

NephroGenex, Inc.  
Form POS AM  
December 07, 2015

As filed with the Securities and Exchange Commission on December 7, 2015  
Registration No. 333-203530

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

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POST-EFFECTIVE AMENDMENT NO. 7 ON  
FORM S-3  
To  
Form S-1  
REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933

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NephroGenex, Inc.  
(Exact name of registrant as specified in its charter)

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Delaware  
(State or other jurisdiction of  
incorporation or organization)

2834  
(Primary Standard Industrial  
Classification Code Number)

20-1295171  
(I.R.S. Employer  
Identification No.)

3200 Beechleaf Court  
Suite 900  
Raleigh, NC 27604  
(609) 986-1780

(Address, including zip code and telephone number,  
including area code, of registrant's principal executive  
offices)

Pierre Legault  
Chief Executive Officer  
NephroGenex, Inc.  
3200 Beechleaf Court, Suite 900  
Raleigh, NC 27604  
(609) 986-1780

(Name, address, including zip code and telephone  
number,  
including area code, of agent for service)

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Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this registration statement.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, check the following box.

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.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) 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.

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.

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

Accelerated filer

Non-accelerated filer

Smaller reporting company

(Do not check if a smaller reporting company)

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Explanatory Note

This Post-Effective Amendment No. 7 on Form S-3 to Form S-1 (this “Registration Statement”) is filed in compliance with Section 10(a)(3) of the Securities Act of 1933 and Rule 401(b) under the Securities Act of 1933. This Registration Statement originally covered an offering of common stock and warrants that was completed in July 2015 and now covers the shares of our common stock issuable from time to time upon exercise of those warrants by the holders.

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 Commission, acting pursuant to said Section 8(a), may determine.

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

PRELIMINARY PROSPECTUS

Subject to Completion, dated December 7, 2015

NephroGenex, Inc.

1,725,000 Shares of Common Stock Issuable

Upon Exercise of Outstanding Warrants

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We are offering 1,725,000 shares of our common stock that are issuable for a purchase price of \$6.25 per share from time to time upon exercise of currently outstanding five-year warrants that we issued in July 2015 in an underwritten public offering that we completed at that time. No other securities are being offered pursuant to this prospectus apart from the shares of our common stock that will be issued upon exercise of those currently outstanding warrants. Our common stock is quoted on the NASDAQ Capital Market under the symbol "NRX." On December 4, 2015, the last reported price per share of our common stock as quoted on the NASDAQ Capital Market was \$1.81. There is no established public trading market for the warrants, and we do not expect a market to develop. In addition, we do not intend to apply for listing of the warrants on any national securities exchange or other nationally recognized trading system.

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Our business and investing in our securities involves significant risks. You should carefully read and consider the "Risk Factors" beginning on page 9 of this prospectus before investing.

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.

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The date of this prospectus is \_\_\_\_\_, 2015

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You should rely only on the information contained in this prospectus. We have not authorized anyone to provide you with information different from that which is contained in this prospectus. This prospectus may be used only where it is legal to sell these securities. The information in this prospectus may only be accurate on the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of securities.

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#### ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC. As permitted by the rules and regulations of the SEC, the registration statement filed by us includes additional information not contained in this prospectus. You may read the registration statement and the other reports we file with the SEC at the SEC's web site or its offices described below under the heading "Where You Can Find More Information."

You should rely only on the information that is contained in this prospectus or that is incorporated by reference into this prospectus. We have not authorized anyone to provide you with information that is in addition to or different from that contained in, or incorporated by reference into, this prospectus. If anyone provides you with different or inconsistent information, you should not rely on it.

The shares of common stock offered by this prospectus are not being offered in any jurisdiction where the offer or sale of such common stock is not permitted. You should not assume that the information contained in, or incorporated by reference into, this prospectus is accurate as of any date other than the date of this prospectus or, in the case of the documents incorporated by reference, the date of such documents, regardless of the date of delivery of this prospectus or any sale of the common stock offered by this prospectus. Our business, financial condition, liquidity, results of operations and prospects may have changed since those dates.

## PROSPECTUS SUMMARY

### Overview

We are a pharmaceutical company focused on the development of therapeutics to treat kidney disease, an area of significant unmet medical need. Since our inception, we have collaborated with the world's leading experts in kidney disease and leveraged our knowledge of pathogenic oxidative chemistries to build a strong portfolio of intellectual property and to advance the development of our drug candidates. We believe that our comprehensive effort to develop a new generation of therapeutics that target kidney disease provides us with a leadership position in this large and attractive market.

Pathogenic oxidative chemistries are collectively a group of oxygen-based chemical reactions that occur in the body during stress, injury, or disease, to form compounds that can induce pathological changes in tissues that effect normal physiological function. These include (i) advanced glycation end-products (AGE's), which are oxidative end products of glucose-modified biomolecules which adversely affect their function; (ii) reactive oxygen species (ROS), which are chemically reactive molecules containing oxygen such as oxygen ions and peroxides that when elevated in the body can induce pathology; and (iii) toxic carbonyls which are reactive compounds that can modify biomolecules and affect their function. These chemistries are generally agreed to be involved in the etiology of diabetic nephropathy, a common complication of diabetes, and in cases of acute kidney injury (AKI). We are developing Pyridorin™ ("Pyridorin"), a small molecule drug that is a unique and broadly acting inhibitor of the pathogenic oxidative chemistries which are elevated in diabetic patients.

We licensed patents covering methods of use and synthesis of Pyridorin from BioStratum, Inc. in May of 2006. We subsequently acquired Pyridorin-related patents from BioStratum through a Series A financing completed in May of 2007. At the time of acquisition, BioStratum, through its contracted investigators, contract research organizations, and collaborators had completed 5 preclinical efficacy studies, 36 preclinical safety studies, 4 Phase 1 studies and 5 Phase 2 studies with Pyridorin. After the acquisition, we conducted a multi-center, randomized, placebo-controlled Phase 2b study, namely PYR-210 and recently completed the Phase 1 QT/QTc (TQT) cardiac safety study. In addition, we worked with the FDA to establish a new regulatory pathway for Pyridorin approval, as well as received support from the European Medicines Agency (EMA) regarding the pivotal Phase 3 program with Pyridorin in diabetic nephropathy.

Pyridorin has demonstrated preliminary evidence of efficacy in slowing the progression of diabetic nephropathy in relevant patient populations in three Phase 2 clinical studies. Based on these results, Pyridorin entered into a Phase 3 program in 2014 termed the PIONEER trial which was agreed to by the U.S. Food and Drug Administration (FDA), with fast track designation, under a Special Protocol Assessment (SPA). This Phase 3 program is using a novel, events-based endpoint based on end stage renal disease (ESRD) or a 50% increase in serum creatinine (SCr). We believe this change will significantly reduce the cost and time for completion of our Phase 3 program compared to the traditional endpoint used in previous pivotal trials for diabetic nephropathy which is a 100% increase in SCr from baseline or end stage renal disease (ESRD). Based on an analysis of the Irbesartan Type II Diabetic Nephropathy Trial (IDNT) used for the approval of the drug irbesartan, the follow-up time required to reach the new endpoint of a 50% SCr increase would be approximately 50% less than the follow-up time required to reach the traditional endpoint in a similar patient population. We believe that we are the first company to use this novel endpoint in a Phase 3 trial.

We are also studying the application of an intravenous formulation of Pyridorin to specific types of AKI in patients at increased risk and where pathogenic oxidative chemistries have been identified as a possible contributing factor to the severity of this condition. Our preclinical program has shown encouraging results in animal models of ischemia-reperfusion AKI including an observed treatment effect on post injury fibrosis.

### Our Lead Product Candidate



The oral form of Pyridorin (pyridoxamine dihydrochloride) is being developed as a chronic, therapeutic agent to slow the progression of diabetic nephropathy. Pyridoxamine is a derivative of vitamin B6 and consists of a different chemical structure. It uniquely possesses activity against a broad range of pathogenic oxidative chemistries, a generally agreed causative factor in the development and progression of diabetic nephropathy. The FDA has ruled that pyridoxamine is an investigational drug candidate and not eligible for sale as a dietary supplement. Its concentration in the blood cannot be increased by taking commercially available vitamin B6.

Diabetic nephropathy is a chronic, degenerative disease of the kidney caused by diabetes. There are approximately 6 million patients with diabetic nephropathy in the United States (approximately 33% of diagnosed diabetics) and this population is expected to grow. According to a 2010 study commissioned by us, approximately 2.8 million diabetic patients have overt nephropathy, approximately 3.5 million patients have early stage diabetic nephropathy and approximately 3.6 million patients are at high risk of progressing to diabetic nephropathy. Patients suffering from diabetic nephropathy progress to End Stage Renal Failure (and require dialysis) or death. There are currently no adequate treatments for diabetic nephropathy.

As a potential therapeutic agent, Pyridorin has demonstrated preliminary evidence of efficacy in slowing the progression of diabetic nephropathy in preclinical models and in three Phase 2 clinical studies. Pyridorin has also been generally well tolerated in all of these studies.

To date, our Pyridorin development program has:

- verified the mechanism of action in in-vitro, animal and human studies;
- verified inhibition of diabetic nephropathy in animal models;
- demonstrated preliminary evidence of efficacy in slowing the progression of diabetic nephropathy in relevant patient populations in three Phase 2 clinical studies; and
- identified the patient population currently being studied in Phase 3 with the highest potential to demonstrate a significant treatment effect.

Based on these results, we have reached agreement with the FDA on an SPA regarding the design of the Phase 3 clinical program required for the registration of the product. This Phase 3 program is evaluating Pyridorin treatment for slowing the progression of diabetic nephropathy in type 2 diabetic patients with overt nephropathy and a baseline serum creatinine level of less than 3.0 mg/dL that are on an established and stable standard of care regimen at screening. In its prior Phase 2 study in this specific patient population, Pyridorin dosed at 300 mg twice daily demonstrated a statistically significant 57% treatment effect.

#### Additional Pipeline Opportunity

In addition to developing Pyridorin as a treatment for diabetic nephropathy, we are also studying the application of an intravenous formulation of Pyridorin for the treatment of specific types of acute kidney injury (AKI) where pathogenic oxidative chemistries have been identified as a possible contributing factor to the severity of this condition. In the U.S., the incidence of AKI varies from 20% to 40% in critical care patients. It is estimated that up to 7% of all patients who visit the hospital will experience AKI. Patients with uncomplicated AKI have a mortality rate of up to 10%, and if renal replacement therapy is required, the mortality rate rises to as high as 80%.

#### Our Strategy

We are committed to applying our leadership position in the field of kidney disease to transform the lives of patients with debilitating, costly diseases or conditions. Each of our ongoing and planned development projects addresses kidney diseases or conditions with high unmet medical need that presents a significant market opportunity. The core elements of our strategy include:

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- advancing Pyridorin through Phase 3 development for the treatment of diabetic nephropathy in patients with type 2 diabetes;
- submission and approval of a new drug application (NDA) in the United States and a Market Authorization Application (MAA) in Europe;
- commercializing Pyridorin using a highly-targeted sales force in the United States and the rest of the world;
- continued development of an intravenous formulation of Pyridorin for AKI, with an investigational new drug application (IND) filing and launch of the initial clinical study during the second half of 2015; and
- deploying capital strategically to develop our portfolio of product candidates and create shareholder value.

#### Corporate Information

We were incorporated in the State of Delaware on May 25, 2004. Our principal executive offices are located at 3200 Beechleaf Court, Suite 900, Raleigh, NC 27604 and our telephone number is (609) 986-1780. Our website address is [www.nephrogenex.com](http://www.nephrogenex.com). The information contained on, or that can be accessed through, our website is not part of this prospectus. Our common stock is listed on the NASDAQ Capital Market and trades under the symbol "NRX."

We have obtained a registered trademark for Pyridorin in the United States. This prospectus contains references to our trademarks and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to in this prospectus, including logos, artwork and other visual displays, may appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other company.

### The Offering

In July 2015, we completed the sale of 1,725,000 five-year warrants to purchase a total of 1,725,000 shares of our common stock. To date, none of these warrants have been exercised. This prospectus covers the 1,725,000 shares of our common stock issuable from time to time upon exercise of the warrants that are currently outstanding. Total common stock outstanding as of September 30, 2015 after this offering if all warrants are exercised is 12,467,387.

Securities being offered by us	1,725,000 shares of common stock issuable at a purchase price of \$6.25 per share from time to time upon exercise of the warrants issued in our July 2015 public offering.
Common stock to be outstanding after this offering if all of the warrants are exercised.	12,467,387 shares.
Use of proceeds	We intend to use the net proceeds received from the exercise of the warrants, if any, for working capital and general corporate purposes. See "Use of Proceeds" for further information.
Risk Factors	See "Risk Factors," as well as other information included in this prospectus, for a discussion of factors you should read and consider carefully before investing in our securities.
Trading Market	Our common stock is quoted on the NASDAQ Capital Market under the symbol "NRX."

The number of shares of common stock to be outstanding after this offering as shown above is based on 10,742,387 shares outstanding as of September 30, 2015 and excludes:

• 1,442,500 shares of our common stock issuable upon the exercise of stock options, with a weighted average exercise price of \$4.46 per share;

• 12,500 shares of our common stock issuable upon the settlement of outstanding restricted stock units;

• 118,603 shares of our common stock issuable upon the exercise of outstanding warrants, with a weighted average exercise price of \$9.86 per share; and

• other shares of our common stock reserved for future issuance under our Amended and Restated 2007 Equity Incentive Plan, as amended.

## RISK FACTORS

An investment in our securities involves a high degree of risk. The risks described below may not be the only ones relating to our company. Additional risks that we currently believe are immaterial may also impair our business operations. Our business, financial condition and future prospects and the trading price of our common stock could be harmed as a result of any of these risks. Investors should also refer to the other information contained in this prospectus, and our other filings from time to time with the SEC.

### Risks Related To Our Financial Position and Need for Additional Capital

We will require substantial additional funding, which may not be available to us on acceptable terms, or at all, and, if not so available, may require us to delay, limit, reduce or cease our operations.

We are currently advancing Pyridorin through clinical development for diabetic nephropathy and an intravenous formulation of Pyridorin for AKI through preclinical development. Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive. We will require substantial additional future capital in order to complete clinical development and commercialize Pyridorin. If the FDA or EMA requires that we perform additional nonclinical studies or clinical trials, our expenses would further increase beyond what we currently expect and the anticipated timing of any potential NDA or MAA would likely be delayed. Further, there can be no assurance that the costs to obtain regulatory approval of Pyridorin as a treatment for diabetic nephropathy in patients with type 2 diabetes or as a treatment for AKI will not increase.

