 9th Floor, New York, NY 10017. Broadfin, Broadfin Capital, LLC and Kevin Kotler have shared voting and investment control of the securities held by Broadfin.
- (6) The address of POZEN Inc. is 1414 Raleigh Road, Suite 400, Chapel Hill, NC 27517. Consists of 500,000 shares of common stock issuable upon exercise of a warrant issued to POZEN Inc. by Pernix in connection with the Asset Purchase and Sale Agreement, dated as of May 13, 2014, by and among Pernix and GlaxoSmithKline plc and certain of its related affiliates. The exercise price is equal to \$4.28 per share and the warrant is exercisable until February 28, 2018.
- (7) The address of Athyrium Opportunities Fund (A) LP is c/o Athyrium Capital Management, LLC, 530 Fifth Avenue, Floor 25, New York, NY 10036. Jeffrey A. Ferrell, Anthony Tutrone, Samuel Porat, Peter Von Lehe and Brian Talbot, as the voting members of this selling stockholder's investment committee, exercise voting and investment control over the convertible notes and the underlying common stock held by such selling stockholder. This selling stockholder is managed by Athyrium Opportunities Associates LP, which in turn is managed by Athyrium Opportunities Associates GP LLC. The members of Athyrium Opportunities Associates GP LLC are Athyrium Capital Management LLC and NB Alternatives GP Holdings LLC.
- (8) The address of Athyrium Opportunities Fund (B) LP is c/o Athyrium Capital Management, LLC, 530 Fifth Avenue, Floor 25, New York, NY 10036. Jeffrey A. Ferrell, Anthony Tutrone, Samuel Porat, Peter Von Lehe and Brian Talbot, as the voting members of this selling stockholder's investment committee, exercise voting and investment control over the convertible notes and the underlying common stock held by such selling stockholder. This selling stockholder is managed by Athyrium Opportunities Associates LP, which in turn is managed by Athyrium Opportunities Associates GP LLC. The members of Athyrium Opportunities Associates GP LLC are Athyrium Capital Management LLC and NB Alternatives GP Holdings LLC.

5

Board Nomination Rights

In conection with our sale of 8.00% Convertible Senior Notes due 2019 to Athyrium Opportunities Fund (A) LP and Athyrium Opportunities Fund (B) LP (together, the "Athyrium Investor") and Cetus Capital II, LLC, Littlejohn Opportunities Master Fund LP and SG Distressed Fund, LP (collectively, the "Cetus Investor"), we entered into a representation agreement whereby we granted to the Athyrium Investor and the Cetus Investor certain board nomination rights.

DESCRIPTION OF OUR CAPITAL STOCK

This section describes the general terms of our capital stock. For more detailed information, you should refer to our certificate of incorporation and our by-laws, copies of which are filed with the SEC as exhibits to the registration statement of which this prospectus is a part.

Overview

We are authorized to issue up to 90,000,000 shares of common stock, \$0.01 par value per share, and up to 10,000,000 shares of preferred stock, \$0.01 par value per share, of which 1,000,000 shares have been designated Series B Junior Participating Stock. As of September 30, 2014, there were 38,204,068 shares of our common stock outstanding and no shares of preferred stock outstanding.

Common Stock

Holders of shares of our common stock are entitled to one vote for each share held of record on all matters to be voted on by stockholders, including the election of directors.

Our certificate of incorporation and by-laws do not provide for cumulative voting rights. Because of this, subject to the voting rights of any outstanding shares of preferred stock, the holders of a majority of our issued and outstanding common stock entitled to vote in any election of directors can elect all of the directors standing for election.

Subject to the preferences that may be applicable to any then outstanding preferred stock, the holders of our outstanding shares of common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities, subject to the satisfaction of any liquidation preference granted to the holders of any outstanding shares of preferred stock.

The terms of our common stock do not include any preemptive, conversion or subscription rights, nor any redemption or sinking fund provisions.

The rights, preferences and privileges of the holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of shares of Series B Junior Participating Stock and holders of shares of any other series of our preferred stock that we may classify and issue in the future.

Stock Exchange Listing

Our common stock is listed on the NASDAQ Global Market. The trading symbol for our common stock is "PTX."

Transfer Agent and Registrar

Computershare is the transfer agent and registrar for our common stock.

