NephroGenex, Inc.
Form 10-K
March 31, 2014

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

ý **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2013

OR

o **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to
Commission file number: 001-36303

NephroGenex, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**20-1295171**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
79 T.W. Alexander Drive 4401 Research Commons Building Suite 290 P.O. Box 14188 Research Triangle Park, NC	**27709** (Zip Code)
(Address of principal executive offices)	

(609) 986-1780
Registrant's telephone number, including area code

Securities registered pursuant to Section 12(b) of the Exchange Act:

Title of each class	**Name of each exchange on which registered**
Common Stock, $0.001 Par Value Per Share	NASDAQ Capital Market

Securities registered pursuant to Section 12(g) of the Exchange Act: **None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes o No ý

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes o No ý

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ý No o

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes o No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. o

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 o	Accelerated filer o	Non-accelerated filer o [Do not check if a smaller reporting company]	Smaller reporting company ý

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes o No ý

The aggregate market value of the registrant's voting and non-voting common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) computed by reference to the price at which the common stock was last sold as of March 17, 2014 was $25,182,571. The registrant has provided this information as of March 17, 2014 because its common stock was not publicly traded as of the last business day of its most recently completed second fiscal quarter.

As of March 17, 2014, the registrant had 8,855,114 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

The following documents (or parts thereof) are incorporated by reference into the following parts of this Form 10-K: Certain information required in Part III of this Annual Report on Form 10-K is incorporated from the Registrant's Proxy Statement for the Annual Meeting of Stockholders to be held on May 15, 2014.

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Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements. All statements other than statements of historical facts contained in this Annual Report on Form 10-K, 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," "should," "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 use of net proceeds from our recently completed initial public offering;
- the accuracy of our estimates regarding expenses, future revenues and capital requirements;
- 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;
- 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 Annual Report on Form 10-K, particularly in Item 1.A. Risk Factors, 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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You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to the Annual Report on Form 10-K with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements whether as a result of new information, future events or otherwise, except as required by applicable law.

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PART I

All brand names or trademarks appearing in this report are the property of their respective holders. Unless the context requires otherwise, references in this report to "NephroGenex," the "Company," "we," "us," and "our" refer to NephroGenex, Inc.

Item 1. BUSINESS

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. 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. In addition, we worked with the FDA to establish a new regulatory pathway for Pyridorin approval.

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 will be further developed in a Phase 3 program agreed to by the U.S. Food and Drug Administration (FDA) under a Special Protocol Assessment (SPA). This Phase 3 program will use a novel endpoint based on 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 the Phase 3 program compared to the traditional endpoint used in previous pivotal trials for diabetic nephropathy. The traditional renal endpoint used in previous pivotal trials for diabetic nephropathy is a 100% increase in SCr from baseline or 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 will be the first company to use this novel endpoint in a Phase 3 trial.

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We are also studying the application of an intravenous formulation of Pyridorin to 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.

Corporate Objectives

There is a large medical need and market opportunity for treatments that can (1) slow the progression of renal disease and thus delay or avoid the onset of end stage renal disease (ESRD); or (2) reduce the severity of acute kidney injury and its associated potential treatment costs and long term complications.

Our principal corporate objective is the maximization of shareholder value by advancing Pyridorin through Phase 3 development and approval. In order to maximize the market potential of Pyridorin, we intend to consider entering into a partnership for the launch and marketing of the product at the end of Phase 3 or possibly earlier, based on interim clinical data. We also intend to consider acquisitions and the development of other clinical candidates as we see appropriate.

We acquired commercial rights to Pyridorin in 2007 and, since then, have been investigating the safety and efficacy of Pyridorin therapy for diseases in which pathogenic oxidative chemistries are an established and/or causative and contributing factor in kidney disease. These include diabetic nephropathy and acute kidney injury.

We anticipate seeking corporate partners to aid us in commercialization and market entry.

Our Strategy

There is a large medical need and market opportunity for treatments that can (1) slow the progression of renal disease and thus delay or prevent the onset of end stage renal disease (ESRD); or (2) reduce the severity of acute kidney injury and potentially its associated treatment costs and long term complications.

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:

- 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;
- maximizing the value of our Pyridorin franchise by expanding into additional indications; and
- deploying capital strategically to develop our portfolio of product candidates and create shareholder value.

Rationale for Development of Pyridorin

Diabetic microvascular complications arise in tissues that are not under direct insulin control and are thus exposed to elevated levels of glucose in hyperglycemic conditions. This exposure leads to a perturbation or deviation of many metabolic pathways and the emergence of non-enzymatic oxidative chemistries that form pathogenic reactive compounds including: (1) reactive oxygen species; (2) reactive carbonyl intermediates (which are reactive compounds containing a carbonyl function group that can

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react with biomolecules and modify their function, a process collectively referred to as carbonyl stress); and (3) glycated protein amino groups and their subsequent advanced glycation end-products (AGEs).