We will continue to require substantial additional capital to continue our clinical development and commercialization activities. Because successful development of our product candidates is uncertain, we are unable to estimate the actual funds we will require to complete research and development and commercialize our products under development.

The amount and timing of our future funding requirements will depend on many factors, including but not limited to:

- the progress, costs, results of and timing of our Phase 3 Pyridorin PIONEER program for the treatment of diabetic nephropathy in patients with type 2 diabetes, and the preclinical and clinical development of an intravenous formulation of Pyridorin for AKI;

• the outcome, costs and timing of seeking and obtaining FDA, EMA and any other regulatory approvals;

• the number and characteristics of product candidates that we pursue;

• the ability of our product candidates to progress through clinical development successfully;

• our need to expand our research and development activities;

• the costs associated with securing and establishing commercialization and manufacturing capabilities;

• market acceptance of our product candidates;

• the costs of acquiring, licensing or investing in businesses, products, product candidates and technologies;

• our ability to maintain, expand and enforce the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights;

- our need and ability to hire additional management and scientific and medical personnel;
- the effect of competing drug candidates and new product approvals;
- our need to implement additional internal systems and infrastructure, including financial and reporting systems; and
- the economic and other terms, timing of and success of our existing licensing arrangements and any collaboration, licensing or other arrangements into which we may enter in the future.

Some of these factors are outside of our control. Based upon our currently expected level of operating expenditures, we believe that we will be able to fund our operations into mid-2016. This period could be shortened if there are any significant increases in planned spending on development programs or more rapid progress of development programs than anticipated. We do not expect our existing capital resources to be sufficient to enable us to complete the commercialization of Pyridorin, if approved, or to initiate any clinical trials or additional development work needed for any other product candidates, other than as described above. Accordingly, we expect that we will need to raise additional funds in the future.

We may seek additional funding through a combination of equity offerings, debt financings, government or other third-party funding, commercialization, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements. Additional funding may not be available to us on acceptable terms or at all. In addition, the terms of any financing may adversely affect the holdings or the rights of our stockholders. In addition, the issuance of additional shares by us, or the possibility of such issuance, may cause the market price of our shares to decline.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail one or more of our research or development programs. We also could be required to seek funds through arrangements with collaborative partners or otherwise that may require us to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us.

We have never been profitable. Currently, we have no products approved for commercial sale, and to date we have not generated any revenue from product sales. As a result, our ability to reduce our losses and reach profitability is unproven, and we may never achieve or sustain profitability.

We have never been profitable and do not expect to be profitable in the foreseeable future. We have not yet submitted any product candidates for approval by regulatory authorities in the United States or elsewhere for our lead indication, the treatment of diabetic nephropathy in patients with type 2 diabetes, or any other indication. We have incurred net losses in each year since our inception, including net losses of \$16.9 million and \$11.5 million for the nine months ended September 30, 2015 and 2014, respectively. We had an accumulated deficit of approximately \$74.7 million as of September 30, 2015.

To date, we have devoted most of our financial resources to our corporate overhead and research and development, including our drug discovery research, preclinical development activities and clinical trials. We have not generated any revenues from product sales. We expect to continue to incur losses for the foreseeable future, and we expect these losses to increase as we continue our development of, and seek regulatory approvals for Pyridorin, prepare for and begin the commercialization of any approved products, and add infrastructure and personnel to support our continuing product development efforts. We anticipate that any such losses could be significant for the next several years as we continue our Phase 3 clinical program of Pyridorin for the treatment of diabetic nephropathy in patients with type 2 diabetes, which we call the PIONEER program, and related activities required for regulatory approval of Pyridorin and pursuing an intravenous formulation of Pyridorin for AKI in clinical trials. If Pyridorin or any of our other product candidates fails in clinical trials or does not gain regulatory approval, or if our product candidates do not achieve market acceptance, we may never become profitable. As a result of the foregoing, we expect to continue to experience net losses and negative cash flows for the foreseeable future. These net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve

profitability. In addition, our expenses could increase if we are required by the FDA or the EMA, to perform studies

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or trials in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates. The amount of future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues.

Borrowings under our credit facility may not be available to us to operate our business and successfully develop and commercialize our primary product candidate.

On November 20, 2014, we entered into a Loan and Security Agreement with East West Bank (“East West”) for a term loan (the “Initial Term Loan”) with an aggregate principal amount of \$7.0 million and, subject to the terms and conditions set forth in the agreement, a second term loan (the “Second Term Loan”) with an aggregate principal amount of \$5.0 million. As security for our obligations under the Loan Agreement, we granted East West a lien in substantially all of our assets, including owned and licensed intellectual property. At our option, we could have borrowed the Second Term Loan on or before May 29, 2015, if we had met certain clinical milestones. As of the date hereof, we have not met the clinical milestones for the Second Term Loan. However, we have made a proposal to East West to amend the clinical milestones necessary for incurrence of the Second Term Loan.

Our loan agreement contains customary affirmative and negative covenants, indemnification provisions and events of default. The affirmative covenants include, among others, covenants requiring us to maintain our legal existence and governmental approvals, deliver certain financial reports and maintain certain intellectual property rights. The negative covenants include, among others, restrictions on transferring or licensing our assets, changing our business, incurring additional indebtedness, engaging in mergers or acquisitions, paying dividends or making other distributions, and creating other liens on our assets, in each case subject to customary exceptions. If we default under the Loan Agreement, East West may accelerate all of our repayment obligations and take control of our pledged assets, potentially requiring us to renegotiate the Loan Agreement on terms less favorable to us or to immediately cease operations. Further, if we are liquidated, East West has the right to repayment would be senior to the rights of the holders of our common shares to receive any proceeds from the liquidation. East West could declare a default under the Loan Agreement upon the occurrence of any event that East West interprets as a material adverse change as defined under the Loan Agreement, thereby requiring us to repay the loan immediately or to attempt to reverse the declaration of default through negotiation or litigation. Any declaration by our lender of an event of default could significantly harm our business and prospects and could cause the price of our common shares to decline. If we raise any additional debt financing, the terms of such additional debt could further restrict our operating and financial flexibility.

As of December 7, 2015, approximately \$6.6 million was outstanding on the loan. In addition, as of December 7, 2015, the Company believes it is compliance with all loan covenants.

We have a limited operating history and we expect a number of factors to cause our operating results to fluctuate on a quarterly and annual basis, which may make it difficult to predict our future performance.

We are a development stage pharmaceutical company with a limited operating history. Our operations to date have been limited to developing our technology and undertaking preclinical studies and clinical trials of our product candidates. We have not yet obtained regulatory approvals for any of our product candidates. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a longer operating history or approved products on the market. Our financial condition and operating results have varied significantly in the past and are expected to continue to significantly fluctuate from quarter-to-quarter or year-to-year due to a variety of factors, many of which are beyond our control. Factors relating to our business that may contribute to these fluctuations include:

any delays in regulatory review and approval of our product candidates in clinical development, including our ability to receive approval from the FDA and the EMA for Pyridorin for the treatment of diabetic nephropathy in patients with type 2 diabetes based on our Phase 3 Pyridorin program, and our other completed and planned clinical trials and nonclinical studies and other work, as the basis for review and approval of Pyridorin for the treatment of diabetic nephropathy in patients with type 2 diabetes;

delays in the commencement, enrollment and timing of clinical trials;

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difficulties in identifying and randomizing patients suffering from our target indications, and kidney disease in patients with type 2 diabetes in particular;

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the success of our clinical trials through all phases of clinical development, including our Phase 3 trial of Pyridorin for the treatment of diabetic nephropathy in patients with type 2 diabetes;

potential side effects of our product candidate that could delay or prevent approval or cause an approved drug to be taken off the market;

our ability to obtain additional funding to develop product candidates;

our ability to identify and develop additional product candidates;

market acceptance of our product candidates;

our ability to establish an effective sales and marketing infrastructure directly or through collaborations with third parties;

competition from existing products or new products that continue to emerge;

the ability of patients or healthcare providers to obtain coverage or sufficient reimbursement for our products;

our ability to adhere to clinical trial requirements directly or with third parties such as contract research organizations (CROs);

our dependency on third-party manufacturers to manufacture our products and key ingredients;

our ability to establish or maintain collaborations, licensing or other arrangements;

the costs to us, and our ability and our third-party collaborators' ability to obtain, maintain and protect our intellectual property rights;

costs related to and outcomes of potential intellectual property litigation;

our ability to adequately support future growth;

our ability to attract and retain key personnel to manage our business effectively; and

potential product liability claims.

Accordingly, the results of any quarterly or annual periods should not be relied upon as indications of future operating performance.

Our recurring losses from operations may raise substantial doubt regarding our ability to continue as a going concern.

Our recurring losses from operations may raise substantial doubt about our ability to continue as a going concern. There is no assurance that sufficient financing will be available when needed to allow us to continue as a going concern. The perception that we may not be able to continue as a going concern may cause others to choose not to deal with us due to concerns about our ability to meet our contractual obligations.

#### Risks Relating to Regulatory Review and Approval of Our Product Candidates

We cannot be certain that Pyridorin will receive regulatory approval, and without regulatory approval we will not be able to market Pyridorin.



Our business currently depends entirely on the successful development and commercialization of Pyridorin. Our ability to generate revenue related to product sales, if ever, will depend on the successful development and regulatory approval of Pyridorin for the treatment of diabetic nephropathy in patients with type 2 diabetes or an intravenous formulation of Pyridorin for AKI.

We currently have no products approved for sale and we cannot guarantee that we will ever have marketable products. The development of a product candidate and issues relating to its approval and marketing are subject to extensive regulation by the FDA in the United States, the EMA in Europe and regulatory authorities in other countries, with regulations differing from country to country. We are not permitted to market our product candidates in the United States or Europe until we receive approval of a NDA from the FDA or a MAA from the EMA, respectively. We have not submitted any marketing applications for any of our product candidates.

NDAs and MAAs must include extensive preclinical and clinical data and supporting information to establish the product candidate's safety and effectiveness for each desired indication. NDAs and MAAs must also include significant information regarding the chemistry, manufacturing and controls for the product. Obtaining approval of a NDA or a MAA is a lengthy, expensive and uncertain process, and we may not be successful in obtaining approval. The FDA and the EMA review processes can take years to complete and approval is never guaranteed. If we submit a NDA to the FDA, the FDA must decide whether to accept or reject the submission for filing. We cannot be certain that any submissions will be accepted for filing and review by the FDA. Regulators in other jurisdictions, such as the EMA, have their own procedures for approval of product candidates. Even if a product is approved, the FDA or the EMA, as the case may be, may limit the indications for which the product may be marketed, require extensive warnings on the product labeling or require expensive and time-consuming clinical trials or reporting as conditions of approval. Regulatory authorities in countries outside of the United States and Europe also have requirements for approval of drug candidates with which we must comply with prior to marketing in those countries. Obtaining regulatory approval for marketing of a product candidate in one country does not ensure that we will be able to obtain regulatory approval in any other country. In addition, delays in approvals or rejections of marketing applications in the United States, Europe or other countries may be based upon many factors, including regulatory requests for additional analyses, reports, data, preclinical studies and clinical trials, regulatory questions regarding different interpretations of data and results, changes in regulatory policy during the period of product development and the emergence of new information regarding our product candidates or other products. Also, regulatory approval for any of our product candidates may be withdrawn.

We have completed three Phase 2 trials for Pyridorin and are enrolling patients for our Phase 3 PIONEER trial. In addition, we have successfully completed a QT/QTc (TQT) cardiac safety study. Before we submit a NDA to the FDA or a MAA to the EMA for Pyridorin for the treatment of diabetic nephropathy in patients with type 2 diabetes, we must successfully conduct two Phase 3 trials. In addition, we must complete other nonclinical studies and clinical trials, such as two nonclinical carcinogenicity studies and a nonclinical cardiac safety study. We cannot predict whether our future trials and studies will be successful or whether regulators will agree with our conclusions regarding the preclinical studies and clinical trials we have conducted to date.

If we are unable to obtain approval from the FDA, the EMA or other regulatory agencies for Pyridorin and our other product candidates, or if, subsequent to approval, we are unable to successfully commercialize Pyridorin or our other product candidates, we will not be able to generate sufficient revenue to become profitable or to continue our operations.

Any statements in this document indicating that Pyridorin has demonstrated preliminary evidence of efficacy are our own and are not based on the FDA's or any other comparable governmental agency's assessment of Pyridorin and do not indicate that Pyridorin will achieve favorable efficacy results in any later stage trials or that the FDA or any comparable agency will ultimately determine that Pyridorin is effective for purposes of granting marketing approval. Delays in the commencement, enrollment and completion of clinical trials could result in increased costs to us and delay or limit our ability to obtain regulatory approval for Pyridorin and our other product candidates.

Delays in the commencement, enrollment and completion of clinical trials could increase our product development costs or limit the regulatory approval of our product candidates. We do not know whether any future trials or studies of our other product candidates will begin on time or will be completed on schedule, if at all. The start or end of a clinical study is often delayed or halted due to changing regulatory requirements, manufacturing

challenges, including delays or shortages in available drug product, required clinical trial administrative actions, slower than anticipated patient enrollment, changing standards of care, availability or prevalence of use of a comparative drug or required prior

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therapy, clinical outcomes or financial constraints. For instance, delays or difficulties in patient enrollment or difficulties in retaining trial participants can result in increased costs, longer development times or termination of a clinical trial. Clinical trials of a new product candidate require the enrollment of a sufficient number of patients, including patients who are suffering from the disease the product candidate is intended to treat and who meet other eligibility criteria. Rates of patient enrollment are affected by many factors, including the size of the patient population, the eligibility criteria for the clinical trial, that include the age and condition of the patients and the stage and severity of disease, the nature of the protocol, the proximity of patients to clinical sites and the availability of effective treatments and/or availability of investigational treatment options for the relevant disease.