Preferred Stock

Pursuant to our certificate of incorporation, our board of directors has the authority, without further action by the stockholders (unless such stockholder action is required by applicable law or NASDAQ Global Market rules), to (1) issue up to 1,000,000 shares of Series B Junior Participating Stock, and (2) designate and issue up to 9,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the preferences, conversion and other rights, voting powers, restrictions, limitations as to dividends, qualifications, and other terms and conditions of the shares of each such series, and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding or above the amount authorized in our certificate of incorporation. These rights, powers, restrictions and limitations could rank senior to and adversely impact holders of our common stock and other series of preferred stock, and may provide the right to receive specified dividend payments and payments on liquidation prior to any payments to holders of common stock or other series of preferred stock. For example, each share of our Series B Junior Participating Stock entitles the holder thereof to 100 votes on all matters submitted to a vote of the holders of the common stock. There are currently no shares of Series B Junior Participating Stock outstanding.

Our board of directors may authorize the issuance of preferred stock with voting, conversion, dividend, liquidation preference and other rights that could adversely affect the voting power or other rights of the holders of our common stock and any other series of preferred stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in our control and may adversely affect the market price of the common stock and the voting and other rights of the holders of common stock. Additionally, the issuance of preferred stock may have the effect of decreasing the market price of our common stock.

Warrants to Purchase Common Stock

As of September 30, 2014, we have outstanding (a) warrants to purchase 469,000 shares of common stock issued in connection with our acquisition of Somaxon Pharmaceuticals, Inc. having exercise prices ranging from \$7.70 to \$90.72 and expiration dates ranging from July 2016 through August 2021, and (b) warrants to purchase 500,000 shares of common stock issued in connection with our acquisition of the Treximet® product from GlaxoSmithKline plc having an exercise price equal to \$4.28 per share and an expiration date of February 28, 2018.

8.00% Convertible Senior Notes due 2019

On February 21, 2014, we issued \$65,000,000 aggregate principal amount of 8.00% Convertible Senior Notes due 2019 (the "Notes"). The Notes were offered and sold only to institutional accredited investors and pursuant to Rule 4(a)(2) of the Securities Act.

The Notes are governed by the terms of an indenture (the "Indenture"), dated as of February 21, 2014, between the company and Wilmington Trust, National Association, as trustee (the "Trustee"). The Notes are the senior unsecured obligations of the company and bear interest at a rate of 8.00% per annum, payable quarterly in arrears on March 15, June 15, September 15 and December 15, beginning on June 15, 2014. The Notes will mature on February 15, 2019, unless earlier converted or repurchased. The Notes will be convertible into shares of our common stock at an initial conversion rate of 277.7778 shares of common stock per \$1,000 principal amount of the Notes, which corresponds to an initial conversion price of approximately \$3.60 per share of common stock.

The conversion rate is subject to adjustment from time to time upon the occurrence of certain events, including, but not limited to, the issuance of stock dividends, payment of cash dividends and the below-market-price issuance of common stock. At any time prior to the close of business on the business day immediately preceding the maturity date, holders may convert all or any portion of their Notes at their option. If, upon the occurrence of a change of control, as described in the Indenture, a holder elects to convert its Notes in connection with such change of control, such holder may be entitled to an increase in the conversion rate as described in the Indenture. To the extent such increase in the conversion rate would result in the conversion price of the Notes to be less than \$2.3278 per share (subject to adjustment) and equal to or greater than \$2.09 per share (subject to adjustment), we will be obligated to deliver cash in lieu of any share that was not delivered on account of such limitation.

We may not redeem the Notes prior to the maturity date and no "sinking fund" is provided for the Notes, which means that we are not required to periodically redeem or retire the Notes. Upon the occurrence of a change of control, as described in the Indenture, holders of the Notes may require us to repurchase for cash all or part of their Notes at a repurchase price equal to 100% plus a specified percentage (that is initially 40% and declines over the life of the notes) of the principal amount of the Notes to be repurchased, plus accrued and unpaid interest.

The Indenture contains restrictive covenants that, among other things, restrict our ability to: (i) incur debt; (ii) pay dividends and make distributions on, or redeem or repurchase, our capital stock; (iii) make certain investments, purchase certain assets or other restricted payments; (iv) sell assets, including in connection with sale-leaseback transactions; (v) create liens; (vi) enter into transactions with affiliates; (vii) make lease payments in excess of an agreed to threshold; and (viii) merge, consolidate or transfer all or substantially all of our assets. In addition, we are also required to maintain a minimum liquidity of \$8.0 million at all times. Many of these covenants are subject to a number of important limitations and exceptions under the Indenture.

For a complete and detailed description of the terms and conditions of the Notes and the Indenture, see our Current Report on Form 8-K filed with the SEC on February 26, 2014.