One pathway of particular interest is the post-Amadori pathway of AGE formation. The study of this pathway led to the discovery of Pyridorin as a promising drug candidate for diabetic nephropathy. Our founding scientists first isolated protein-Amadori intermediates and utilized them to search for compounds that could specifically block the degradation of protein-Amadori intermediates into AGEs. They examined many previously studied AGE inhibitors in this screening assay, including aminoguanidine (pimagedine). The majority of such AGE inhibitors, including aminoguanidine (Graph 2), did not exhibit inhibitory activity towards formation of the AGE carboxymethlylysine (CML) under these conditions. However, Pyridorin uniquely exhibited potent post-Amadori inhibitory activity (Graph 1). Due to the possible importance of this AGE pathway, this inhibitory activity may form the basis for the activity of Pyridorin in inhibiting the progression of diabetic nephropathy, as evidenced in nonclinical studies and as summarized below.

Chronic hyperglycemia is directly associated with end-organ damage in patients with diabetes. The major target organs affected, namely the kidney, peripheral nerves, retina, and the vasculature, are all exposed to glucose fluctuations since they are not under insulin regulation. This hyperglycemia damage may be initiated by direct chemical reaction of glucose (an aldehyde) with protein amino groups, leading to the formation of harmful products collectively designated as AGEs. It has been established that circulating and tissue levels of AGEs are elevated in patients with poorly controlled diabetes and

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increase dramatically when the glomerular filtration rate (GFR) declines. GFR is the calculation of the flow rate of filtered fluid through the glomerulus that determines how well the kidney is filtering the blood.

In extensive in-vitro studies, Pyridorin has been shown to inhibit AGE formation and scavenge ROS and toxic carbonyl compounds. For example, Pyridorin has been shown to:

- inhibit the degradation of glycated proteins to AGEs;
- inhibit lipoxidation (lipid oxidation) by trapping lipoxidation intermediates, (reactive lipid compounds that form during the oxidation of lipids that normally proceed to lipid oxidation end-products), particularly 1,4-dicarbonyls;
- scavenge glycoaldehyde and dicarbonyls intermediates of carbonyl stress such as glyoxal and methylglyoxal;
- trap the hydroxyl radical (which is a highly reactive and short-lived neutral form of the hydroxide ion (HO-); and
- bind redox transition metal ions (such as Cu2+, Mn2+, and Fe 2+),which interfere with their catalytic role in oxidative reactions (redox chemical reactions are common physiological chemical reactions involving the transfer of electrons).

All of the above processes and reactive compounds have been implicated directly or indirectly in the development of diabetic microvascular disease, the basis of diabetic complications.

Pyridorin Targets Specific
Pathogenic Oxidative Chemistries

The above graphic is for illustrative purposes only.

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Preclinical Efficacy Results

The ability of Pyridorin to slow the progression of diabetic nephropathy in animals has been examined in several preventative and interventional preclinical studies. These include a "proof-of-principle" rat model of AGE-albumin induced nephropathy (Khalifah, et al, J. Am. Soc. Nephrol. 1997 Sep; 8:641A), an STZ-treated rat classical model of type 1 diabetic nephropathy (Degenhardt, et al, Kidney Int. 2002; 61:939-950), a db/db mouse spontaneous model of type 2 diabetic nephropathy Zheng, et al, Kidney Int. 2006; 70: 507-514), the Zucker fa/fa rat model of non-diabetic, hyperlipidemic nephropathy (Alderson, et al, Kidney Int. 2003; 63:2123-2133), and the type 2 diabetic KK-Ay/Ta mouse (Tanimoto, et al, Metabolism. 56:160-7, 2007).

In the first model, AGE-modified rat serum albumin (RSA), which is the most abundant protein in rat blood plasma, was injected daily for 6 weeks into normoglycemic rats to mimic damage from circulating AGE-modified plasma proteins. These normoglycemic rats were given daily tail vein injections of AGE-modified RSA at 50 mg/kg/day with and without concomitant treatment with 25 mg/kg/day Pyridorin in the drinking water. Another AGE inhibitor, aminoguanidine (pimagedine) was also evaluated in this model for comparative purposes. At the time of this study, aminoguanidine was being developed by Alteon for the treatment of diabetic nephropathy. Previous studies have demonstrated that such daily injections of AGE-modified RSA induce pathological changes in the kidney consistent with the onset of diabetic nephropathy. As expected, overt nephropathy did not develop during this short-term study. However, statistically significant early diabetic-like morphological changes were observed in the glomerulus, such as an increase in glomerular volume, an increase in albumin deposition (Graph 3), and a decrease in heparin sulfate, a component of the kidney anionic filtration barrier (Graph 4).