A product candidate can unexpectedly fail at any stage of preclinical and clinical development. The historical failure rate for product candidates is high due to scientific feasibility, safety, efficacy, changing standards of medical care and other variables. The results from preclinical testing or early clinical trials of a product candidate may not predict the results that will be obtained in later phase clinical trials of the product candidate. We, the FDA or other applicable regulatory authorities may suspend clinical trials of a product candidate at any time for various reasons, including a belief that subjects participating in such trials are being exposed to unacceptable health risks or adverse side effects. We may not have the financial resources to continue development of, or to enter into collaborations for, a product candidate if we experience any problems or other unforeseen events that delay or prevent regulatory approval of, or our ability to commercialize, product candidates, including:

- inability to obtain sufficient funds required for a clinical trial;

- inability to reach agreements on acceptable terms with prospective CROs and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

- negative or inconclusive results from our clinical trials or the clinical trials of others for product candidates similar to ours, leading to a decision or requirement to conduct additional preclinical testing or clinical trials or abandon a program;

- serious and unexpected drug-related side effects experienced by subjects in our clinical trials or by individuals using drugs similar to our product candidates;

- inability to obtain approval from institutional review boards (IRBs), to conduct a clinical trial at their respective sites;

- inability to obtain approval from regulatory authorities outside the United States to conduct a clinical trial in their respective country;

- conditions imposed by the FDA or comparable foreign authorities regarding the scope or design of our clinical trials;

- delays in enrolling research subjects in clinical trials;

- high drop-out rates of research subjects;

- high screen fail rates of research subjects;

- inadequate supply or quality of product candidate components or materials or other supplies necessary for the conduct of our clinical trials;

- greater than anticipated clinical trial costs;

- poor effectiveness of our product candidates during clinical trials;

- unfavorable FDA or other regulatory agency inspection and review of a clinical trial site or vendor;



• failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;

• delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular; or

• varying interpretations of data by the FDA and similar foreign regulatory agencies.

Although the FDA has agreed to our endpoint for approval for the pivotal Phase 3 PIONEER program, other regulatory agencies outside the United States may not agree to our proposed endpoint for approval of Pyridorin for the treatment of diabetic nephropathy in patients with type 2 diabetes, in which case we would need to complete one or more additional clinical trials in order to seek approval outside the United States.

Regulatory authorities in other countries in which we may seek approval for and market Pyridorin may require additional nonclinical studies and/or clinical trials prior to granting approval. It may be expensive and time consuming to conduct and complete additional nonclinical studies and clinical trials that other regulatory authorities may require us to perform. As such, any requirement by other regulatory authorities that we conduct additional nonclinical studies or clinical trials could materially and adversely affect our business, financial condition and results of operations. Furthermore, even if we receive regulatory approval of Pyridorin for the treatment of diabetic nephropathy in patients with type 2 diabetes, the labeling for Pyridorin in the United States, Europe or other countries in which we seek approval may include limitations that could impact the commercial success of Pyridorin. Clinical failure can occur at any stage of clinical development and we have never conducted a Phase 3 trial or submitted a NDA or MAA before. The results of earlier clinical trials are not necessarily predictive of future results and any product candidate we or our potential future collaborators advance through clinical trials may not have favorable results in later clinical trials or receive regulatory approval.

Clinical failure can occur at any stage of our clinical development. Clinical trials may produce negative or inconclusive results, and we or our collaborators may decide, or regulators may require us, to conduct additional clinical trials or nonclinical studies. In addition, data obtained from trials and studies are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may delay, limit or prevent regulatory approval. Success in preclinical studies and early clinical trials does not ensure that subsequent clinical trials will generate the same or similar results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate. A number of companies in the pharmaceutical industry, including those with greater resources and experience than us, have suffered significant setbacks in Phase 3 clinical trials, even after seeing promising results in earlier clinical trials.

Pyridorin did not reach its primary endpoint in the intent to treat (ITT) population in the Phase 2b trial (PYR-210). However, in a prespecified subgroup of patients on stable long term standard of care, Pyridorin showed a dose-dependent treatment effect of approximately 50%. This subgroup is the patient population that will be studied in the Phase 3 program. Subgroup analysis carries the inherent risk that the results may not be repeatable in a subsequent trial. It is possible that the treatment effect observed in this subgroup of PYR-210 may not repeat in our Phase 3 trials.

Pyridorin has demonstrated a promising treatment effect in Phase 2 clinical trials using a rate of change in SCr endpoint. The Phase 3 PIONEER trial is utilizing a new  $\geq 50\%$  SCr increase event endpoint or ESRD. While there is a strong correlation between the rate of change of SCr and the 50% SCr increase event endpoint, no clinical trials have been conducted using this new endpoint. We cannot assure you that our PIONEER Pyridorin program will achieve positive results using this new endpoint.

In addition, the design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well-advanced. We may be unable to design and execute a clinical trial to support regulatory approval. Further, clinical trials of potential products often reveal that it is not practical or feasible to continue development efforts.

If Pyridorin is found to be unsafe or lack efficacy, we will not be able to obtain regulatory approval for it and our business would be harmed. For example, if the results of our Phase 3 Pyridorin program do not achieve the primary





efficacy endpoints or demonstrate expected safety, the prospects for approval of Pyridorin would be materially and adversely affected.

In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in composition of the patient populations, adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. We do not know whether any Phase 2, Phase 3 or other clinical trials we or any of our potential future collaborators may conduct will demonstrate the consistent or adequate efficacy and safety that would be required to obtain regulatory approval and market Pyridorin. If we are unable to bring Pyridorin to market, or to acquire other products that are on the market or can be developed, our ability to create long-term stockholder value will be limited.

Our product candidates may have undesirable side effects which may delay or prevent marketing approval, or, if approval is received, require them to be taken off the market, require them to include safety warnings or otherwise limit their sales.

Pyridorin targets a broad range of pathogenic oxidative chemistries, including advanced glycation end-products, toxic carbonyls, and reactive oxygen species that develop in patients with diabetes and are considered a principal causative factor in the development and progression of diabetic microvascular disease. Unforeseen side effects from any of our product candidates could arise either during clinical development or, if approved, after the approved product has been marketed. The most common side effects observed in clinical trials of Pyridorin were a slight increase in diarrhea and constipation. No patients were withdrawn from the study for these side effects. Additional or unforeseen side effects from these or any of our other product candidates could arise either during clinical development or, if approved, after the approved product has been marketed.

The range and potential severity of possible side effects from systemic therapies is significant. The results of future clinical trials may show that Pyridorin causes undesirable or unacceptable side effects, which could interrupt, delay or halt clinical trials, and result in delay of, or failure to obtain, marketing approval from the FDA and other regulatory authorities, or result in marketing approval from the FDA and other regulatory authorities with restrictive label warnings.

If any of our product candidates receives marketing approval and we or others later identify undesirable or unacceptable side effects caused by such products:

- regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication or field alerts to physicians and pharmacies;

- we may be required to change instructions regarding the way the product is administered, conduct additional clinical trials or change the labeling of the product;

- we may be subject to limitations on how we may promote the product;

- sales of the product may decrease significantly;

- regulatory authorities may require us to take our approved product off the market;

- we may be subject to litigation or product liability claims; and

- our reputation may suffer.

Any of these events could prevent us or our potential future collaborators from achieving or maintaining market acceptance of the affected product or could substantially increase commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenues from the sale of our products.

Reimbursement decisions by third-party payors may have an adverse effect on pricing and market acceptance. If there is not sufficient reimbursement for our products, it is less likely that they will be widely used.

Market acceptance and sales of Pyridorin or any other product candidates that we develop, if approved, will depend on reimbursement policies and may be affected, among other things, by future healthcare reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will cover and establish payment levels. We cannot be certain that reimbursement will be available for

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Pyridorin or any other product candidates that we develop. Also, we cannot be certain that reimbursement policies will not reduce the demand for, or the price paid for, our products. If reimbursement is not available or is available on a limited basis, we may not be able to successfully commercialize Pyridorin or any other product candidates that we develop.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) changed the way Medicare covers and pays for pharmaceutical products. The legislation established Medicare Part D, which expanded Medicare coverage for outpatient prescription drug purchases by the elderly but provided authority for limiting the number of drugs that will be covered in any therapeutic class. The MMA also introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. Any negotiated prices for our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain in the United States. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

The United States and several other jurisdictions are considering, or have already enacted, a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access to healthcare. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. We expect to experience pricing pressures in connection with the sale of Pyridorin and any other products that we develop, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative proposals.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act (collectively, ACA) became law in the United States. The goal of ACA is to reduce the cost of health care and substantially change the way health care is financed by both governmental and private insurers. While we cannot predict what impact on federal reimbursement policies this legislation will have in general or on our business specifically, the ACA may result in downward pressure on pharmaceutical reimbursement, which could negatively affect market acceptance of Pyridorin or any future product candidates. In addition, some members of the U.S. Congress have been seeking to overturn at least portions of the legislation and we expect they will continue to review and assess this legislation and alternative health care reform proposals. We cannot predict whether new proposals will be made or adopted, when they may be adopted or what impact they may have on us if they are adopted.

In the European Union (EU), prescription drug pricing and reimbursement is subject to governmental control and reimbursement mechanisms used by private and public health insurers in the EU vary by member state. For the public systems, reimbursement is determined by guidelines established by the legislator or responsible national authority. As elsewhere, inclusion in reimbursement catalogues focuses on the medical usefulness, need, quality and economic benefits to patients and the health care system. Acceptance for reimbursement comes with cost, use and often volume restrictions, which can vary by member state. In those member states that impose price controls, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some member states, we or our partners may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies.

Some EU member states require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some member states, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we or our partners might obtain marketing approval for a product in a particular member state, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues that are generated from the sale of the product in that country. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, or if there is competition from lower priced cross-border sales, our profitability may be negatively affected.

If we do not obtain protection under the Hatch-Waxman Act and similar legislation outside of the United States by extending the patent terms and obtaining data exclusivity for our product candidates, our business may be materially harmed.

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Depending upon the timing, duration and specifics of FDA marketing approval of Pyridorin and our other product candidates, if any, one or more of our U.S. patents may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially. In the event that we are unable to obtain any patent term extensions, the issued patents for methods of using Pyridorin are expected to expire in June 2024 assuming they withstand any challenge.

If we market products in a manner that violates healthcare fraud and abuse laws, or if we violate government price reporting laws, we may be subject to civil or criminal penalties.

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal healthcare laws, commonly referred to as “fraud and abuse” laws, have been applied in recent years to restrict certain marketing practices in the pharmaceutical industry. Other jurisdictions such as Europe have similar laws. These laws include false claims and anti-kickback statutes. If we market our products and our products are paid for by governmental programs, it is possible that some of our business activities could be subject to challenge under one or more of these laws.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, or causing to be made, a false statement to get a false claim paid. The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service covered by Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers or formulary managers on the other. Although there are several statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Most states also have statutes or regulations similar to the federal anti-kickback law and federal false claims laws, which apply to items and services covered by Medicaid and other state programs, or, in several states, apply regardless of the payor. Administrative, civil and criminal sanctions may be imposed under these federal and state laws.

Over the past few years, a number of pharmaceutical and other healthcare companies have been prosecuted under these laws for a variety of promotional and marketing activities, such as: providing free trips, free goods, sham consulting fees and grants and other monetary benefits to prescribers; reporting inflated average wholesale prices that were then used by federal programs to set reimbursement rates; engaging in off-label promotion; and submitting inflated best price information to the Medicaid Rebate Program to reduce liability for Medicaid rebates. If the FDA and EMA and other regulatory agencies do not find the manufacturing facilities of our future contract manufacturers acceptable for commercial production, we may not be able to commercialize any of our product candidates.

We do not intend to manufacture the pharmaceutical products that we plan to sell. We currently have agreements with and are negotiating additional agreements with contract manufacturers for the production of the active pharmaceutical ingredients and the formulation of drug product for our Phase 3 trial of Pyridorin for the treatment of diabetic nephropathy in patients with type 2 diabetes and the other trials and nonclinical studies that we believe we will need to conduct prior to seeking regulatory approval. However, we do not have agreements for commercial supplies of Pyridorin or any of our other product candidates and we may not be able to reach agreements with these or other contract manufacturers for sufficient supplies to commercialize Pyridorin if it is approved. Additionally, the

facilities used by any contract manufacturer to manufacture Pyridorin or any of our other product candidates must be the subject of a satisfactory inspection before the FDA or the regulators in other jurisdictions approve the product candidate manufactured at that facility. We are completely dependent on these third-party manufacturers for compliance with the

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requirements of U.S. and non-U.S. regulators for the manufacture of our finished products. If our manufacturers cannot successfully manufacture material that conform to our specifications and cGMP and other requirements of any governmental agency whose jurisdiction to which we are subject, our product candidates will not be approved or, if already approved, may be subject to recalls. Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured the product candidates, including:

- the possibility that we are unable to enter into a manufacturing agreement with a third party to manufacture our product candidates;

- the possible breach of the manufacturing agreements by the third parties because of factors beyond our control; and

- the possibility of termination or nonrenewal of the agreements by the third parties before we are able to arrange for a qualified replacement third-party manufacturer.

Any of these factors could cause the delay of approval or commercialization of our product candidates, cause us to incur higher costs or prevent us from commercializing our product candidates successfully. Furthermore, if any of our product candidates are approved and contract manufacturers fail to deliver the required commercial quantities of finished product on a timely basis and at commercially reasonable prices and we are unable to find one or more replacement manufacturers capable of production at a substantially equivalent cost, in substantially equivalent volumes and quality and on a timely basis, we would likely be unable to meet demand for our products and could lose potential revenue. It may take several years to establish an alternative source of supply for our product candidates and to have any such new source approved by the government agencies that regulate our products.

Even if our product candidates receive regulatory approval, we may still face future development and regulatory difficulties.

Our product candidates, if approved, will also be subject to ongoing regulatory requirements for labeling, packaging, storage, advertising, promotion, record-keeping and submission of safety and other post-market information. In addition, approved products, manufacturers and manufacturers' facilities are required to comply with extensive FDA and EMA requirements and requirements of other similar agencies, including ensuring that quality control and manufacturing procedures conform to cGMPs. As such, we and our contract manufacturers are subject to continual review and periodic inspections to assess compliance with cGMPs. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. We will also be required to report certain adverse reactions and production problems, if any, to the FDA and EMA and other similar agencies and to comply with certain requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. Accordingly, we may not promote our approved products, if any, for indications or uses for which they are not approved.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, it may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If our product candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters;

- mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners;

- require us or our potential future collaborators to enter into a consent decree or permanent injunction, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;

- impose other administrative or judicial civil or criminal penalties;





- withdraw regulatory approval;

- refuse to approve pending applications or supplements to approved applications filed by us or our potential future collaborators;

- impose restrictions on operations, including costly new manufacturing requirements; or

- seize or detain products.

#### Risks Relating to the Commercialization of Our Products

Even if approved, our product candidates may not achieve broad market acceptance among physicians, patients and healthcare payors, and as a result our revenues generated from their sales may be limited.