Registration Rights

On February 21, 2014, in connection with our private placement of the Notes, we entered into registration rights agreements with each of the purchasers of the Notes pursuant to which we agreed to provide certain registration rights with respect to the common stock issuable upon conversion of the Notes. We are filing the registration statement to which this prospectus forms a part in satisfaction of certain piggy back registration rights exercised by certain of the Selling Stockholders.

DESCRIPTION OF CERTAIN PROVISIONS OF MARYLAND LAW AND OUR CERTIFICATE OF INCORPORATION AND BY-LAWS

The following summary of certain provisions of Maryland law and of our certificate of incorporation and by-laws does not purport to be complete and is subject to and qualified in its entirety by reference to Maryland law and to our certificate of incorporation and by-laws, copies of which are filed with the SEC as exhibits to the registration statement of which this prospectus forms a part.

Our Board of Directors

Our by-laws provide that the number of directors of our company may be established by our board of directors but may not be fewer than the minimum number permitted under the Maryland General Corporate Law (the "MGCL") nor more than 9. Our board currently is set at five directors. As of September 30, 2014, our board of directors had four members and one vacancy remaining to be filled. In accordance with the provisions of Section 3-804(c) of the MGCL, our certificate of incorporation and by-laws, a vacancy on our board of directors, including a vacancy created by an increase in the number of directors, will be filled by the remaining directors until a successor is elected and qualifies. However, a vacancy created by the removal of a director pursuant to the affirmative vote of the stockholders holding not less than two-thirds of all the votes entitled to be cast for the election of directors, will be filled by a plurality of all the votes cast at a meeting of stockholders duly called and at which a quorum is present. Pursuant to our by-laws, each of our directors is elected by our stockholders to serve until the next annual meeting and until his or her successor is duly elected and qualifies under the MGCL. Except as provided with respect to any other class or series of stock, including any Series B Junior Participating Stock, the holders of our common stock possess the exclusive voting power. Each share of our Series B Junior Participating Stock entitles the holder thereof to 100 votes on all matters submitted to a vote of the holders of our common stock. Holders of shares of our common stock have no right to cumulative voting in the election of directors. Consequently, at each annual meeting of stockholders and subject to any outstanding shares of Series B Junior Participating Stock or other preferred stock, the holders of a majority of the shares of our issued and outstanding common stock have the ability to elect all of our directors.

Business Combinations

Under the MGCL, certain "business combinations" (defined in the MGCL) between a Maryland corporation and any interested stockholder, or an affiliate of such an interested stockholder, are prohibited for five years after the most recent date on which the interested stockholder becomes an interested stockholder. The MGCL defines an interested stockholder as any person who:

is the beneficial owner, directly or indirectly, of 10% or more of the voting power of the outstanding voting stock of the corporation, or

is an affiliate or associate of the corporation who, at any time within the two-year period prior to the date in question, was the beneficial owner, directly or indirectly, of 10% or more of the voting power of the then outstanding voting stock of the corporation.

A person is not an interested stockholder under the statute if our board of directors approved in advance the most recent transaction by which the person otherwise would have become an interested stockholder. However, in approving a transaction, our board of directors may provide that its approval is subject to compliance at or after the time of the approval, with any terms and conditions determined by it.

Business combinations are defined by the MGCL to include certain mergers, consolidations, share exchanges and asset transfers, some issuances and reclassifications of equity securities, the adoption of a plan of liquidation or dissolution or the receipt by an interested stockholder or its affiliate of any loan advance, guarantee, pledge or other financial assistance or tax advantage provided by the company.

After the five-year moratorium period described above, any business combination between the company and an interested stockholder generally must be recommended by our board of directors and approved by the affirmative vote of at least:

80% of the votes entitled to be cast by holders of outstanding shares of voting stock of the corporation, and

two-thirds (2/3) of the votes entitled to be cast by holders of voting stock of the corporation other than shares held by the interested stockholder with whom (or with whose affiliate) the business combination is to be effected or by an affiliate or associate of the interested stockholder voting together in a single voting group, unless, among other conditions, the corporation's common stockholders receive a minimum price (as described in the MGCL) for their shares and the consideration is received in cash or in the same form as previously paid by the interested stockholder for its shares.

These provisions of the MGCL do not apply, however, to business combinations that are approved or exempted by a board of directors prior to the time that the interested stockholder becomes an interested stockholder.