Treatment with Pyridorin protected the animals from the damaging effects of AGE-albumin with regard to all three parameters mentioned above. All of the results were statistically significant when compared to untreated animals. Treatment with similar amounts of aminoguanidine did not lead to significant amelioration except for a partial reduction in albumin deposition.

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Results from an STZ-treated rat model of type 1 diabetic nephropathy are shown in Graphs 5 and 6 below. Pyridorin inhibited the development of albuminuria compared to untreated animals ($p = 0.0001$ at 27 weeks). It also inhibited the increase in plasma creatinine levels compared to untreated animals ($p = 0.0001$ at 28 weeks). Increases in albuminuria and plasma creatinine levels are indications of decreasing kidney function. Additionally, at equal doses, Pyridorin exhibited an improvement over aminoguanidine in preventing increases in plasma creatinine ($p = 0.021$ at 28 weeks) and albuminuria.

In addition to these results on kidney function, this study demonstrated that Pyridorin significantly inhibited AGE formation in skin collagen, as measured by standard methods of quantifying AGE levels (i.e. pepsin digestibility, AGE fluorescence, and carboxymethyllysine AGE content).

In a second STZ study similar in design to the above, treatment with Pyridorin at 1 g/L drinking water was compared to treatment with the ACE inhibitor enalapril (the standard of care treatment for diabetic nephropathy) dosed at 50 mg/L drinking water (Alderson, et al, Diabetologia 2004; 47:1385-1395). At 28 weeks, Pyridorin significantly inhibited the development of albuminuria relative to both untreated diabetic controls (43 mg/24 hr versus 12mg/24 hr) and diabetic animals treated with enalapril (26 mg/24 hr versus 12 mg/24 hr). The differences were statistically significant. Pyridorin also significantly reduced the increases in plasma creatinine relative to both untreated diabetic controls (110 µmol/L versus 45 µmol/L) and diabetic animals treated with enalapril (70 µmol/L versus 45 µmol/L). The differences were statistically significant.

Pyridorin has also been evaluated in a standard model of type 2 diabetic nephropathy. The db/db mouse is a commonly used mouse model of type 2 diabetes and develops histologic changes in the kidney which are very similar to those observed in humans with diabetic nephropathy. The study was designed to evaluate the effects of Pyridorin in established diabetic nephropathy. In mice with biopsy-proven diabetic nephropathy, Pyridorin orally administered at 250 mg/kg/day for 2 months resulted in a 43% reduction in the urinary albumin/creatinine ratio. In contrast, the placebo group albumin/creatinine ratio increased 215% ($p<0.05$). The ACE inhibitor treated group increased 40%.

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Microscopic lesions of glomerulosclerosis in the kidney were also reduced in the Pyridorin group when compared with control animals ($p<0.05$).

A second db/db mouse study of 16-week treatment duration was conducted to assess the combination of Pyridorin plus the ACE inhibitor enalapril versus enalapril alone. As in the initial study, there were significant effects on urinary albumin/creatinine ratio. In the placebo group albumin/creatinine ratio increased approximately 350% over 16 weeks. The enalapril treated group increased approximately 220%. The Pyridorin plus enalapril group increased approximately 50% ($p<0.05$ compared to control). There was also a reduction in glomerular lesions in the Pyridorin plus ACE inhibitor group ($p<0.05$ compared to control). In addition, Pyridorin plus enalapril significantly improved survival versus the control or enalapril alone ($p<0.05$).

Pyridorin has also been studied in a non-diabetic, "syndrome X-like" model to assess its effects on the development of nephropathy in the absence of diabetes. In this study, the development of nephropathy and dyslipidemia in treated and untreated obese fa/fa rats was compared to those in lean Fa/fa littermates. Pyridorin, administered at 1 g/L in the drinking water, markedly inhibited the development of dyslipidemia and nephropathy in the fa/fa rats. A 10-fold increase in albuminurea was observed in the untreated obese fa/fa rats over 32 weeks as well as an increase in plasma creatinine from 0.9 mg/dL to 1.5 mg/dL. Pyridorin provided nearly complete protection against increases in both of these parameters ($p<0.0001$). Pyridorin also inhibited the thickening of the aortic and coronary vasculature observed in the untreated obese fa/fa rats by approximately 90% ($p<0.05$). Furthermore, Pyridorin significantly reduced AGE levels in the rat skin collagen when compared to the untreated fa/fa group ($p<0.05$).

Pyridorin was also studied in the type 2 diabetic KK-Ay/Ta mouse. KK-Ay/Ta mice were given Pyridorin (200 or 400 mg/kg per day) starting at 8 weeks of age for 12 weeks. Pyridorin therapy, especially at 400 mg/kg per day, prevented an increase in albuminuria relative to untreated controls (increase of 6.4 mg/L versus 43.5 mg/L, $p<0.05$). Accumulations or Carboxymethyllysine (an AGE) and nitrotyrosine in the kidney were also decreased ($p<0.05$). TGF-β1 and laminin-β1 messenger RNA expressions in kidneys were significantly lower than those in the controls ($p<0.05$).