The commercial success of Pyridorin, if approved, will depend upon its acceptance among the medical community, including physicians, health care payors and patients. The degree of market acceptance of Pyridorin or future product candidates will depend on a number of factors, including:

- limitations or warnings contained in our product candidates' FDA-approved labeling;

- changes in the standard of care or availability of alternative therapies at similar or lower costs for the targeted indications for any of our product candidates;

- limitations in the approved clinical indications for our product candidates;

- demonstrated clinical safety and efficacy compared to other products;

- lack of significant adverse side effects;

- sales, marketing and distribution support;

- availability of reimbursement from managed care plans and other third-party payors;

- timing of market introduction and perceived effectiveness of competitive products;

- the degree of cost-effectiveness;

- availability of alternative therapies at similar or lower cost, including generics and over-the-counter products;

- enforcement by the FDA and EMA of laws and rulings that prohibit the sale of pyridoxamine as a dietary supplement;

- the extent to which our product candidates are approved for inclusion on formularies of hospitals and managed care organizations;

- whether our product candidates are designated under physician treatment guidelines for the treatment of the indications for which we have received regulatory approval;

- adverse publicity about our product candidates or favorable publicity about competitive products;

- convenience and ease of administration of our product candidates;

- potential product liability claims; and



countries accepting the EMA and FDA approvals without study conduct in their respective countries or among a patient population representative of their respective country.

If our product candidates are approved, but do not achieve an adequate level of acceptance by physicians, patients, the medical community and healthcare payors, sufficient revenue may not be generated from these products and we may not become or remain profitable. In addition, efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may never be successful. We have no sales, marketing or distribution experience and we will have to invest significant resources to develop those capabilities or enter into acceptable third-party sales and marketing arrangements.

We have no sales, marketing or distribution experience. To develop sales, distribution and marketing capabilities, we will have to invest significant amounts of financial and management resources, some of which will be committed prior to any confirmation that Pyridorin or any of our other product candidates will be approved. For product candidates where we decide to perform sales, marketing and distribution functions ourselves or through third parties, we could face a number of additional risks, including:

- we or our third-party sales collaborators may not be able to attract and build an effective marketing or sales force;

- the cost of securing or establishing a marketing or sales force may exceed the revenues generated by any products; and

- our direct sales and marketing efforts may not be successful.

We may have limited or no control over the sales, marketing and distribution activities of these third parties. Our future revenues may depend heavily on the success of the efforts of these third parties.

We may not be successful in establishing and maintaining development and commercialization collaborations, which could adversely affect our ability to develop certain of our product candidates and our financial condition and operating results.

Because developing pharmaceutical products, conducting clinical trials, obtaining regulatory approval, establishing manufacturing capabilities and marketing approved products are expensive, we may seek to enter into collaborations with companies that have more experience. Additionally, if any of our product candidates receives marketing approval, we may enter into sales and marketing arrangements with third parties with respect to our unlicensed territories. If we are unable to enter into arrangements on acceptable terms, if at all, we may be unable to effectively market and sell our products in our target markets. We expect to face competition in seeking appropriate collaborators. Moreover, collaboration arrangements are complex and time consuming to negotiate, document and implement and they may require substantial resources to maintain. We may not be successful in our efforts to establish and implement collaborations or other alternative arrangements for the development of our product candidates.

When we collaborate with a third party for development and commercialization of a product candidate, we can expect to relinquish some or all of the control over the future success of that product candidate to the third party. For example, we may relinquish the rights to Pyridorin in jurisdictions outside of the United States. Our collaboration partner may not devote sufficient resources to the commercialization of our product candidates or may otherwise fail in their commercialization. The terms of any collaboration or other arrangement that we establish may not be favorable to us. In addition, any collaboration that we enter into may be unsuccessful in the development and commercialization of our product candidates. In some cases, we may be responsible for continuing preclinical and initial clinical development of a product candidate or research program under a collaboration arrangement, and the payment we receive from our collaboration partner may be insufficient to cover the cost of this development. If we are unable to reach agreements with suitable collaborators for our product candidates, we would face increased costs, we may be forced to limit the number of our product candidates we can commercially develop or the territories in which we commercialize them and we might fail to commercialize products or programs for which a suitable collaborator cannot be found. If we fail to achieve successful collaborations, our operating results and financial condition will be materially and adversely affected.



The success of the company depends greatly on the success of Pyridorin's development in diabetic nephropathy, and the company's pipeline of product candidates beyond this lead indication is limited.

We are evaluating the application of an intravenous formulation of Pyridorin to specific types of acute renal injury in which pathogenic oxidative chemistries have been identified as likely causative factors in the onset, severity and progression of this condition. These include ischemia-reperfusion and contrast-dye-induced acute renal injury, which can arise in cardiac and vascular surgeries. However, the intravenous formulation of Pyridorin has never been evaluated in a clinical setting and there is no clinical evidence that the therapy will be effective in additional indications. Moreover, the completion of development, securing of approval and commercialization of an intravenous formulation of Pyridorin for additional indications will require substantial additional funding and is prone to the risks of failure inherent in drug development. We cannot provide you any assurance that we will be able to successfully advance any of these indications through the development process. Even if we receive FDA approval to market an intravenous formulation of Pyridorin for additional indications, we cannot provide assurance that this will be successfully commercialized, widely accepted in the marketplace or more effective than other commercially available alternatives.

If serious adverse events or other undesirable side effects are identified during the development of Pyridorin for one indication, we may need to abandon our development of Pyridorin for other indications.

Product candidates in clinical stages of development have a high risk of failure. We cannot predict when or if Pyridorin will prove effective or safe in humans or will receive regulatory approval. To date, the most common side effects observed in clinical trials of Pyridorin were a slight increase in diarrhea and constipation. New side effects could, however, be identified as we expand the size of our clinical trials and apply Pyridorin to other indications. If new side effects are found during the development of Pyridorin for any indication, if known side effects are shown to be more severe than previously observed or if Pyridorin is found to have other unexpected characteristics, we may need to abandon our development of Pyridorin for kidney disease in patients with type 2 diabetes and other potential indications. Additional or more severe adverse side effects with respect to Pyridorin may develop in future clinical trials, which could delay or preclude regulatory approval of Pyridorin or limit its commercial use.

#### Risks Relating to Our Business and Strategy

We face competition from other biotechnology and pharmaceutical companies and our operating results will suffer if we fail to compete effectively.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We have competitors in the United States, Europe and other jurisdictions, including major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical and generic drug companies and universities and other research institutions. Many of our competitors have greater financial and other resources, such as larger research and development staff and more experienced marketing and manufacturing organizations. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients and manufacturing pharmaceutical products. These companies also have significantly greater research, sales and marketing capabilities and collaborative arrangements in our target markets with leading companies and research institutions. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make the product candidates that we develop obsolete. As a result of all of these factors, our competitors may succeed in obtaining patent protection and/or FDA approval or discovering, developing and commercializing drugs for the diseases that we are targeting before we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Some of the pharmaceutical and biotechnology companies we expect to compete with include AbbVie Inc., Bayer Corporation, Bristol-Meyers Squibb, Thrasos Therapeutics, Inc., Genkyotex S.A., Janssen Pharmaceutical, Inc., Pfizer Inc., Chemocentryx, Inc., Eli Lilly and Company, and Mitsubishi Tanabe Pharma. In addition, many universities and private and public research institutes may become active in our target disease areas. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis, technologies and drug products that are more effective or less costly than Pyridorin or any other product candidates that we are currently developing or that we may develop, which could render our products obsolete and noncompetitive.

We believe that our ability to successfully compete will depend on, among other things:

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- the results of our and our potential strategic collaborators' clinical trials and preclinical studies;
- our ability to recruit and randomize patients for our clinical trials;
- the efficacy, safety and reliability of our product candidates;
- the speed at which we develop our product candidates;
- our ability to design and successfully execute appropriate clinical trials;
- our ability to maintain a good relationship with regulatory authorities;
- the timing and scope of regulatory approvals, if any;
- our ability to commercialize and market any of our product candidates that receive regulatory approval;
- the price of our products;
  - adequate levels of reimbursement under private and governmental health insurance plans, including Medicare;
- our ability to protect intellectual property rights related to our products;
- our ability to manufacture and sell commercial quantities of any approved products to the market; and
  - acceptance of our product candidates by physicians and other health care providers.

If our competitors market products that are more effective, safer or less expensive or that reach the market sooner than our future products, if any, we may not achieve commercial success. In addition, the biopharmaceutical industry is characterized by rapid technological change. Because our research approach integrates many technologies, it may be difficult for us to stay abreast of the rapid changes in each technology. If we fail to stay at the forefront of technological change, we may be unable to compete effectively. Technological advances or products developed by our competitors may render our technologies or product candidates obsolete, less competitive or not economical. We depend on third-party contractors for a substantial portion of our operations and may not be able to control their work as effectively as if we performed these functions ourselves.

We outsource substantial portions of our operations to third-party service providers, including the conduct of preclinical studies and clinical trials, collection and analysis of data, and manufacturing. Our agreements with third-party service providers and CROs are on a study-by-study and project-by-project basis. Typically, we may terminate the agreements with notice and are responsible for the supplier's previously incurred costs. In addition, any CRO that we retain will be subject to the FDA's and EMA's regulatory requirements and similar standards outside of the United States and Europe and we do not have control over compliance with these regulations by these providers. Consequently, if these providers do not adhere to applicable governing practices and standards, the development and commercialization of our product candidates could be delayed or stopped, which could severely harm our business and financial condition.

Because we have relied on third parties, our internal capacity to perform these functions is limited to management oversight. Outsourcing these functions involves the risk that third parties may not perform to our standards, may not produce results in a timely manner or may fail to perform at all. Although we have not experienced any significant difficulties with our third-party contractors, it is possible that we could experience difficulties in the future. In addition, the use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated. There are a limited number of



third-party service providers that specialize or have the expertise required to achieve our business objectives. Identifying, qualifying and managing performance of third-party service providers can be difficult, time consuming and cause delays in our development programs. We currently have a small number of employees, which limits the internal resources we have available to

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identify and monitor third-party service providers. To the extent we are unable to identify, retain and successfully manage the performance of third-party service providers in the future, our business may be adversely affected, and we may be subject to the imposition of civil or criminal penalties if their conduct of clinical trials violates applicable law. A variety of risks associated with our possible international business relationships could materially adversely affect our business.

We may enter into agreements with other third parties for the development and commercialization of Pyridorin or our other product candidates in international markets. International business relationships subject us to additional risks that may materially adversely affect our ability to attain or sustain profitable operations, including:

- differing regulatory requirements for drug approvals internationally;

- potentially reduced protection for intellectual property rights;

- potential third-party patent rights in countries outside of the United States;

- the potential for so-called “parallel importing,” which is what occurs when a local seller, faced with relatively high local prices, opts to import goods from another jurisdiction with relatively low prices, rather than buying them locally;

- unexpected changes in tariffs, trade barriers and regulatory requirements;

- economic weakness, including inflation, or political instability, particularly in non-U.S. economies and markets, including several countries in Europe;

- compliance with tax, employment, immigration and labor laws for employees traveling abroad;

- taxes in other countries;

- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;

- workforce uncertainty in countries where labor unrest is more common than in the United States;

- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and

- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters, including earthquakes, volcanoes, typhoons, floods, hurricanes and fires.

We will need to expand our operations and increase the size of our company, and we may experience difficulties in managing growth.

As of December 7, 2015, we had nine employees. As we increase the number of ongoing product development programs and advance our product candidates through preclinical studies and clinical trials, we will need to increase our product development, scientific and administrative headcount to manage these programs. In addition, to meet our obligations as a public company, we may need to increase our general and administrative capabilities. Our management, personnel and systems currently in place may not be adequate to support this future growth. Our need to effectively manage our operations, growth and various projects requires that we:

- successfully attract and recruit new employees or consultants with the expertise and experience we will require;

- manage our clinical programs effectively, which we anticipate being conducted at numerous clinical sites, among multiple vendors and countries;



develop a marketing and sales infrastructure; and

continue to improve our operational, financial and management controls, reporting systems and procedures.

If we are unable to successfully manage this growth and increased complexity of operations, our business may be adversely affected.

Our recurring losses from operations may raise substantial doubt regarding our ability to continue as a going concern.

Our recurring losses from operations may raise substantial doubt about our ability to continue as a going concern. There is no assurance that sufficient financing will be available when needed to allow us to continue as a going concern. The perception that we may not be able to continue as a going concern may cause others to choose not to deal with us due to concerns about our ability to meet our contractual obligations.

We may not be able to manage our business effectively if we are unable to attract and retain key personnel and consultants.

We may not be able to attract or retain qualified management, finance, scientific and clinical personnel and consultants due to the intense competition for qualified personnel and consultants among biotechnology, pharmaceutical and other businesses. If we are not able to attract and retain necessary personnel and consultants to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the development, regulatory, commercialization and business development expertise of Pierre Legault, our chief executive officer; John P. Hamill, our chief financial officer; and our other key employees and consultants. If we lose one or more of our executive officers or key employees or consultants, our ability to implement our business strategy successfully could be seriously harmed. Any of our executive officers or key employees or consultants may terminate their employment at any time. Replacing executive officers, key employees and consultants may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize products successfully. Competition to hire and retain employees and consultants from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel and consultants. Our failure to retain key personnel or consultants could materially harm our business.

In addition, we have scientific and clinical advisors and consultants who assist us in formulating our research, development and clinical strategies. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us and typically they will not enter into non-compete agreements with us. If a conflict of interest arises between their work for us and their work for another entity, we may lose their services. In addition, our advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours.

We may experience challenges as certain executive roles are being changed.

Dr. J. Wesley Fox is focused on strategy, strategic products, a Scientific Advisory Board, investor relations and other activities. Dr. Jaikrishna Patel serves as our Chief Medical Officer effective as of July 27, 2015. As such, he will have a significant role in our PIONEER clinical trial program. He also focuses on new areas and is taking over the activities recently performed by contractors and consultants.

If either Dr. Fox or Dr. Patel ceases to fulfill his respective new responsibilities, our business, financial condition and results of operations could be materially and adversely affected. Additionally, we cannot provide any assurance

that this transitional period will not result in a disruption that adversely impacts our business and employee morale.

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Failure to continue improving our accounting systems and controls could impair our ability to comply with the financial reporting and internal controls requirements for publicly traded companies.

As a public company, we operate in an increasingly demanding regulatory environment, which requires us to comply with the Sarbanes-Oxley Act of 2002, and the related rules and regulations of the SEC, expanded disclosure requirements, accelerated reporting requirements and more complex accounting rules. Company responsibilities required by the Sarbanes-Oxley Act include establishing corporate oversight and adequate internal control over financial reporting and disclosure controls and procedures. Effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent financial fraud.