Control Share Acquisitions

The MGCL provides that "control shares" of a Maryland corporation acquired in a "control share acquisition" have no voting rights except to the extent approved at a special meeting by the affirmative vote of two-thirds of the votes entitled to be cast on the matter, excluding shares of stock in a corporation in respect of which any of the following persons is entitled to exercise or direct the exercise of the voting power of shares of stock of the corporation in the election of directors:

a person who makes or proposes to make a control share acquisition,

an officer of the corporation, or

an employee of the corporation who is also a director of the corporation.

"Control shares" are voting shares of stock which, if aggregated with all other such shares of stock previously acquired by the acquiror or in respect of which the acquiror is able to exercise or direct the exercise of voting power (except solely by virtue of a revocable proxy), would entitle the acquiror to exercise voting power in electing directors within one of the following ranges of voting power:

one-tenth or more but less than one-third,

one-third or more but less than a majority, or

a majority or more of all voting power.

Control shares do not include shares the acquiring person is then entitled to vote as a result of having previously obtained stockholder approval in accordance with the MGCL. A "control share acquisition" means the acquisition of control shares, subject to certain exceptions.

A person who has made or proposes to make a control share acquisition, upon satisfaction of certain conditions (including an undertaking to pay expenses), may compel our board of directors to call a special meeting of stockholders to be held within 50 days of demand to consider the voting rights of the control shares. If no request for a meeting is made, the corporation may itself present the question at any stockholders meeting. If voting rights of control shares are not approved at the meeting or if the acquiring person does not deliver the statement as required by the MGCL, then, subject to certain conditions and limitations, the corporation may redeem any or all of the control shares (except those for which voting rights have previously been approved) for fair value.

Fair value is determined, without regard to the absence of voting rights for the control shares, as of the date of the last control share acquisition by the acquiror or of any meeting of stockholders at which the voting rights of such shares are considered and not approved. If voting rights for control shares are approved by the stockholders at a special meeting and the acquiror becomes entitled to vote a majority of the shares entitled to vote, all other stockholders may exercise appraisal rights. The fair value of the shares as determined for purposes of such appraisal rights may not be less than the highest price per share paid by the acquiror in the control share acquisition. The control share acquisition statute does not apply (1) to shares acquired in a merger, consolidation or share exchange if the corporation is a party to the transaction or (2) to acquisitions approved or exempted by a corporation's charter or by-laws.

Our by-laws contain a provision exempting from the control share acquisition statute any and all acquisitions of our capital stock. We cannot provide you any assurance that our board of directors will not amend or eliminate this provision at any time in the future, and our board of directors may do so on a retroactive basis.

Subtitle 8

Title 3, Subtitle 8 of the MGCL permits a Maryland corporation with a class of equity securities registered under the Exchange Act and at least three independent directors to elect to be subject, by provision in its charter or by-laws or a resolution of its board of directors and notwithstanding any contrary provision in the charter or by-laws, to any of (1) a classified board, (2) a two-thirds vote requirement for removing a director, (3) a requirement that the number of directors be fixed only by vote of the directors, (4) a requirement that a vacancy on the board be filled only by the remaining directors and for the remainder of the full term of the class of directors in which the vacancy occurred, or (5) a majority requirement for the calling of a special meeting of stockholders. Pursuant to Subtitle 8, we have elected to provide, except in vacancies created by the affirmative vote of the stockholders holding not less than two-thirds of all the votes entitled to be cast for the election of directors, that vacancies on our board may be filled only by the remaining directors and for the remainder of the full term of the directorship in which the vacancy occurred. Through provisions in our certificate of incorporation and by-laws unrelated to Subtitle 8, we already require a two-thirds vote for the removal of any director from the board, vest in the board the exclusive power to fix the number of directorships and fill vacancies, subject to the limitations set forth in our by-laws, and require, unless called by our president, a majority of our board of directors or a majority of our independent directors, the written request of stockholders entitled to cast not less than a majority of all votes entitled to be cast at such meeting to call a special meeting. We have not elected to create a classified board; however, our board may elect to do so in the future without stockholder approval.

Charter Amendments and Extraordinary Transactions

Under the MGCL, a Maryland corporation generally cannot dissolve, amend its charter, merge, sell all or substantially all of its assets or engage in a share exchange unless approved by the affirmative vote of stockholders entitled to cast at least two-thirds of the votes entitled to be cast on the matter unless a lesser percentage (but not less than a majority of all of the votes entitled to be cast on the matter) is set forth in the corporation's charter. Our certificate of incorporation does not provide for a lesser percentage of votes for stockholder approval of the dissolution, merger, sale of all or substantially all of the company's assets or share exchange on the part of the company. However, because operating assets may be held by a corporation's subsidiaries, as in our situation, this may mean that a subsidiary of a corporation can transfer all of its assets or engage in other extraordinary actions without any vote of the corporation's stockholders.