Preclinical Safety Summary

Pyridorin was studied in acute and chronic rat, rabbit and dog studies for up to one year. Acute and chronic toxicology studies were conducted by Quintiles Preclinical Services. Developmental & reproductive toxicology studies were conducted by Charles River Laboratories Inc. All of these studies were sponsored by BioStratum, Inc. There were no observable side effects seen at blood levels as high 100x over therapeutic blood levels in humans. In a full battery of genotoxicity tests, no mutagenicity or clastogenicity was observed. These studies were conducted by Bioreliance Labs, Quintiles Toxicology/Pathology Services, and Sequani Ltd and sponsored by BioStratum, Inc. Human hepatic cytochrome P450 enzymes are involved in the metabolism and elimination of many widely used drugs. Any induction or inhibition of these enzymes can potentially lead to drug-drug interactions. In human hepatic cell assays, Pyridorin had no effect on cytochrome P450 enzymes. Thus, the potential for Pyridorin to interact with the metabolism of other drugs in-vivo is unlikely. The P450 enzyme studies were conducted by RTI International and sponsored by BioStratum, Inc.

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Clinical Safety Summary

An investigational new drug application (IND) was filed for Pyridorin by BioStratum, Inc. on July 30, 1999. The sponsorship of the IND was transferred to NephroGenex on July 10, 2007.

The safety, tolerability, and pharmacokinetics of Pyridorin was investigated in four Phase 1 studies conducted in healthy male volunteers. A summary of these studies is provided in the table below:

Protocol #	**440-01 (PO)**	**440-01 (IV)**	**440-02**	**PYR-103**
Conducted	Sep 99 - Nov 99	Sep 99 - Nov 99	Nov 99 - Dec 99	Mar 2001
CRO/Sponsor	MDS Harris/BioStratum	MDS Harris/BioStratum	MDS Harris/BioStratum	PPD Development/BioStratum
Location(s)	Lincoln, NE	Lincoln, NE	N. Ireland	Morrisville, NC
Active/Placebo	16/8	4/2	18/6	6/0
Type of Subject M/F	Healthy 24/0	Healthy 6/0	Healthy 24/0	Healthy 6/0
Age range	19 - 41 yrs	19 - 41 yrs	18 - 45 yrs	19 - 50 yrs
Study Design	Ascending Single dose Randomized Double Blind Placebo control	Single dose Randomized Double Blind	Ascending Multiple dose Randomized Double Blind Placebo control	Single dose High fat meal vs fasted 2-way crossover
Route of admin.	Oral	I.V.	Oral	Oral
Dose	3 mg/kg 10 mg/kg 30 mg/kg 50 mg/kg	10 mg/kg	5mg/kg BID 15 mg/kg BID 25 mg/kg BID	500 mg
Duration	Single dose	Single dose	7 days	Single dose
Results	No safety signal	No safety signal	No safety signal	No safety signal

In all four of these studies, Pyridorin was well tolerated with no drug-related toxicity observed in any patients. Based on its benign profile in healthy patients, the decision was made by BioStratum to advance Pyridorin into Phase 2 testing in patients with diabetic nephropathy. The safety, tolerability, and pharmacokinetics of Pyridorin was investigated by BioStratum in a Phase 2 study conducted in patients with Type 1 diabetic nephropathy. In addition, the safety, tolerability and biological activity of Pyridorin was investigated in another Phase 2 study conducted in Type 2 diabetic patients with microalbuminuria (ACR≤ 300 mg/g). This study was conducted in Japan under the sponsorship and management of Kowa Company Ltd.

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A summary of these two studies is provided in the table below:

Protocol #	PYR-202	K-163-04
Conducted	Nov 2000 - Mar 2001	2005 - 2006
CRO/Sponsor	PPD Development/BioStratum	Kowa
Location(s)	USA (5 sites)	Japan
Active/Placebo	9/3	68/67
Type of Subject M/F	Type 1 Diabetic nephropathy 8/4	Type 2 Diabetes w/microalbuminurea 107/28
Age range	28 - 54 yrs	20 - 70 yrs
Study Design	Multiple dose Randomized Escalating dose Double Blind Placebo control	Multiple dose Randomized Double Blind Placebo control
Route of admin.	Oral	Oral
Dose	50 mg BID for 7 days then 250 mg BID for 7 days then 500 mg BID for 28 days	300 mg BID
Duration	6 weeks	26 weeks
Results	No safety signal	No safety signal No effect on microalbuminuria

In both of these studies, Pyridorin was well tolerated with no drug-related toxicity observed in any patients. Based on its benign profile in diabetic nephropathy patients, the decision was made by BioStratum to continue evaluation of the safety, tolerability and biological activity of Pyridorin in type 1 and type 2 diabetic nephropathy patients with macroalbuminuria (ACR >300 mg/g).