We have implemented a system of internal controls over financial reporting and preparing the documentation necessary to perform the evaluation needed to comply with Section 404(a) of the Sarbanes-Oxley Act. We may need to retain additional finance capabilities and build our financial infrastructure as a public company, including complying with the requirements of Section 404 of the Sarbanes-Oxley Act. We plan to continue improving our financial infrastructure with the enhancement of internal controls and additional training for our financial and accounting staff.

Section 404(a) of the Sarbanes-Oxley Act requires annual management assessments of the effectiveness of our internal control over financial reporting, starting with the second annual report that we would expect to file with the SEC. However, for as long as we remain an “emerging growth company” as defined in the JOBS Act, we have and intend to continue to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not “emerging growth companies” including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act. We may continue to take advantage of these reporting exemptions until we are no longer an “emerging growth company.” We will remain an “emerging growth company” until the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of \$1 billion or more; (ii) December 31, 2019; (iii) the date on which we have issued more than \$1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

If we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be harmed and investors could lose confidence in our reported financial information.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading, which could significantly harm our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with the regulations of the FDA and non-U.S. regulators, provide accurate information to the FDA and non-U.S. regulators, comply with health care fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of conduct, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

We face potential product liability exposure, and if successful claims are brought against us, we may incur substantial liability for a product candidate and may have to limit its commercialization.

The use of our product candidates in clinical trials and the sale of any products for which we may obtain marketing approval expose us to the risk of product liability claims. Product liability claims may be brought against us or our potential future collaborators by participants enrolled in our clinical trials, patients, health care providers or others using, administering or selling our products. If we cannot successfully defend ourselves against any such

claims, we would incur substantial liabilities. Regardless of merit or eventual outcome, product liability claims may result in:

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- withdrawal of clinical trial participants;
- termination of clinical trial sites or entire trial programs;
- costs of related litigation;
- substantial monetary awards to patients or other claimants;
- decreased demand for our product candidates and loss of revenues;
- impairment of our business reputation;
- diversion of management and scientific resources from our business operations; and
- the inability to commercialize our product candidates.

We currently maintain products liability insurance (\$20 million coverage) which covers our clinical trials liability. Our insurance coverage may not reimburse us or may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to product liability. We intend to expand our insurance coverage for products to include the sale of commercial products if we obtain marketing approval for our product candidates in development, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us, particularly if judgments exceed our insurance coverage, could decrease our cash resources and adversely affect our business.

We purchase commercially available insurance at limits suggested by our insurance broker based on our business operations. Our insurance policies do not cover all of our business exposures thus leaving us exposed to significant uninsured liabilities.

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability (\$2 million coverage), umbrella liability (\$2 million coverage), employment practices liability, property, auto, workers' compensation, and directors' and officers' insurance. We currently maintain products liability insurance (\$20 million coverage) which covers our clinical trials liability. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our financial position and results of operations.

If we engage in an acquisition, reorganization or business combination, we will incur a variety of risks that could adversely affect our business operations or our stockholders.

From time to time we have considered, and we will continue to consider in the future, strategic business initiatives intended to further the expansion and development of our business. These initiatives may include acquiring businesses, technologies or products or entering into a business combination with another company. If we pursue such a strategy, we could, among other things:

- issue equity securities that would dilute our current stockholders' percentage ownership;
- incur substantial debt that may place strains on our operations;
- spend substantial operational, financial and management resources to integrate new businesses, technologies and products;
- assume substantial actual or contingent liabilities;

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reprioritize our development programs and even cease development and commercialization of our product candidates;  
or

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merge with, or otherwise enter into a business combination with, another company in which our stockholders would receive cash and/or shares of the other company on terms that certain of our stockholders may not deem desirable.

Although we intend to evaluate and consider acquisitions, reorganizations and business combinations in the future, we have no agreements or understandings with respect to any acquisition, reorganization or business combination at this time.

#### Risks Relating to Our Intellectual Property

It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection. If our patent position does not adequately protect our product candidates, others could compete against us more directly, which would harm our business, possibly materially.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection of our current and future product candidates and the methods used to develop and manufacture them, as well as successfully defending these patents against third-party challenges. Our ability to stop third parties from making, using, selling, offering to sell or importing our products depends on the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our product candidates, discovery programs and processes.

The patent positions of biotechnology and pharmaceutical companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved.

No consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the United States or in many jurisdictions outside of the United States. Changes in either the patent laws or interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be enforced in the patents that may be issued from the applications we currently or, may in the future, own or license from third parties. Further, if any patents we obtain or license are deemed invalid and unenforceable, our ability to commercialize or license our technology could be adversely affected.

In the future others may file patent applications covering products and technologies that are similar, identical or competitive to ours or important to our business. We cannot be certain that any patent application owned by a third party will not have priority over patent applications filed or in-licensed by us, or that we or our licensors will not be involved in interference, opposition or invalidity proceedings before U.S. or non-U.S. patent offices.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

• others may be able to develop a platform similar to, or better than, ours in a way that is not covered by the claims of our patents;

• others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of our patents;

• we might not have been the first to make the inventions covered by our pending patent applications;

• we might not have been the first to file patent applications for these inventions;

• others may independently develop similar or alternative technologies or duplicate any of our technologies;

• any patents that we obtain may not provide us with any competitive advantages;



we may not develop additional proprietary technologies that are patentable; or

the patents of others may have an adverse effect on our business.

As of December 7, 2015, we were the owner of record or the licensee of 26 issued or granted U.S. and non-U.S. patents relating to Pyridorin™ with claims directed to methods of making Pyridorin™, and methods of using Pyridorin™ in various indications. We were also the owner of record or licensee of 4 pending U.S. and non-U.S. patent applications relating to Pyridorin™ in these areas. In addition, as of December 7, 2015, we were the owner of record of 2 issued US patents and 2 pending U.S. and non-U.S. applications relating to our product candidates other than Pyridorin™, with claims directed to pharmaceutical compounds, pharmaceutical compositions and methods of using these compounds in various indications.

Patents covering methods of using Pyridorin expire in 2024 if the appropriate maintenance fee renewal, annuity, or other government fees are paid, unless a patent term extension based on regulatory delay is obtained. We expect that expiration in 2016 of some of our method-of-use patents, or their foreign equivalents, covering use of Pyridorin for treating diabetic nephropathy will have a limited impact on our ability to protect our intellectual property in the United States, Europe, and Canada, where we have additional issued patents covering this use that extend until 2024. In other countries, our patent protection covering use of Pyridorin for treating diabetic nephropathy will expire in 2016. We will attempt to mitigate the effect of patent expiration by seeking data exclusivity, or the foreign equivalent thereof, in conjunction with product approval, as well as by filing additional patent applications covering improvements in our intellectual property.

We expect that the other patents and patent applications for the Pyridorin portfolio, if issued, and if the appropriate maintenance, renewal, annuity or other governmental fees are paid, would expire from 2016 to 2035. We own pending applications in the United States and Europe covering Pyridorin analogs, and uses of such analogs as therapeutics to treat a variety of disorders, including kidney disorders such as nephropathy. Patent protection, to the extent it issues, would be expected to extend to 2027, unless a patent term extension based on regulatory delay is obtained.

Due to the patent laws of a country, or the decisions of a patent examiner in a country, or our own filing strategies, we may not obtain patent coverage for all of our product candidates or methods involving these candidates in the parent patent application. We plan to pursue divisional patent applications or continuation patent applications in the United States and other countries to obtain claim coverage for inventions which were disclosed but not claimed in the parent patent application.

We may also rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or feasible. However, trade secrets are difficult to protect. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our information to competitors. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. Pyridorin does not have composition of matter patent protection.

Although we own and exclusively license patents and patent applications with claims directed to the methods of use of Pyridorin (pyridoxamine) to treat diabetic nephropathy and other conditions, and methods for its synthesis, we are unaware of any composition of matter patent protection for Pyridorin in the United States or elsewhere. As a result, competitors may be able to offer and sell products including pyridoxamine so long as these competitors do not infringe any other patents that we or third parties hold, including synthesis and method of use patents. However, method of use patents, in particular, are more difficult to enforce than composition of matter patents because of the risk of off-label sale or use of the subject compounds. Physicians are permitted to prescribe an approved product for uses that are not described in the product's labeling. Although off-label prescriptions may infringe our method of use patents, the practice is common across medical specialties and such infringement is difficult to prevent or prosecute. Off-label sales would limit our ability to generate revenue from the sale of Pyridorin, if approved for commercial sale.

In addition, other third parties have obtained patents in the United States and elsewhere relating to methods of use of pyridoxamine for the treatment of certain diseases. As a result, it is possible that we could face competition

from third party products that have pyridoxamine as the active pharmaceutical ingredient. If a third party were to obtain FDA

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approval in the United States for the use of pyridoxamine, or regulatory approval in another jurisdiction, for an indication before we did, such third party would be first to market and could establish the price for pyridoxamine in these jurisdictions. This could adversely impact our ability to implement our pricing strategy for the product and may limit our ability to maximize the commercial potential of Pyridorin in the United States and elsewhere. The presence of a lower priced competitive product with the same active pharmaceutical ingredients as our product could lead to use of the competitive product for our diabetic nephropathy indication. This could lead to pricing pressure for Pyridorin, which would adversely affect our ability to generate revenue from the sale of Pyridorin for treating diabetic nephropathy. This would also limit the length of data exclusivity and patent term extension available if we later obtain approval to market Pyridorin for treating diabetic nephropathy.

We may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights.

If we choose to go to court to stop another party from using the inventions claimed in any patents we obtain, that individual or company has the right to ask the court to rule that such patents are invalid or should not be enforced against that third party. These lawsuits are expensive and would consume time and resources and divert the attention of managerial and scientific personnel even if we were successful in stopping the infringement of such patents. In addition, there is a risk that the court will decide that such patents are not valid and that we do not have the right to stop the other party from using the inventions. There is also the risk that, even if the validity of such patents is upheld, the court will refuse to stop the other party on the ground that such other party's activities do not infringe our rights to such patents. In addition, in recent years the U.S. Supreme Court modified some tests used by the U.S. Patent and Trademark Office (USPTO) in granting patents over the past 20 years, which may decrease the likelihood that we will be able to obtain patents and increase the likelihood of challenge of any patents we obtain or license.

We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing our product candidates.

Our success will depend in part on our ability to operate without infringing the proprietary rights of third parties. We cannot guarantee that our products, or manufacture or use of our product candidates, will not infringe third-party patents. Furthermore, a third party may claim that we or our manufacturing or commercialization collaborators are using inventions covered by the third party's patent rights and may go to court to stop us from engaging in our normal operations and activities, including making or selling our product candidates. These lawsuits are costly and could affect our results of operations and divert the attention of managerial and scientific personnel. There is a risk that a court would decide that we or our commercialization collaborators are infringing the third party's patents and would order us or our collaborators to stop the activities covered by the patents. In that event, we or our commercialization collaborators may not have a viable way around the patent and may need to halt commercialization of the relevant product. In addition, there is a risk that a court will order us or our collaborators to pay the other party damages for having violated the other party's patents. In the future, we may agree to indemnify our commercial collaborators against certain intellectual property infringement claims brought by third parties. The pharmaceutical and biotechnology industries have produced a proliferation of patents, and it is not always clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid, and we may not be able to do this. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and divert management's time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, which may not be available, defend an infringement action or challenge the validity of the patents in court. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, develop or obtain non-infringing technology, fail to defend an infringement action successfully or have infringed patents declared invalid, we may incur substantial monetary damages, encounter significant delays in bringing our product candidates to market and be precluded from manufacturing or selling our product candidates.

We cannot be certain that others have not filed patent applications for technology covered by our pending applications, or that we were the first to invent the technology, because:

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some patent applications in the United States may be maintained in secrecy until the patents are issued;

patent applications in the United States are typically not published until 18 months after the priority date; and

publications in the scientific literature often lag behind actual discoveries.

Our competitors may have filed, and may in the future file, patent applications covering technology similar to ours. Any such patent application may have priority over our patent applications, which could further require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application on inventions similar to ours, we may have to participate in an interference proceeding declared by the USPTO to determine priority of invention in the United States. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful if, unbeknownst to us, the other party had independently arrived at the same or similar invention prior to our own invention, resulting in a loss of our U.S. patent position with respect to such inventions. Other countries have similar laws that permit secrecy of patent applications, and may be entitled to priority over our applications in such jurisdictions.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We employ an outside firm and rely on our outside counsel to pay these fees due to non-U.S. patent agencies and this outside firm has systems in place to ensure compliance on payment of fees. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers. If we are not able to adequately prevent disclosure of trade secrets and other proprietary information, the value of our technology and products could be significantly diminished.

As is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees, or we, have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

We rely on trade secrets to protect our proprietary technologies, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to protect our trade secrets and other proprietary information. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's



disclosure policies may change in the future, if at all.

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Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position. Failure to secure trademark registrations could adversely affect our business.

If we seek to register additional trademarks, our trademark applications may not be allowed for registration or our registered trademarks may not be maintained or enforced. During trademark registration proceedings, we may receive rejections. Although we are given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many other jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we do not secure registrations for our trademarks, we may encounter more difficulty in enforcing them against third parties than we otherwise would.

If the FDA, EMA or other regulatory agencies fail to monitor and enforce the illegal sale of pyridoxamine as a dietary supplement, the commercial success of Pyridorin may be limited.

Following the publication of the initial Phase 2 studies that evaluated pyridoxamine therapy in diabetic nephropathy patients, a number of dietary supplement companies began selling pyridoxamine over the internet. In January 2009, the FDA ruled that pyridoxamine is an investigational drug candidate not eligible for sale as a dietary supplement. A significant decline in product availability occurred after the issuance of the above mentioned FDA ruling. However, approximately 5 sites on the internet can be found that continue to illegally sell pyridoxamine. In at least one example, the FDA has taken action against a dietary supplement company and prohibited such company from selling an FDA approved active drug ingredient in a dietary supplement. However, there is no guarantee that the FDA will take action against other companies that illegally sell pyridoxamine after its approval. Food and dietary supplements in Europe are regulated by Directive 2002/46/EC, European Commission, Health and Consumers Directorate-General. Those approved are listed in Annex I and II of Directive 2002/46/EC. Pyridoxamine is not included on either list, and therefore the sale of pyridoxamine in foods and supplements in Europe is not permitted. The European Commission, Health and Consumers Directorate-General has indicated to us in April of this year that no applications for pyridoxamine have been received and that any new product intended for preventing, curing or treating diseases, would fall under the scope of medicinal products and not dietary supplements products. We are not aware of any direct action that this agency has taken against a company illegally selling an EMA approved drug for preventing, curing or treating disease, in the European Union. It is possible that this agency would not be successful in prohibiting such sales. We will rely on the FDA, EMA and other regulatory agencies to enforce laws and rulings that prohibit the illegal sale of pyridoxamine as a dietary supplement. If these agencies fail to enforce such laws and rulings, the commercial success of Pyridorin may be limited.