Our certificate of incorporation generally provides that charter amendments requiring stockholder approval must be declared advisable by our board of directors and approved by the affirmative vote of stockholders entitled to cast a majority of all of the votes entitled to be cast on the matter. However, the affirmative vote of stockholders holding at least two-thirds of all of the votes entitled to be cast thereon is required to amend, alter, change, repeal or adopt any provisions inconsistent with the sections of our certificate of incorporation relating to removal of directors, the prohibition on cumulative voting in the election of directors, the requirements for independent directors, the prohibition on preemptive rights (except as provided in the terms of any series of preferred stock), indemnification and limitation of liability of directors and officers, and amendment of the charter. Currently, there are no provisions of our certificate of incorporation relating to holders of our capital stock.

In addition, our board may, upon the vote of a majority of our board of directors acting without stockholder approval, increase (up to the maximum number authorized under our certificate of incorporation but unissued) or decrease (to an amount not less than the total amount then outstanding) the number of shares of stock of any class that the corporation has authority to issue.

By-law Amendments

Our board of directors has the exclusive power to adopt, alter or repeal any provision of our by-laws and to make new by-laws, provided that amendment of certain provisions in our by-laws requires the affirmative vote of 80% of our entire board of directors.

Advance Notice of Director Nominations and New Business

Our by-laws provide that:

with respect to an annual meeting of stockholders, nominations of individuals for election to our board of directors and the proposal of business to be considered by stockholders may be made only:

pursuant to our notice of the meeting;

by or at the direction of our board of directors; or

by a stockholder who is entitled to vote at the meeting and has complied with the advance notice procedures set forth in our by-laws; and

with respect to special meetings of stockholders, only the business specified in our company's notice of meeting may be brought before the meeting of stockholders and nominations of individuals for election to our board of directors may be made only pursuant to our notice of the meeting, provided that the president, a majority of the board of directors (or of the independent directors) or the secretary of the company (upon request of holders of shares entitled to cast a majority of all the votes entitled to be cast at such meeting), shall be permitted to call and propose matters to be acted on at a special meeting.

The advance notice procedures of our by-laws generally provide that, to be timely, a stockholder's notice with respect to director nominations or proposals for an annual meeting must be delivered to our corporate secretary at our principal executive office not less than 90 nor more than 120 days prior to the first anniversary of the date of our preceding year's annual meeting.

Anti-takeover Effect of Certain Provisions of Maryland Law and of Our Certificate of Incorporation and By-laws

The provisions of our certificate of incorporation on removal of directors and the advance notice provisions of the by-laws could delay, defer or prevent a transaction or a change in control of our company that might involve a premium price for holders of our common stock or otherwise be in their best interest. Likewise, if our board of directors were to opt in to the business combination provisions of the MGCL or certain of the provisions of Title 3, Subtitle 8 of the MGCL, to the extent we have not already done so, or if the provision in the by-laws opting out of the control share acquisition provisions of the MGCL were rescinded, these provisions of the MGCL could have similar anti-takeover effects.

PLAN OF DISTRIBUTION

The Selling Stockholders and any of their donees, pledgees, transferees or other successors in interest may, from time to time after the date of this prospectus, sell, transfer or otherwise dispose of any or all of their shares of common stock offered hereby on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These sales may be made directly to purchasers or through underwriters, broker-dealers or agents, who may receive compensation in the form of discounts, concessions or commissions from the Selling Stockholders or the purchasers. These discounts, concessions or commissions as to any particular underwriter, broker-dealer or agent may be in excess of those customary in the types of transactions involved. These sales 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.

The Selling Stockholders may use any one or more of the following methods when disposing of shares or interests therein:

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 effected after the date the registration statement of which this prospectus is a part is declared effective by the SEC;

13

loans to broker-dealers or other financial institutions that in turn may sell the shares;

through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;

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

by pledge to secure debts and other obligations or on foreclosure of a pledge;

a combination of any such methods of sale; and

any other method permitted by applicable law.

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, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act amending identity of the Selling Stockholders to include the pledgees, transferees 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 donees, transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

The Selling Stockholders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act, provided that they meet the criteria and conform to the requirements of that rule.