In two randomized, placebo-controlled, Phase 2 studies of 24-week treatment duration, patients with nephropathy due to either type 1 or type 2 diabetes showed no consistent across-study differences between Pyridorin and placebo groups in the type or incidence of adverse event reporting or in vital signs, weight, blood pressure, electrocardiograms (ECGs), general chemistry, urinalysis, hematology or special laboratories (coagulation and thyroid function tests). In the first study, the adverse events defined as definitely, probably, or possibly related to the study drug as determined by the investigator, were reported in 26.2% and 33.3% Pyridorin and Placebo patients respectively. In the second study, the adverse events defined as definitely, probably, or possibly related to the study drug as determined by the investigator, were reported in 35.1% and 44.4% Pyridorin and Placebo patients respectively. The types of serious adverse events (SAEs) observed were quite varied and very similar to what is typically observed in diabetic nephropathy patients. Cardiac related events were the most common followed by infections. While a numerical imbalance in SAE reporting was seen, the lack of a specific type of SAE reported in patients receiving Pyridorin, the similarity to the types of SAEs reported in other diabetic nephropathy studies, and the significant baseline medical conditions in these patients suggest that the SAEs were related to the underlying medical conditions, not an effect attributable to Pyridorin. In a retrospective ECG analysis using pooled data from the two 24-week studies, there was no evidence for an effect of Pyridorin on the QT/QTc interval, either at the group level or at the individual patient

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level (using Fridericia's and Bazett's formulae). The QT/QTc interval is a measure of the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle. In general, the QT interval represents electrical depolarization and repolarization of the left and right ventricles. A lengthened QT interval is a biomarker for ventricular tachyarrhythmias and a risk factor for sudden death. Fridericia's and Bazett's formulae are two different correction methods commonly used to correct for heart rate differences when calculating the QT interval.

In a 12-month Phase 2 study treatment with Pyridorin, up to 300 mg twice daily (BID) was generally well tolerated. Most of the AEs were mild or moderate in severity and there was a slight increase in the incidence of diarrhea and constipation in the 300 mg BID group relative to placebo. The pattern and occurrence of AEs were consistent with the patient population under study. The overall incidence of AEs and AEs deemed drug-related was similar among the treatment groups. The types of serious adverse events (SAEs) observed were quite varied and very similar to what is observed in diabetic nephropathy patients. Cardiac related events were the most common followed by infections. There were no meaningful differences in SAEs between the placebo group and the Pyridorin group. The observed SAEs were attributed to underlying baseline medical conditions in these patients and not attributed to Pyridorin therapy.

Phase 2 Efficacy Results

PYR-206

PYR-206 was a Phase 2, multi-center, placebo-controlled, randomized, double-blind study which evaluated the safety and tolerability of Pyridorin administered orally via 50 mg capsules BID for 24 weeks to patients with nephropathy due to type 1 or type 2 diabetes.This study was conducted by BioStratum Inc. which utilized the services of the contract research organization Pharmaceutical Product Development (PPD). The study was conducted from October 2001 to January 2003 in the United States.

Although PYR-206 was designed as a safety and tolerability study, post-hoc analyses were performed on various efficacy parameters, including serum creatinine (SCr), urinary creatinine clearance, and TGF-β1. Creatinine is a breakdown product of creatine. Its level in serum reflects the efficiency of the kidney to remove waste products from the blood. Serum creatinine is the most commonly used indicator of renal function. The SCr change from baseline was analyzed for all patients and for the patient subgroups listed in Table 1 below using a repeated measures mixed model with baseline SCr as a fixed covariate.

Treatment with Pyridorin reduced the change in SCr concentration from baseline by 27% for all patients (65 Pyridorin and 63 placebo). While the treatment was not statistically significant in the Intent to Treat (ITT) patient population, which included all patients that received at least one dose of study drug, this effect was statistically significant for a subgroup of patients with type 2 diabetes and a starting baseline SCr ≥ 1.3 mg/dL (Table 1 and Figure 1).