#### Risks Relating to Owning Our Common Stock

The trading market in our common stock has been extremely limited and substantially less liquid than the average trading market for a stock quoted on the NASDAQ Capital Market.

Since our initial listing on the NASDAQ Capital Market on February 11, 2014, the trading market in our common stock has been limited. The quotation of our common stock on the NASDAQ Capital Market does not assure that a meaningful, consistent and liquid trading market currently exists. We cannot predict whether a more active market for our common stock will develop in the future. An absence of an active trading market could adversely affect our stockholders' ability to sell our common stock at current market prices in short time periods, or possibly at all. Additionally, market visibility for our common stock may be limited and such lack of visibility may have a depressive effect on the market price for our common stock. As of December 7, 2015, 51.2% of our outstanding shares of common stock were held by our officers, directors, beneficial owners of 5% or more of our securities and their respective affiliates, which adversely affects the liquidity of the trading market for our common stock, in as much as federal securities laws restrict sales of our shares by these stockholders. If our affiliates continue to hold their shares of common stock, there will be limited trading volume in our common stock, which may make it more difficult for investors to sell their shares or increase the volatility of our stock price.

Our share price may be volatile, which could subject us to securities class action litigation and result in substantial losses to our stockholders.



The trading price of our common stock is highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. Our stock price is likely to remain volatile. The stock market in general and the market for pharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their common stock at or above the price at which it was purchased. The market price for our common stock may be influenced by many factors, including:

• results of our clinical trials;

• results of clinical trials of our competitors' products;

• regulatory actions with respect to our products or our competitors' products;

• actual or anticipated fluctuations in our financial condition and operating results;

• actual or anticipated changes in our growth rate relative to our competitors;

• actual or anticipated fluctuations in our competitors' operating results or changes in their growth rate;

• competition from existing products or new products that may emerge;

• announcements by us, our potential future collaborators or our competitors of significant acquisitions, strategic collaborations, joint ventures, or capital commitments;

• issuance of new or updated research or reports by securities analysts;

• fluctuations in the valuation of companies perceived by investors to be comparable to us;

• share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;

• additions or departures of key management or scientific personnel;

• disputes or other developments related to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;

• announcement or expectation of additional financing efforts;

• sales of our common stock by us, our insiders or our other stockholders;

• market conditions for biopharmaceutical stocks in general; and

• general economic and market conditions.

Furthermore, the stock markets have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many companies. These fluctuations often have been unrelated or disproportionate to the operating performance of those companies. These broad market and industry fluctuations, as well as general economic, political and market conditions such as recessions, interest rate changes or international currency fluctuations, may negatively impact the market price of shares of our common stock, regardless of our actual operating performance. In addition, such fluctuations could subject us to securities class action litigation, which could result in substantial costs and divert our management's attention from other business concerns, which

could seriously harm our business. As a result of this volatility, our stockholders could incur substantial losses. We have a significant stockholder, which will limit your ability to influence corporate matters and may give rise to conflicts of interest.

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Care Capital III LLC, together with its affiliates (collectively, Care Capital) is our largest stockholder. As of December 7, 2015, Care Capital beneficially owned 4,241,097 shares of our common stock. The shares of common stock beneficially owned by Care Capital represent approximately 32.8% of our outstanding shares of common stock. Accordingly, Care Capital exerts significant influence over us and any action requiring the approval of the holders of our common stock, including the election of directors and approval of significant corporate transactions. This concentration of voting power makes it less likely that any other holder of common stock or directors of our business will be able to affect the way we are managed and could delay or prevent an acquisition of us on terms that other stockholders may desire. In addition, if Care Capital obtains a majority of our common stock, Care Capital would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, Care Capital would be able to control the election of directors, amendments to our organizational documents and approval of any merger, consolidation, sale of all or substantially all of our assets or other business combination or reorganization. In addition, if Care Capital obtains a majority of our common stock, we would be deemed a “controlled company” for purposes of NASDAQ listing requirements. Under NASDAQ rules, a “controlled company” may elect not to comply with certain NASDAQ corporate governance requirements, including (i) the requirement that a majority of our board of directors consist of independent directors, (ii) the requirement that the compensation of our officers be determined or recommended to the board by a majority of independent directors or a compensation committee that is composed entirely of independent directors, and (iii) the requirement that director nominees be selected or recommended to the board by a majority of independent directors or a nominating committee that is composed of entirely independent directors.

Furthermore, the interests of Care Capital may not always coincide with your interests or the interests of other stockholders and Care Capital may act in a manner that advances its best interests and not necessarily those of other stockholders, including seeking a premium value for its common stock, and might affect the prevailing market price for our common stock. Our board of directors, which currently consists of six directors, including two designated by Care Capital, has the power to set the number of directors on our board from time to time. Richard J. Markham and Robert R. Seltzer, partners at Care Capital, are members of our board of directors and some of its committees. Being a public company has increased our expenses and administrative burden.

As a public company, we are incurring, and will continue to incur significant legal, insurance, accounting and other expenses. In addition, we are required to bear all of the internal and external costs of preparing and distributing periodic public reports in compliance with our obligations under the securities laws.

In addition, laws, regulations and standards applicable to public companies relating to corporate governance and public disclosure, including the Sarbanes-Oxley Act and related regulations implemented by the SEC and the NASDAQ Stock Market, are creating uncertainty for public companies, increasing legal and financial compliance costs and making some activities more time consuming. These laws, regulations and standards are subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment will result in increased general and administrative expenses and may divert management’s time and attention from product development activities. If our efforts to comply with new laws, regulations and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to practice, regulatory authorities may initiate legal proceedings against us and our business may be harmed. In connection with our initial public offering, we increased our directors’ and officers’ insurance coverage, which increased our insurance cost. In the future, it will be more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. These factors could also make it more difficult for us to attract and retain qualified members of our board of directors, particularly to serve on our audit committee and compensation committee, and qualified executive officers.

We are an “emerging growth company” and we will continue to avail ourselves of the reduced disclosure requirements applicable to emerging growth companies, which could make our common stock less attractive to investors.

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012 (the JOBS Act) and we have and intend to continue to take advantage of certain exemptions from various reporting requirements

that are applicable to other public companies that are not “emerging growth companies” including not being required

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to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. We cannot predict if investors will find our common stock less attractive because we have and may continue to rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

We may take advantage of these reporting exemptions until we are no longer an “emerging growth company.” We will remain an “emerging growth company” until the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of \$1 billion or more; (ii) December 31, 2019; (iii) the date on which we have issued more than \$1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

If we fail to maintain an effective system of internal control over financial reporting in the future, we may not be able to accurately report our financial condition, results of operations or cash flows, which may adversely affect investor confidence in us and, as a result, the value of our common stock.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. Commencing with our annual report on Form 10-K for the year ending December 31, 2015, we will be required, under Section 404 of the Sarbanes-Oxley Act, to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting. This assessment will need to include disclosure of any material weaknesses identified by our management in our internal control over financial reporting. A material weakness is a control deficiency, or combination of control deficiencies, in internal control over financial reporting that results in more than a reasonable possibility that a material misstatement of annual or interim financial statements will not be prevented or detected on a timely basis. Section 404 of the Sarbanes-Oxley Act also generally requires an attestation from our independent registered public accounting firm on the effectiveness of our internal control over financial reporting. However, for as long as we remain an emerging growth company, as defined in the JOBS Act, we intend to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies including, but not limited to, not being required to comply with the independent registered public accounting firm’s requirement to attest to the effectiveness of our internal controls over financial reporting.

Our compliance with Section 404 will require that we incur substantial accounting expense and expend significant management efforts. We currently do not have an internal audit group, and we will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge, and compile the system and process documentation necessary to perform the evaluation needed to comply with Section 404. We may not be able to complete our evaluation, testing and any required remediation in a timely fashion. During the evaluation and testing process, if we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to assert that our internal control over financial reporting is effective. We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting once that firm begins its Section 404 reviews, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by the NASDAQ, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets. Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to the periodic reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized



and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures

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or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosure due to error or fraud may occur and not be detected.

Future sales of our common stock, or the perception that future sales may occur, may cause the market price of our common stock to decline, even if our business is doing well.

Sales of substantial amounts of our common stock, or the perception that these sales may occur, could materially and adversely affect the price of our common stock and could impair our ability to raise capital through the sale of additional equity securities.

We had outstanding 12,946,018 shares of common stock as of December 7, 2015, 4,254,097 of which are restricted securities that may be sold only in accordance with the resale restrictions under Rule 144 of the Securities Act of 1933, as amended. In addition, as of December 7, 2015, we had outstanding options to purchase 1,592,133 shares of our common stock, 891,617 shares of common stock were issuable upon the settlement of outstanding restricted stock units and we had outstanding warrants to purchase 10,039,682 shares of our common stock. Shares issued upon the exercise of stock options or upon the settlement of outstanding restricted stock units generally will be eligible for sale in the public market, except that affiliates will continue to be subject to volume limitations and other requirements of Rule 144 under the Securities Act. The issuance or sale of such shares could depress the market price of our common stock.

In the future, we also may issue our securities if we need to raise additional capital. The number of new shares of our common stock issued in connection with raising additional capital could constitute a material portion of the then-outstanding shares of our common stock. We are unable to predict the effect that transactions on our stock may have on the prevailing market price of our common stock.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

The trading market for our common stock will depend on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. There can be no assurance that analysts will continue to cover us or provide favorable coverage. If one or more of the analysts who cover us downgrade our stock or change their opinion of our stock, our share price would likely decline. If one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

NASDAQ may delist our securities from its exchange, which could limit investors' ability to make transactions in our securities and subject us to additional trading restrictions.

If we fail to maintain the listing of our common stock on the NASDAQ Capital Market, the liquidity for our common stock would be significantly impaired, which may substantially decrease the trading price of our common stock. We cannot assure you that, in the future, our securities will meet the continued listing requirements to be listed on NASDAQ. If NASDAQ delists our common stock from trading on its exchange, we could face significant material adverse consequences, including:

- limited availability of market quotations for our securities;

a determination that our common stock is a "penny stock" which will require brokers trading in our common stock to adhere to more stringent rules and possibly resulting in a reduced level of trading activity in the secondary trading market for our common stock;

- limited amount of news and analyst coverage for our company; and

- decreased ability to issue additional securities or obtain additional financing in the future.

If our shares become subject to the penny stock rules, it would become more difficult to trade our shares.



The SEC has adopted rules that regulate broker-dealer practices in connection with transactions in penny stocks. Penny stocks are generally equity securities with a price of less than \$5.00, other than securities registered on certain national securities exchanges or authorized for quotation on certain automated quotation systems, provided that current price and volume information with respect to transactions in such securities is provided by the exchange or system. If we do not obtain or retain a listing on The NASDAQ Capital Market and if the price of our common stock is less than \$5.00, our common stock will be deemed a penny stock. The penny stock rules require a broker-dealer, before a transaction in a penny stock not otherwise exempt from those rules, to deliver a standardized risk disclosure document containing specified information. In addition, the penny stock rules require that before effecting any transaction in a penny stock not otherwise exempt from those rules, a broker-dealer must make a special written determination that the penny stock is a suitable investment for the purchaser and receive (i) the purchaser's written acknowledgment of the receipt of a risk disclosure statement; (ii) a written agreement to transactions involving penny stocks; and (iii) a signed and dated copy of a written suitability statement. These disclosure requirements may have the effect of reducing the trading activity in the secondary market for our common stock, and therefore stockholders may have difficulty selling their shares.

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our restated certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders. These provisions include:

- authorizing the issuance of "blank check" convertible preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;

- limiting the removal of directors by the stockholders;

- creating a staggered board of directors;

- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;

- eliminating the ability of stockholders to call a special meeting of stockholders;

- permitting our board of directors to accelerate the vesting of outstanding equity awards upon certain transactions that result in a change of control; and

- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

These provisions may also frustrate or prevent any attempts by our stockholders to replace or remove our current management or members of our board of directors. In addition, we are subject to Section 203 of the Delaware General Corporation Law (DGCL), which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with an interested stockholder for a period of three years following the date on which the stockholder became an interested stockholder, unless such transactions are approved by our board of directors. This provision could have the effect of delaying or preventing a change of control, whether or not it is desired by or beneficial to our stockholders. Further, other provisions of Delaware law may also discourage, delay or prevent someone from acquiring us or merging with us.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful stockholder claims against us and may reduce the amount of money available to us.

As permitted by Section 102(b)(7) of the DGCL, our restated certificate of incorporation limits the liability of our directors to the fullest extent permitted by law. In addition, as permitted by Section 145 of the DGCL, our restated certificate of incorporation and restated bylaws provide that we shall indemnify, to the fullest extent authorized by the

DGCL, each person who is involved in any litigation or other proceeding because such person is or was a director or

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officer of our company or is or was serving as an officer or director of another entity at our request, against all expense, loss or liability reasonably incurred or suffered in connection therewith. Our restated certificate of incorporation provides that the right to indemnification includes the right to be paid expenses incurred in defending any proceeding in advance of its final disposition, provided, however, that such advance payment will only be made upon delivery to us of an undertaking, by or on behalf of the director or officer, to repay all amounts so advanced if it is ultimately determined that such director is not entitled to indemnification. If we do not pay a proper claim for indemnification in full within 60 days after we receive a written claim for such indemnification, except in the case of a claim for an advancement of expenses, in which case such period is 20 days, our restated certificate of incorporation and our restated bylaws authorize the claimant to bring an action against us and prescribe what constitutes a defense to such action.

Section 145 of the DGCL permits a corporation to indemnify any director or officer of the corporation against expenses (including attorney's fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with any action, suit or proceeding brought by reason of the fact that such person is or was a director or officer of the corporation, if such person acted in good faith and in a manner that he reasonably believed to be in, or not opposed to, the best interests of the corporation, and, with respect to any criminal action or proceeding, if he or she had no reason to believe his or her conduct was unlawful. In a derivative action, (i.e., one brought by or on behalf of the corporation), indemnification may be provided only for expenses actually and reasonably incurred by any director or officer in connection with the defense or settlement of such an action or suit if such person acted in good faith and in a manner that he or she reasonably believed to be in, or not opposed to, the best interests of the corporation, except that no indemnification shall be provided if such person shall have been adjudged to be liable to the corporation, unless and only to the extent that the court in which the action or suit was brought shall determine that the defendant is fairly and reasonably entitled to indemnity for such expenses despite such adjudication of liability.