The aggregate proceeds to the Selling Stockholders from the sale of the common stock offered by them will be the purchase price of the common stock less discounts or commissions, if any. The Selling Stockholders reserve the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of common stock to be made directly or through agents. We will not receive any of the proceeds from this offering.

The Selling Stockholders and any underwriters, broker-dealers or agents that participate in the sale of the common stock or interests therein may be "underwriters" within the meaning of Section 2(a)(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the shares may be underwriting discounts and commissions under the Securities Act. The Selling Stockholders who are "underwriters" within the meaning of Section 2(a)(11) of the Securities Act. The Selling Stockholders who are "underwriters" within the meaning of Section 2(a)(11) of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act. To the extent any Selling Stockholder may be deemed to be an "underwriter," it may be subject to statutory liabilities, including, but not limited to, Sections 11, 12 and 17 of the Securities Act.

The Selling Stockholders have advised us that they have not entered into any written or oral agreements, understandings or arrangements with any underwriter or broker-dealer regarding the sale of the shares covered by this prospectus. There is no underwriter or coordinating broker acting in connection with the proposed sale of the shares covered by this prospectus by the Selling Stockholders.

The Selling Stockholders may decide not to sell any of the common stock described in this prospectus. We cannot assure holders that any Selling Stockholder will use this prospectus to sell any or all of the common stock. In addition, a Selling Stockholder may transfer, devise or gift the common stock by other means not described in this prospectus.

To the extent required, the shares of our common stock to be sold, the name or names of the Selling Stockholders, the respective purchase prices and public offering prices, the names of any agents, dealer or underwriter, any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the common stock may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the common stock may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have advised the Selling Stockholders that the anti-manipulation rules of Regulation M under the Exchange Act, may apply to the activities of the Selling Stockholders and their affiliates. In addition, to the extent applicable we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the Selling Stockholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The Selling Stockholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

We have agreed with the Selling Stockholders to keep the registration statement of which this prospectus constitutes a part continuously effective until the earlier to occur of such time as all securities registered hereunder have been sold, the Selling Stockholders agree to terminate the registration, or the registration rights of the Selling Stockholders terminate.

We have agreed, among other things, to pay all expenses of the registration of the shares of common stock, including, without limitation, SEC filing fees and expenses of compliance with state securities or "blue sky" laws; provided, however, that the Selling Stockholders will pay all underwriting discounts and selling commissions applicable to the sale of the shares of common stock.

We have agreed to indemnify the Selling Stockholders against liabilities, including liabilities under the Securities Act and state securities laws, relating to the registration of the shares offered by this prospectus. The Selling Stockholders have, subject to certain limitations, agreed to indemnify us against liabilities under the Securities Act that may arise from any written information furnished to us by the Selling Stockholders specifically for use in this prospectus.

LEGAL MATTERS

Certain legal matters with respect to the securities offered hereby have been passed upon by Goodwin Procter LLP, New York, New York.

15

EXPERTS

Cherry Bekaert LLP, independent registered public accounting firm, has audited (i) our consolidated financial statements and management's assessment of the effectiveness of internal control over financial reporting included in our Annual Report on Form 10-K for the year ended December 31, 2013, and (ii) the statement of assets acquired of the Treximet® product line as of August 20, 2014 included in our Current Report on Form 8-K/A dated August 19, 2014, which are incorporated by reference in this prospectus and elsewhere in the registration statement. These financial statements and management's assessment of the effectiveness of internal control over financial reporting are incorporated by reference in reliance on Cherry Bekaert LLP's report, given on their authority as experts in accounting and auditing.

The audited historical statements of revenues and certain direct expenses of the Treximet® product line of GlaxoSmithKline plc included as exhibit 99.3 to Pernix Therapeutics Holdings Inc.'s Current Report on Form 8-K dated August 19, 2014 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, independent accountants, given on the authority of said firm as experts in auditing and accounting.

DOCUMENTS INCORPORATED BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with it, which means that we can disclose important information to you by referring you to those documents. The information we incorporate by reference is considered part of this prospectus. Statements in this prospectus regarding the contents of any contract or other document may not be complete. You should refer to the copy of the contract or other document filed as an exhibit to the registration statement. Later information filed with the SEC will update and supersede information we have included or incorporated by reference in this prospectus.