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Table 1: PYR-206 Serum Creatinine Change from Baseline Analysis

Patient Population	Treatment Group	N	Baseline SCr(1)	SCr Change from Baseline(2)	Treatment Effect(3)
All Patients	Pyridorin	65	1.27 ± 0.34	0.12 ± 0.40	-27%
	Placebo	63	1.33 ± 0.38	0.16 ± 0.28	
Type 2 Diabetes	Pyridorin	40	1.28 ± 0.34	0.08 ± 0.29	-53%
	Placebo	40	1.30 ± 0.36	0.17 ± 0.30	
Baseline SCr ≥ 1.3 mg/dL	Pyridorin	34	1.54 ± 0.21	0.13 ± 0.53	-50%
	Placebo	30	1.65 ± 0.28	0.26 ± 0.33	
Type 2, Baseline SCr ≥ 1.3 mg/dL	Pyridorin	22	1.53 ± 0.20	0.06 ± 0.37	-79%**
	Placebo	19	1.59 ± 0.73	0.29 ± 0.35	

(1) Mean ± SD in mg/dL

(2) Unadjusted mean within group change from baseline in mg/dL

(3) Difference relative to placebo in unadjusted mean change from baseline where a negative value indicates a lesser change from baseline in Pyridorin patients (*i.e.* reno-protection)

** Statistically significant, p<0.01

Figure 1. PYR-206 Serum Creatinine Change from Baseline Analysis in Patients with Type 2 Diabetes and a Baseline SCr ≥ 1.3 mg/dL

(1) Mean ± SEM; P= 0.0074 (Repeated measures mixed model analysis with baseline serum creatinine as a fixed covariate)

In the total patient population, Pyridorin also reduced the rate of rise in SCr levels by 23% relative to placebo. The rise in SCr was 0.161 mg/dL/yr and 0.210 mg/dL/yr in the Pyridorin (n=65) and placebo (n=63) groups, respectively. In the sub-population of patients with more substantial renal impairment as evidenced by a baseline SCr level of ≥ 1.3 mg/dL, the ability of Pyridorin to preserve renal function was more pronounced with a 59% reduction in the rate of rise in SCr relative to placebo. In this sub-population of patients, the rise in SCr was 0.183 mg/dL/yr and 0.445 mg/dL/yr in the Pyridorin (n=34) and placebo (n=31) groups, respectively. This result suggests Pyridorin therapy may be slowing the progression of kidney disease in diabetic patients with more substantial renal

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impairment exhibiting a larger increase in SCr over the treatment period. However, it is part of a post-hoc analysis, and this effect may not be observed in a subsequent study.

Urinary creatinine clearance findings were consistent with the beneficial effects of Pyridorin on slowing the decline of renal function with an 18% reduction in the decline of creatinine clearance in the Pyridorin group relative to patients treated with placebo in the total patient population.

Urinary excretion of TGF-β1, a factor implicated in the pathogenesis of chronic renal failure in diabetic nephropathy, was also assessed. The mean change from baseline to endpoint in urinary TGF-β1 levels was -9.34 and 14.38 pg/mg creatinine in the Pyridorin and placebo patients respectively, with a relative change from baseline of -24.7% and 41.8%, respectively, in the total patient population. As in the case of the observed changes in SCr and urinary creatinine clearance, these results on urinary TGF-β1 are part of a post-hoc analysis, and they may not repeat in a subsequent clinical study.

PYR-205/207

PYR-205 and PYR-207 were identical in design, with the exception of the patient entrance criteria for SCr (≤ 2.0 mg/dL and > 2.0 mg/dL but ≤ 3.5 mg/dL, respectively). The data were merged, as prespecified in the Statistical Analysis Plan, and analyzed as a single study. PYR-205 and 207 were Phase 2, international, multi-center, randomized, double-blind, placebo-controlled, escalating dose studies to evaluate the safety, tolerability, and biologic activity of Pyridorin given orally in a sequential fashion to patients with diabetic nephropathy due to type 1 or type 2 diabetes at:

50 mg BID for two weeks,

100 mg BID for two weeks, and

250 mg BID for 20 weeks.

This study was conducted by BioStratum Inc. which utilized the services of the contract research organizations Pharmaceutical Product Development (PPD), Cato Research, and PharmaNet. The study was conducted from July 2002 to September 2003 in the United States, Belgium, the United Kingdom, Canada and South Africa.

In PYR-205/207, baseline renal function was more impaired than patients studied in PYR-206. In PYR-205/207, Pyridorin reduced the change from baseline SCr in either a statistically significant fashion or trending toward a significant p-value close to 0.05 in all prospectively defined patient sub-groups. The reno-protective effect of Pyridorin as compared to placebo was seen to an equal degree across all patient groups with an approximate 70% reduction relative to placebo in the increase of baseline SCr (Table 2 and Figure 2).