The rights conferred in the restated certificate of incorporation and the restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons. We have entered into or plan to enter into indemnification agreements with each of our officers and directors.

The above limitations on liability and our indemnification obligations limit the personal liability of our directors and officers for monetary damages for breach of their fiduciary duty as directors by shifting the burden of such losses and expenses to us. Although we have increased the coverage under our directors' and officers' liability insurance, certain liabilities or expenses covered by our indemnification obligations may not be covered by such insurance or the coverage limitation amounts may be exceeded. As a result, we may need to use a significant amount of our funds to satisfy our indemnification obligations, which could severely harm our business and financial condition and limit the funds available to stockholders who may choose to bring a claim against our company.

We do not anticipate paying cash dividends, and accordingly, stockholders must rely on stock appreciation for any return on their investment.

We do not anticipate paying cash dividends in the future. As a result, only appreciation of the market price of our common stock, which may never occur, will provide a return to stockholders. Investors seeking cash dividends should not invest in our common stock.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

As of December 31, 2014, we had federal net operating loss carryforwards (NOLs) of \$31.8 million million which expire from 2024 through 2034. Our ability to utilize our NOLs may be limited under Section 382 of the Internal Revenue Code. The limitations apply if an ownership change, as defined by Section 382, occurs. Generally, an ownership change occurs when certain shareholders increase their aggregate ownership by more than 50 percentage points over their lowest ownership percentage in a testing period (typically three years). Although we have not undergone a Section 382 analysis, it is possible that the utilization of the NOLs, could be substantially limited. Additionally, U.S. tax laws limit the time during which these carryforwards may be utilized against future taxes. As a result, we may not be able to take full advantage of these carryforwards for federal and state tax purposes. Future changes in stock ownership may also trigger an ownership change and, consequently, a Section 382 limitation.



#### CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus and those documents incorporated by reference in the prospectus contain forward-looking statements. All statements other than statements of historical facts contained in this prospectus and in the documents incorporated by reference in this prospectus, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

The words “anticipate,” “believe,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “target,” “will,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, among other things, statements about:

- our ability to obtain additional financing;
- our ability to borrow under our credit facility;
- our limited operating history and our recurring losses from operations;
- the success and timing of our preclinical studies and clinical trials;
- our ability to obtain and maintain regulatory approval of Pyridorin and any other product candidates we may develop, and the labeling under any approval we may obtain;
- regulatory developments in the United States and other countries;
- the performance of third-party manufacturers;
- our plans to develop and commercialize our product candidates;
- our ability to obtain and maintain intellectual property protection for our product candidates;
- the successful development of our sales and marketing capabilities;
- the potential markets for our product candidates and our ability to serve those markets;
- competition from other biotechnology and pharmaceutical companies;
- the rate and degree of market acceptance of any future products;
- the success of competing drugs that are or become available; and
- the loss of key scientific or management personnel.

These forward-looking statements are only predictions and we may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, so you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our business, financial condition and operating results. We have included important factors in the cautionary statements included in this prospectus, particularly in the “Risk Factors” section, that could cause actual future results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the



potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

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The forward-looking statements in this prospectus represent our views as of the date of this prospectus. We anticipate that subsequent events and developments will cause our views to change.

However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this prospectus.

This prospectus contains estimates made, and other statistical data published, by independent parties and by us relating to market size and growth and other data about our industry. We obtained the industry and market data in this prospectus from our own research as well as from industry and general publications, surveys and studies conducted by third parties. This data involves a number of assumptions and limitations and contains projections and estimates of the future performance of the industries in which we operate that are subject to a high degree of uncertainty. We caution you not to give undue weight to such projections, assumptions and estimates.

#### USE OF PROCEEDS

If all of the warrants to purchase the 1,725,000 shares of our common stock are exercised for cash, the total amount of proceeds that we would receive is approximately \$10.8 million. We would expect to use the proceeds from the exercise of the warrants, if any, for our working capital and general corporate purposes. The amounts and timing of our actual use of net proceeds will vary depending on numerous factors, including our ability to obtain additional financing, the relative success and cost of our research, preclinical and clinical development programs. As a result, management will have broad discretion in the application of the net proceeds, and investors will be relying on our judgment regarding the application of the net proceeds of this offering. In addition, we might decide to postpone or not pursue other clinical trials or preclinical activities if the net proceeds from this offering and the other sources of cash are less than expected.

**DILUTION**

Purchasers of the securities offered by this prospectus will suffer immediate and substantial dilution in the net tangible book value per share of the common stock they purchase through the exercise of warrants. Our net tangible book value as of September 30, 2015 was approximately \$1.06 per share of our common stock. We calculate net tangible book value per share by dividing our net tangible book value, which is tangible assets less total liabilities, by the number of outstanding shares of our common stock as of September 30, 2015.

Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers in this offering and the net tangible book value per share of our common stock immediately after this offering. After giving effect to the sale of the 1,725,000 shares of common stock upon exercise of all of the warrants covered by this prospectus at the warrant exercise price of \$6.25 per share, our as adjusted net tangible book value as of September 30, 2015 would have been approximately \$1.78 per share of common stock. This represents an immediate increase in net tangible book value of \$0.72 share of common stock to our existing stockholders and an immediate dilution in net tangible book value of \$4.47 per share of common stock to purchasers in this offering. The following table illustrates this per share dilution:

Public offering price per share		\$6.25
Net tangible book value per share as of September 30, 2015	\$1.06	
Increase per share attributable to this offering	0.72	
As adjusted net tangible book value per share as of September 30, 2015 after this offering		1.78
Dilution per share to investors participating in this offering		\$4.47

The number of shares of common stock to be outstanding after this offering as shown above is based on 10,742,387 shares outstanding as of September 30, 2015 and excludes:

- 1,442,500 shares of our common stock issuable upon the exercise of stock options, with a weighted average exercise price of \$4.46 per share;

- 12,500 shares of our common stock issuable upon the settlement of outstanding restricted stock units;

- 118,603 shares of our common stock issuable upon the exercise of outstanding warrants, with a weighted average exercise price of \$9.86 per share; and

- other shares of our common stock reserved for future issuance under our Amended and Restated 2007 Equity Incentive Plan, as amended.

To the extent that any other options or warrants are exercised, new options are issued under our equity incentive plan, or we otherwise issue additional shares of common stock in the future, at a price less than the warrant exercise price in this offering, there will be further dilution to new investors.

PLAN OF DISTRIBUTION

We will deliver shares of our common stock upon exercise of the warrants we issued in July 2015. As of the date of this prospectus, these warrants were exercisable for a total of 1,725,000 shares of our common stock, and no more of these warrants will be issued. We will not issue fractional shares upon exercise of these warrants. Each of these warrants contains instructions for exercise. In order to exercise any of these warrants, the holder must deliver to us or our transfer agent the information required in the warrants, along with payment of the exercise price for the shares to be purchased. We will then deliver shares of our common stock in the manner described below in the section titled “Description of Securities – July 2015 Warrants.”

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## DESCRIPTION OF SECURITIES WE ARE OFFERING

We are presently authorized to issue 100,000,000 shares of common stock, \$0.001 par value per share, and 5,000,000 shares of preferred stock, \$0.001 par value per share. As of the date of this prospectus, we had 12,946,018 shares of common stock issued and outstanding and no shares of preferred stock issued and outstanding.

### Common Stock

Holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders, and do not have cumulative voting rights. Subject to preferences that may be applicable to any outstanding shares of preferred stock, holders of common stock are entitled to receive ratably such dividends, if any, as may be declared from time to time by our board of directors out of funds legally available for dividend payments. All outstanding shares of common stock are fully paid and nonassessable, and the shares of common stock to be issued upon completion of this offering will be fully paid and nonassessable. The holders of common stock have no preferences or rights of conversion, exchange, pre-emptive or other subscription rights. There are no redemption or sinking fund provisions applicable to the common stock. In the event of any liquidation, dissolution or winding-up of our affairs, holders of common stock will be entitled to share ratably in any of our assets remaining after payment or provision for payment of all of our debts and obligations and after liquidation payments to holders of outstanding shares of preferred stock, if any.

### July 2015 Warrants

The following summary description of the material features of the warrants that we issued in July 2015 is necessarily general and is qualified in its entirety by reference to the form of warrant, a copy of which has been filed with the SEC as an exhibit to the registration statement of which this prospectus is a part. See “Where You Can Find More Information.”

**Form.** The warrants have been issued as individual warrant agreements to the investors. You should review a copy of the form of warrant, which is filed as an exhibit to the registration statement of which this prospectus forms a part, for a complete description of the terms and conditions applicable to the warrants.

**Exercisability.** The warrants are exercisable at any time after their original issuance, July 22, 2015, and at any time up to the date that is five years after their original issuance. The warrants are exercisable, at the option of each holder, in whole or in part by delivering to us a duly executed exercise notice and, at any time a registration statement registering the issuance of the shares of common stock underlying the warrants under the Securities Act is effective and available for the issuance of such shares, or an exemption from registration under the Securities Act is available for the issuance of such shares, by payment in full in immediately available funds for the number of shares of common stock purchased upon such exercise. If a registration statement registering the issuance of the shares of common stock underlying the warrants under the Securities Act is not effective or available and an exemption from registration under the Securities Act is not available for the issuance of such shares, the holder may, in its sole discretion, elect to exercise the warrant through a cashless exercise, in which case the holder would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the warrant. No fractional shares of common stock will be issued in connection with the exercise of a warrant. In lieu of fractional shares, we will pay the holder an amount in cash equal to the fractional amount multiplied by the exercise price.

**Exercise Limitation.** A holder does not have the right to exercise any portion of the warrant if the holder (together with its affiliates) would beneficially own in excess of 4.99% of the number of shares of our common stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the warrants. However, any holder may increase or decrease such percentage to any other percentage not in excess of 9.99% upon at least 61 days' prior notice from the holder to us.

**Exercise Price.** The exercise price per whole share of common stock purchasable upon exercise of the warrants is \$6.25 per share of common stock. The exercise price is subject to appropriate adjustment in the event of

certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common stock and also upon any distributions of assets, including cash, stock or other property to our stockholders.

**Transferability.** Subject to applicable laws, the warrants may be offered for sale, sold, transferred or assigned without our consent.

**Exchange Listing.** We do not plan on applying to list the warrants on The NASDAQ Capital Market, any other national securities exchange or any other nationally recognized trading system.

**Fundamental Transactions.** In the event of a fundamental transaction, as described in the warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common stock, or any person or group becoming the beneficial owner of 50% of the voting power represented by our outstanding common stock, the holders of the warrants will be entitled to receive upon exercise of the warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the warrants immediately prior to such fundamental transaction.

**Rights as a Stockholder.** Except as otherwise provided in the warrants or by virtue of such holder's ownership of shares of our common stock, the holder of a warrant does not have the rights or privileges of a holder of our common stock, including any voting rights, until the holder exercises the warrant.

#### Preferred Stock

Our preferred stock, if issued, would have priority over our common stock with respect to dividends and other distributions, including the distribution of assets upon liquidation. Our board of directors has the authority, without further stockholder authorization, to issue from time to time shares of preferred stock in one or more series and to fix the terms, limitations, relative rights and preferences and variations of each series. Although we have no present plans to issue any shares of preferred stock, the issuance of shares.

#### Shares Eligible For Future Sale

Prior to our initial public offering in February 2014, there was no public market for our common stock and a liquid trading market for our common stock may not develop or be sustained after this offering. Future sales of substantial amounts of our common stock in the public market, including shares issued upon exercise of outstanding options and warrants, or the anticipation of these sales, could adversely affect prevailing market prices from time to time and could impair our ability to raise equity capital in the future.

As of the date of this prospectus, we had 12,946,018 shares of common stock issued and outstanding. Of those shares, all of the shares sold in this offering and all 3,100,000 shares sold in our initial public offering will be freely tradable, except that any shares held by our "affiliates," as that term is defined in Rule 144 under the Securities Act, or Rule 144, may only be sold in compliance with the limitations described below.

#### Rule 144

In general, under Rule 144, any person who is not our affiliate and has held their shares for at least six months, including the holding period of any prior owner other than one of our affiliates, may sell shares without restriction, subject to the availability of current public information about us. In addition, under Rule 144, any person who is not an affiliate of ours and has held their shares for at least one year, including the holding period of any prior owner other than one of our affiliates, would be entitled to sell an unlimited number of shares without regard to whether current public information about us is available.

Sales under Rule 144 by our affiliates are also subject to manner of sale provisions and notice requirements, and to the availability of current public information about us.

#### Rule 701

In general, under Rule 701 of the Securities Act, any of our stockholders who purchased shares from us in connection with a qualified compensatory stock plan or other written agreement before we became subject to the reporting requirements of Section 13 or 15(d) of the Exchange Act is eligible to resell those shares in reliance on Rule 144. An affiliate of the issuer can resell shares in reliance on Rule 144 without having to comply with the holding



period requirements of Rule 144, and a non-affiliate of the issuer can resell shares in reliance on Rule 144 without having to comply with the holding period requirements of Rule 144 and without regard to the volume of such sales or the availability of public information about the issuer.

As of December 7, 2015, options to purchase a total of 1,592,133 shares of common stock were outstanding, of which 731,617 were vested and 891,617 shares of common stock are issuable upon the settlement of outstanding restricted stock units. In addition, there were 10,039,682 shares of our common stock that underlie outstanding warrants. Of the total number of shares of our common stock issuable under these options, substantially all are subject to contractual lock-up agreements with the underwriters described below, and will become eligible for sale at the expiration of those agreements unless held by an affiliate of ours.

In addition to the shares of common stock issuable upon exercise of warrants covered by this prospectus, another 2,529,353 shares of our common stock issuable upon exercise of other currently exercisable options, restricted stock units or warrants are eligible to be sold pursuant to currently effective registration statements.

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

The provisions of Delaware law and our restated certificate of incorporation and restated bylaws could discourage or make it more difficult to accomplish a proxy contest or other change in our management or the acquisition of control by a holder of a substantial amount of our voting stock. It is possible that these provisions could make it more difficult to accomplish, or could deter, transactions that stockholders may otherwise consider to be in their best interests or in our best interests. These provisions are intended to enhance the likelihood of continuity and stability in the composition of our board of directors and in the policies formulated by the board of directors and to discourage certain types of transactions that may involve an actual or threatened change of our control. These provisions are designed to reduce our vulnerability to an unsolicited acquisition proposal and to discourage certain tactics that may be used in proxy fights. Such provisions also may have the effect of preventing changes in our management.