We incorporate by reference the documents listed below, which have been filed with the SEC (other than Current Reports or portions thereof furnished under Item 2.02 or Item 7.01 of Form 8-K):

- 1. Our Annual Report on Form 10-K for the fiscal year ended December 31, 2013;
 - 2. Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2014;
 - 3. Our Quarterly Report on Form 10-Q for the quarter ended June 30, 2014
- 4. Our Current Reports on Form 8-K or 8-K/A as filed on February 4, 2014, February 7, 2014, February 26, 2014, February 28, 2014, March 11, 2014, March 17, 2014, March 21, 2014, April 3, 2014, April 28, 2014, April 30, 2014, May 8, 2014, May 16, 2014, June 19, 2014, June 25, 2014, August 22, 2014, and October 9, 2014;
 - 5. Our Definitive Proxy Statement on Schedule 14A as filed on April 28, 2014; and
- 6. The description of our capital stock contained in Form 8-A filed with the SEC on February 7, 1997, as amended by that certain Form 8-A filed with the SEC on March 15, 2010.

We also incorporate by reference any filings made with the SEC after the date of the initial filing of the registration statement of which this prospectus forms a part including filings made prior to the effectiveness of the registration statement, under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 until the offering of the securities made by this prospectus is completed or terminated.

We will provide without charge to each person, including any beneficial owner, to whom this prospectus is delivered, upon the written or oral request of that person, a copy of any and all of the information that has been incorporated in this prospectus by reference other than exhibits unless those exhibits are specifically incorporated by reference into the documents. Requests for these copies should be directed to our investor relations department at the following address and telephone number: Pernix Therapeutics Holdings, Inc., 10 North Park Place, Suite 201, Morristown, New Jersey 07960, (800) 793-2145.

WHERE YOU CAN FIND MORE INFORMATION

We file reports, proxy statements and other information with the SEC. You may read and copy the reports, proxy statements and other information that we file with the SEC at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for information about the operation of its Public Reference Room and for its prescribed rates to obtain copies of such material. The SEC also maintains an Internet site that contains reports, proxy and information statements and other information regarding registrants, like us, that file electronically with the SEC. The address of the SEC's Internet site is www.sec.gov. Our Internet site is www.pernixtx.com. Information contained on our Internet site is not a part of this prospectus.

This prospectus provides you with a general description of the common stock being registered. This prospectus is part of a registration statement that we have filed with the SEC. To see more detail, you should read the registration statement and the exhibits and schedules filed with, or incorporated by reference into, our registration statement.

This registration statement, including the exhibits contained or incorporated by reference therein, can be read at the SEC web site or at the SEC office referred to above. Any statement made or incorporated by reference in this prospectus concerning the contents of any contract, agreement or other document is only a summary of the actual contract, agreement or other document. If we have filed or incorporated by reference any contract, agreement or other document as an exhibit to the registration statement, you should read the exhibit for a more complete understanding of the document or matter involved. Each statement regarding a contract, agreement or other document is qualified in its entirety by reference to the actual document.

PART II INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution.

The following table sets forth the various expenses to be incurred in connection with the sale and distribution of the securities being registered hereby, all of which will be borne by Pernix Therapeutics Holdings, Inc. All the amounts shown are estimates, except for the SEC registration fee:

SEC Registration Fee	\$20,035
Legal Fees and Expenses	\$50,000
Accounting Fees and Expenses	\$7,500
Printing and Miscellaneous Fees	\$22,465
Total	\$100,000

Item 15. Indemnification of Directors and Officers.

Maryland General Corporation Law. Section 2-405.2 of Maryland General Corporation Law ("MGCL") permits a Maryland corporation to include in its charter a provision limiting the liability of its directors and officers to the corporation and its stockholders for money damages, except (i) to the extent that it is proved that the director or officer actually received an improper benefit or profit in money, property or services or (ii) if a judgment or other final adjudication is entered in a proceeding based on a finding that the director's or officer's action, or failure to act, was the result of active and deliberate dishonesty and was material to the cause of action adjudicated in the proceeding.