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Table 2: PYR-205/207 Serum Creatinine Change from Baseline Analysis

Patient Population	Treatment Group	N	Baseline SCr(1)	SCr Change from Baseline(2)	Treatment Effect(3)
All Patients	Pyridorin	57	1.75 ± 0.64	0.11 ± 0.26	-68%*
	Placebo	27	1.96 ± 0.86	0.34 ± 0.92	
Type 2 Diabetes	Pyridorin	45	1.74 ± 0.67	0.12 ± 0.27	-68%*
	Placebo	22	1.94 ± 0.92	0.38 ± 1.02	
Baseline SCr ≥ 1.3 mg/dL	Pyridorin	42	2.00 ± 0.55	0.12 ± 0.30	-74%*
	Placebo	19	2.37 ± 0.67	0.47 ± 1.09	
Type 2, Baseline SCr ≥ 1.3 mg/dL	Pyridorin	33	2.00 ± 0.58	0.14 ± 0.31	-75%
	Placebo	15	2.40 ± 0.73	0.55 ± 1.22	

(1) Mean ± SD in mg/dL

(2) Unadjusted mean within group change from baseline in mg/dL

(3) Difference relative to placebo in unadjusted mean change from baseline, where a negative value indicates a lesser change from baseline in Pyridorin patients (*i.e.*, reno-protection)

(4) Determined using repeated measures mixed model analysis with baseline SCr as a fixed covariate and treatment effect being the difference relative to placebo in change from baseline measured in mg/dL.

* Statistically significant, $p<0.05$

Figure 2. PYR-206 Serum Creatinine Change from Baseline Analysis in Patients with Type 2 Diabetes and a Baseline SCr ≥ 1.3 mg/dL

(1)

Mean ± SEM; P= 0.058 (Repeated measures mixed model analysis with baseline serum creatinine as a fixed covariate)

Relative to placebo, Pyridorin treatment also slowed the rate of SCr increase (slope analysis) by approximately 70% in all populations analyzed. The rise in SCr was 0.177 mg/dL/yr in Pyridorin group (n=57) and 0.629 mg/dL/yr in the placebo group (n=27), with a P value of 0.062.

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No significant between-group differences were observed in urinary albumin excretion. Short term effects on proteinuria are usually only seen with anti-hypertensive drugs that improve renal hemodynamics. Pyridorin treatment did not affect blood pressure.

AGE measurements were performed in plasma of patients with more advanced renal disease (all PYR-207 patients) using gas chromatography-mass spectrometry. Whereas carboxymethyllysine (CML) and carboxyethyllysine (CEL) levels increased from baseline by 0.02 and 0.015 mmol/mol Lys, respectively, in the placebo group, CML and CEL levels were decreased from baseline by 0.04 and 0.01 mmol/mol Lys in the Pyridorin-treated group. These data suggest that Pyridorin-induced inhibition of AGE formation occurs concomitantly with the beneficial effects of Pyridorin on renal function, thus lending support to the hypothesis that Pyridorin exerts beneficial effects on renal function via an AGE-dependent mechanism.

The mean change from baseline to endpoint in urinary TGF-β1 levels was -9.7 pg/mg creatinine in Pyridorin patients and +14.2 pg/mg creatinine in placebo patients with a relative change from baseline of -13.1% and 55.7% in the Pyridorin and placebo groups, respectively. These relative differences in TGF-β1 levels could represent one of the mechanisms by which Pyridorin could potentially slow the progressive decline in renal function.

PYR-210

PYR-210 was a randomized, double-blind, placebo-controlled study of Pyridorin at doses of 150 mg BID, 300 mg twice daily (BID) or placebo for 12 months. PYR-210 was designed to further study the efficacy and safety of Pyridorin in patients with overt nephropathy due to type 2 diabetes and to identify the appropriate dose and patient population for Phase 3 pivotal trials.

We conducted the study and utilized the services of the contract research organization Medpace. The study was conducted from August 2008 to August 2010 in the United States, Australia and Israel.

The population selected had macroalbuminuria and impaired renal function. Although previous pivotal trials for diabetic nephropathy (notably, the IDNT study of the drug Irbesartan and the RENAAL study of the drug Losartan) have excluded patients with baseline SCr values ≥ 3.0 mg/dL, patients with higher bSCr values (up to 3.7 mg/dL) were included in the PYR-210 study in order to evaluate Pyridorin safety in more advanced renal disease patients. Pre-specified efficacy analyses according to starting baseline SCr levels were included in the statistical analysis plan. Patients were required to be on an established diabetic nephropathy standard of care (SOC) at screening. Specifically, patients must have received a renin-aldosterone-angiotensin-system (RAAS) inhibitor (ACE-I) or an ARB for at least 3 months prior to screening where the dose of the ACE-I or the ARB was considered appropriate for that patient and had been stable for at least 2 months. Patients were also required to be on stable blood pressure medications (other than an ACE-I or ARB) for 2 months prior to screening.