**Delaware Statutory Business Combinations Provision.** We are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law. Section 203 prohibits a publicly-held Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. For purposes of Section 203, a “business combination” is defined broadly to include a merger, asset sale or other transaction resulting in a financial benefit to the interested stockholder, and, subject to certain exceptions, an “interested stockholder” is a person who, together with his or her affiliates and associates, owns, or within three years prior, did own, 15% or more of the corporation’s voting stock.

**Classified Board of Directors; Removal of Directors for Cause.** Our restated certificate of incorporation and restated bylaws provide that, our board of directors is divided into three classes. Each year the stockholders will elect the members of one of the three classes to a three-year term of office. All directors elected to our classified board of directors will serve until the election and qualification of their respective successors or their earlier resignation or removal. The board of directors is authorized to create new directorships and to fill such positions so created and is permitted to specify the class to which any such new position is assigned. The person filling such position would serve for the term applicable to that class. The board of directors, or its remaining members, even if less than a quorum, is also empowered to fill vacancies on the board of directors occurring for any reason for the remainder of the term of the class of directors in which the vacancy occurred. Members of the board of directors may only be removed for cause and only by the affirmative vote of at least 80% of our outstanding voting stock. These provisions are likely to increase the time required for stockholders to change the composition of the board of directors. For example, at least two annual meetings will be necessary for stockholders to effect a change in a majority of the members of the board of directors.

**Advance Notice Provisions for Stockholder Proposals and Stockholder Nominations of Directors.** Our restated bylaws provide that, for nominations to the board of directors or for other business to be properly brought by a stockholder before a meeting of stockholders, the stockholder must first have given timely notice of the proposal in writing to our Secretary. For an annual meeting, a stockholder’s notice generally must be delivered not less than 90 days nor more than 120 days prior to the anniversary of the mailing date of the proxy statement for the previous



year's annual meeting. For a special meeting, the notice must generally be delivered not earlier than the 90th day prior to the meeting and not later than the later of (1) the 60th day prior to the meeting or (2) the 10th day following the day on which public

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announcement of the meeting is first made. Detailed requirements as to the form of the notice and information required in the notice are specified in the restated bylaws. If it is determined that business was not properly brought before a meeting in accordance with our bylaw provisions, such business will not be conducted at the meeting.

**Special Meetings of Stockholders.** Special meetings of the stockholders may be called only by our board of directors pursuant to a resolution adopted by a majority of the total number of directors.

**No Stockholder Action by Written Consent.** Any action to be effected by our stockholders must be effected at a duly called annual or special meeting of the stockholders.

**Super Majority Stockholder Vote Required for Certain Actions.** The Delaware General Corporation Law provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or by-laws, unless the corporation's certificate of incorporation or by-laws, as the case may be, requires a greater percentage. Our restated certificate of incorporation requires the affirmative vote of the holders of at least 80% of our outstanding voting stock to amend or repeal any of the provisions discussed in this section of this prospectus entitled "Anti-Takeover Effects of Delaware Law and Our Restated Certificate of Incorporation and Restated Bylaws," or to reduce the number of authorized shares of common stock or preferred stock. This 80% stockholder vote would be in addition to any separate class vote that might in the future be required pursuant to the terms of any preferred stock that might then be outstanding. An 80% vote is also required for any amendment to, or repeal of, our restated bylaws by the stockholders. Our restated bylaws may be amended or repealed by a simple majority vote of the board of directors.

**Blank-Check Preferred Stock.** Our board of directors will be authorized to issue, without stockholder approval, preferred stock, the rights of which will be determined at the discretion of the board of directors and that, if issued, could operate as a "poison pill" to dilute the stock ownership of a potential hostile acquirer to prevent an acquisition that our board of directors does not approve.

**Transfer Agent and Registrar**

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

**Stock Market Listing**

Our common stock is listed on the NASDAQ Capital Market under the symbol "NRX."

## LEGAL MATTERS

The validity of the shares of the common stock and warrants offered by this prospectus will be passed upon for us by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., New York, New York. Legal matters in connection with this offering were passed upon for the underwriters in the July 2015 public offering by Reed Smith LLP, New York, New York.

## EXPERTS

The balance sheets of NephroGenex, Inc. as of December 31, 2014 and 2013, and the related statements of comprehensive loss, stockholders' equity (deficit), and cash flows for each of the years then ended have been audited by EisnerAmper LLP, independent registered public accounting firm, as stated in their report which is incorporated herein by reference. Such financial statements have been incorporated herein by reference in reliance on the report of such firm given upon their authority as experts in accounting and auditing.

## WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock underlying the warrants being offered by this prospectus. This prospectus does not contain all of the information in the registration statement and its exhibits. For further information with respect to us and the common stock offered by this prospectus, we refer you to the registration statement and its exhibits. Statements contained in this prospectus as to the contents of any contract or any other document referred to are not necessarily complete, and in each instance, we refer you to the copy of the contract or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference.

You can read our SEC filings, including the registration statement, over the Internet at the SEC's website at [www.sec.gov](http://www.sec.gov). You may also read and copy any document we file with the SEC at its public reference facilities at 100 F Street NE, Washington, D.C. 20549. You may also obtain copies of these documents at prescribed rates by writing to the Public Reference Section of the SEC at 100 F Street N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference facilities.

We are subject to the information and periodic reporting requirements of the Exchange Act, and we file periodic reports, proxy statements and other information with the SEC. These periodic reports, proxy statements and other information are available for inspection and copying at the public reference room and website of the SEC referred to above. We maintain a website at <http://www.nephrogenex.com>. You may access our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act with the SEC free of charge at our website as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not incorporated by reference in, and is not part of, this prospectus.

## INCORPORATION OF INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" into this prospectus the information we have filed with the SEC. The information we incorporate by reference into this prospectus is an important part of this prospectus. Any statement in a document we incorporate by reference into this prospectus will be considered to be modified or superseded to the extent a statement contained in this prospectus or any other subsequently filed document that is

incorporated by reference into this prospectus modifies or supersedes that statement. The modified or superseded statement will not be considered to be a part of this prospectus, except as modified or superseded.

We incorporate by reference into this prospectus the information contained in the documents listed below, which is considered to be a part of this prospectus:

Our Annual Report on Form 10-K for the year ended December 31, 2014 filed with the SEC on March 24, 2015;

Our Quarterly Reports on Form 10-Q for the quarter ended March 31, 2015 filed on May 13, 2015, for the quarter ended June 30, 2015 filed on August 12, 2015 and for the quarter ended September 30, 2015 filed on November 12, 2015;

Our Current Reports on Form 8-K filed on January 7, 2015, February 5, 2015, May 1, 2015, July 22, 2015, July 27, 2015, August 6, 2015, August 7, 2015, November 9, 2015 and November 13, 2015;

the description of our common stock contained in our Registration Statement on Form 8-A, filed on February 6, 2014, pursuant to Section 12(b) of the Exchange Act, which incorporates by reference the description of the shares of our common stock contained in our Registration Statement on Form S-1, as amended (File No. 333-193023) filed on December 23, 2013 and declared effective by the SEC on February 11, 2014, and any amendment or report filed with the SEC for purposes of updating such description.

We also incorporate by reference into this prospectus all documents filed pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus and prior to the termination of the offering; provided, however, that we are not incorporating any information furnished under Item 2.02 or Item 7.01 of any Current Report on Form 8-K we may subsequently file.

You may request, orally or in writing, a copy of any or all of the documents incorporated herein by reference. These documents will be provided to you at no cost, by contacting: Secretary, John P. Hamill, NephroGenex, Inc., 3200 Beechleaf Court, Suite 900, Raleigh, North Carolina, 27604 or call (609) 986-1780.

Copies of these documents are also available, without charge, through the "Investors & Media" section of our website ([www.nephrogenex.com](http://www.nephrogenex.com)) as soon as reasonably practicable after they are filed with the SEC. The information contained on our website is not a part of this prospectus.

## PART II – INFORMATION NOT REQUIRED IN PROSPECTUS

## ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION

We estimate that expenses in connection with the distribution (including the July 2015 public offering) described in this registration statement (other than brokerage commissions, discounts or other expenses relating to the sale of the shares by the selling stockholders) will be as set forth below. We will pay all of the expenses with respect to the distribution, and such amounts, with the exception of the Securities and Exchange Commission registration fee, are estimates.

SEC registration fee	\$1,879.17	
FINRA filing fee	5,675.00	
Printing and Engraving fees	85,000.00	
Accounting fees and expenses	57,500.00	*
Legal fees and expenses	282,500.00	*
Transfer Agent fees	6,500.00	
Miscellaneous	20,945.83	
Total	\$460,000.00	

\* Includes \$7,500 of expenses related solely to the post-effective amendments.

## ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS

Our certificate of incorporation provides that we shall indemnify, to the fullest extent authorized by the Delaware General Corporation Law, each person who is involved in any litigation or other proceeding because such person is or was a director or officer of NephroGenex, Inc. or is or was serving as an officer or director of another entity at our request, against all expense, loss or liability reasonably incurred or suffered in connection therewith. Our certificate of incorporation provides that the right to indemnification includes the right to be paid expenses incurred in defending any proceeding in advance of its final disposition, provided, however, that such advance payment will only be made upon delivery to us of an undertaking, by or on behalf of the director or officer, to repay all amounts so advanced if it is ultimately determined that such director is not entitled to indemnification. If we do not pay a proper claim for indemnification in full within 60 days after we receive a written claim for such indemnification, the certificate of incorporation and our bylaws authorize the claimant to bring an action against us and prescribe what constitutes a defense to such action.

Section 145 of the Delaware General Corporation Law permits a corporation to indemnify any director or officer of the corporation against expenses (including attorney's fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with any action, suit or proceeding brought by reason of the fact that such person is or was a director or officer of the corporation, if such person acted in good faith and in a manner that he reasonably believed to be in, or not opposed to, the best interests of the corporation, and, with respect to any criminal action or proceeding, if he or she had no reason to believe his or her conduct was unlawful. In a derivative action, (i.e., one brought by or on behalf of the corporation), indemnification may be provided only for expenses actually and reasonably incurred by any director or officer in connection with the defense or settlement of such an action or suit if such person acted in good faith and in a manner that he or she reasonably believed to be in, or not opposed to, the best interests of the corporation, except that no indemnification shall be provided if such person shall have been adjudged to be liable to the corporation, unless and only to the extent that the court in which the action or suit was brought shall determine that the defendant is fairly and reasonably entitled to indemnity for such expenses despite such adjudication of liability.



Pursuant to Section 102(b)(7) of the Delaware General Corporation Law, our certificate of incorporation eliminates the liability of a director to us or our stockholders for monetary damages for such a breach of fiduciary duty as a director, except for liabilities arising:

from any breach of the director's duty of loyalty to us or our stockholders;

from acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law;

under Section 174 of the Delaware General Corporation Law; and

from any transaction from which the director derived an improper personal benefit.

We carry insurance policies insuring our directors and officers against certain liabilities that they may incur in their capacity as directors and officers.

#### ITEM 16. EXHIBITS

The Exhibit Index that follows the signature page of this registration statement lists the exhibits that are filed with this registration statement, and such Exhibit Index is incorporated herein by reference.

#### ITEM 17. UNDERTAKINGS

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers or persons controlling the registrant pursuant to the foregoing provisions, the registrant has been informed 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 Securities 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.

The undersigned registrant hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus 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, the Registrant has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in City of Raleigh, State of North Carolina, on December 7, 2015.

NEPHROGENEX, INC.

By: /s/ Pierre Legault  
 Pierre Legault  
 Chief Executive Officer

Pursuant to the requirements of the Securities Act, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
/s/ PIERRE LEGAULT Pierre Legault	Chief Executive Officer, President and Director (Principal Executive Officer)	December 7, 2015
/s/ JOHN P. HAMILL John P. Hamill	Chief Financial Officer (Principal Financial and Accounting Officer)	December 7, 2015
* Richard Markham	Director	December 7, 2015
* James Mitchum	Director	December 7, 2015
* Robert R. Seltzer	Director	December 7, 2015
* Eugene Steiner, M.D., PhD.	Director	December 7, 2015
* Marco Taglietti, M.D.	Director	December 7, 2015

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\*Pursuant to Power of Attorney

By: /s/ Pierre Legault  
 Pierre Legault

EXHIBIT INDEX

Exhibit Number	Description of Exhibit
1.1	Form of Underwriting Agreement (incorporated by reference to Exhibit 1.1 of the Registrant's Registration Statement on Form S-1 (File No. 333-203530), as amended, filed with the SEC on July 16, 2015).
3.1	Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 of the Registrant's Current Report on Form 8-K, filed with the SEC on February 14, 2014)
3.2	Restated Bylaws (incorporated by reference to Exhibit 3.2 of the Registrant's Current Report on Form 8-K, filed with the SEC on February 14, 2014).
4.1	Form of Common Stock Certificate (incorporated by reference to Exhibit 4.1 of the Registrant's Registration Statement on Form S-1 (File No. 333-193023), as amended, filed with the SEC on January 10, 2014).
4.2	Form of Representative's Warrant (incorporated by reference to Exhibit 4.2 of the Registrant's Registration Statement on Form S-1 (File No. 333-193023), as amended, filed with the SEC on January 29, 2014)
4.3	Form of Warrants issued to the lenders under the Loan and Security Agreement, dated as of November 20, 2014, by and among NephroGenex, Inc. and East West Bank (incorporated by reference to Exhibit 10.3 to the Registrant's Current Report on Form 8-K, filed with the SEC on November 20, 2014)
4.4	Amended and Restated Investors' Rights Agreement, dated February 28, 2008, as amended February 14, 2014 (incorporated by reference to Exhibit 4.3 of the Registrant's annual report on Form 10-K, filed with the SEC on March 31, 2014).
4.5	Form of Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.1 of the Registrant's Current Report on Form 8-K, filed with the SEC on July 22, 2015).
5.1	Opinion of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., counsel to the Registrant, with respect to the legality of securities being registered (incorporated by reference to Exhibit 5.1 of the Registrant's registration statement on Form S-1/A, filed with the SEC on July 16, 2015).
23.1	Consent of EisnerAmper LLP, independent registered public accounting firm.
23.2	Consent of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. (incorporated by reference to Exhibit 5.1 of the Registrant's registration statement on Form S-1/A, filed with the SEC on July 16, 2015).
24.1	Power of Attorney (included on the signature page to the initial filing).