Section 2-418(d) of the MGCL requires a corporation (unless its charter provides otherwise) to indemnify a present or former director of the corporation who has been successful, on the merits or otherwise, in the defense of any proceeding to which such director was made a party by reason of the director's service in that capacity. Section 2-418(b) of the MGCL permits a corporation to indemnify its present or former directors against judgments, penalties, fines, settlements and reasonable expenses actually incurred by the director in connection with any proceeding to which the director is made a party by reason of the director's service as a director, unless it is established that (1) the act or omission of the director was material to the matter giving rise to the proceeding and was committed in bad faith or was the result of active and deliberate dishonesty, (2) the director actually received an improper personal benefit in money, property or services or (3) in the case of any criminal proceeding, the director had reasonable cause to believe that the act or omission was unlawful. If, however, the proceeding was one by or in the right of the corporation and the director was adjudged liable to the corporation, the corporation may not indemnify the director. Section 2-418(f) permits a corporation to pay or reimburse reasonable expenses incurred by a director who is a party to such a proceeding in advance of the final disposition of the proceeding upon receipt by the corporation of (i) a written affirmation by the director of the director's good faith belief that the standard of conduct necessary for indemnification has been met, and (ii) a written undertaking (that may be unsecured but must be an unlimited general obligation) by or on behalf of the director to repay the amount if it shall ultimately be determined that the standard of conduct has not been met. Section 2-418(j) of the MGCL also requires a corporation to indemnify an officer of the corporation to the same extent that it must indemnify a director as provided in Section 2-418(d) of the MGCL unless limited by the charter and permits a corporation to indemnify and advance expenses to its officers, employees and agents to the same extent that it may indemnify and advance expenses to its directors.

The indemnification provided by statute is not exclusive of any other rights, by indemnification or otherwise, to which a director or officer may be entitled under the charter, by-laws, a resolution of shareholders or directors, an agreement or otherwise.

A Maryland corporation may purchase and maintain insurance on behalf of any person who is or was a director or officer, whether or not the corporation would have the power to indemnify a director or officer against liability under the provision of Section 2-418. Further, a corporation may provide similar protection, including a trust fund, letter of credit or surety bond, not inconsistent with the statute.

Pernix Therapeutics Holdings, Inc. Our certificate of incorporation and by-laws limit the liability of our directors and officers for money damages to the company and its stockholders to the fullest extent permitted from time to time by the MGCL.

Our certificate of incorporation and by-laws provide for indemnification of our officers and directors to the fullest extent permitted under MGCL Section 2-418. Our certificate of incorporation and by-laws also provide that the expenses of officers and directors incurred in defending any action, suit or proceeding, whether civil, criminal, administrative or investigative, shall be paid by us in advance of the final disposition of the action, suit or proceeding to the fullest extent permitted under MGCL Section 2-418.

Our certificate of incorporation and by-laws also require us to purchase and maintain director and officer insurance.

Item 16. Exhibits.

A list of exhibits filed with this registration statement on Form S-3 is set forth on the Exhibit Index and is incorporated herein by reference.

Item 17. Undertakings.

The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

a. To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

b. To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in the volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement;

c. To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

PROVIDED, HOWEVER, that paragraphs (1)(a), (1)(b) and (1)(c) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser, if the registrant is subject to Rule 430C, each prospectus filed pursuant to Rule 424(b) as part of a registration statement relating to an offering, other than registration statements relying on Rule 430B or other than prospectuses filed in reliance on Rule 430A, shall be deemed to be part of and included in the registration statement as of the date it is first used after effectiveness. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such first use, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such date of first use.

(5) That, for the purpose of determining liability of the registrant under the Securities Act to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

a. Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;

b. Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;

c. The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or used or its securities provided by or on behalf of the undersigned registrant; and

d. Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the provisions set forth in Item 15 above, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the city of Morristown, the State of New Jersey, on this 7th day of November, 2014.

PERNIX THERAPEUTICS HOLDINGS, INC.

By:

/s/ Douglas L. Drysdale Douglas L. Drysdale President and Chief Executive Officer

POWER OF ATTORNEY

We, the undersigned officers and directors of Pernix Therapeutics Holdings, Inc. hereby severally constitute and appoint Douglas L. Drysdale and Sanjay S. Patel, and each of them singly, our true and lawful attorneys, with full power to them and each of them singly, to sign for us in our names in the capacities indicated below, any and all amendments (including post-effective amendments) to this registration statement on Form S-3, and to file the same with the Securities and Exchange Commission, and generally to do all such things in our names and on our behalf in our capacities as officers and directors to enable Pernix Therapeutics Holdings, Inc. to comply with the provisions of the Securities Act, and all requirements of the Securities and Exchange Commission, hereby ratifying and confirming our signatures as they may be signed by our said attorneys, or any of them, to said registration statement and any and all amendments thereto.

Pursuant to the requirements of the Securities Act of 1933, as amended, this registration statement on Form S-3 has been signed by the following persons in the capacities and on the dates indicated.

SignatureTitleDatePresident, Chief Executive Officer
and ChairmanPresident, Chief Executive Officer
(Principal Executive Officer)November 7, 2014

/s/ Sanjay S. Patel