Patients not on an established, stable regimen of SOC were allowed to enter a screening phase (designated the "run-in period") during which ACE-I/ARB or blood pressure dosing was initiated or adjusted to establish SOC. This was followed by a run-in period of at least 2 months at these same doses before patients could be randomized. These patients were required to meet the other entry criteria at the screening visit. Because changes in ACE-I/ARB or blood pressure medications are known to affect baseline SCr values, a pre-specified analysis of patients on an established standard of care at screening, excluding run-in patients, was included in the statistical analysis plan.

Eligible patients also had:

- a history of overt diabetic nephropathy defined by a SCr measurement of 1.3 mg/dl to 3.3 mg/dl (women) or 1.5 mg/dl to 3.5 mg/dl (men), inclusive, and

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a 24-hour urine collection Protein to Creatinine Ratio (PCR) > 1200 mg/g.

The trial did not reach its primary endpoint on the intent to treat (ITT) population. In the overall patient population, Pyridorin did not demonstrate a significant treatment effect on the progressive increase in serum creatinine concentration that these patients experienced over one year. However, results from the pre-specified analysis of patients on established SOC at screening showed a treatment effect of 45% for Pyridorin 300 mg BID and 21% for Pyridorin 150 mg BID treatment as compared to placebo treatment. This analysis included patients with a baseline SCr ≥ 3.0 mg/dL, which is higher than the baseline SCr used in the precedent IDNT and RENAAL clinical studies and represents patients who are not appropriate for a pivotal trial in diabetic nephropathy due to their baseline instability and advanced stage of renal insufficiency. Nonetheless, these patients were included in PYR-210 for the purposes of a broad safety assessment. When patients with a baseline SCr < 3.0 mg/dL (the patient population studied in the RENAAL trial of Losartan) that were on established SOC at screening were analyzed, a statistically significant treatment effect of 57% for the Pyridorin 300 mg dose (p=0.0094) and 45% for the Pyridorin 150 mg dose (p=0.0414) was observed. The more robust treatment effect observed in the Pyridorin 300 mg BID group over the Pyridorin 150 mg BID group suggests a potential dose response in this patient population. This subgroup is the patient population that will be studied in the Phase 3 trial. Our 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 be repeated in the Phase 3 trials.

A summary of these results is shown in Table 3.

Table 3: Change in Serum Creatinine (mg/dl) From Baseline to Endpoint in Various Subgroups from PYR-210

Patient Population	Treatment Group	N	Baseline SCr	SCr Change from Baseline	Treatment Effect
ITT Population	Pyridorin 300mg	105	2.17 ± 0.57	0.36 ± 0.57	N/A
	Pyridorin 150mg	99	2.22 ± 0.55	0.42 ± 0.72	N/A
	Placebo	103	2.20 ± 0.56	0.36 ± 0.70	
Patients requiring a run-in period(1)	Pyridorin 300mg	36	2.32 ± 0.59	0.62 ± 0.75	N/A
	Pyridorin 150mg	30	2.33 ± 0.56	0.73 ± 0.90	N/A
	Placebo	34	2.34 ± 0.67	0.31 ± 0.68	
Patients on SOC @ screening in the RENAAL population (bSCr < 3.0)(1) *(FDA approved patient population for Phase 3)*	Pyridorin 300mg	64	2.01 ± 0.49	0.18 ± 0.34	-57%**
	Pyridorin 150mg	60	2.03 ± 0.40	0.23 ± 0.45	-45%*
	Placebo	63	2.04 ± 0.40	0.42 ± 0.70	

(1) A separate analysis of this group was pre-specified in the statistical analysis plan.

(2) The patient population used in the RENAAL clinical trial of Losartan is considered to be the established population used for pivotal trials in diabetic nephropathy.

* Statistically significant, p<0.05

** Statistically significant, p<0.01

Patients who were not on a stable regimen of SOC at screening, and required a run-in period, are also shown in Table 3. These patients did not show a Pyridorin treatment effect. The analysis of the ITT patient population also showed no Pyridorin treatment effect. Since the patients on SOC did show a Pyridorin treatment effect, it is possible that inclusion of patients requiring a run-in period

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confounded the analysis of the ITT population. It is generally accepted that the initiation or change in ACEi/ARB or blood pressure medication dosing in overt diabetic nephropathy patients with established renal insufficiency can result in an increase in SCr levels (or a decrease in GFR). A recently published post-hoc analysis of the RENAAL study showed that patients assigned to Losartan (an ARB marketed by Merck & Co. Inc.) had a greater acute fall in eGFR during the first three months compared to patients assigned to placebo. A post-hoc analysis of the database of the IDNT study indicates that this effect of a blood pressure medication can persist for up to 6 months. Since the run-in period in PYR-210 only required stable doses of ACEi/ARB or blood pressure medications for 2 months prior to randomization, it is likely that some run-in patients had not reached a stable SCr baseline value prior to randomization. In addition, there was an increased number of post-randomization blood pressure medication changes in the run-in patients as compared to patients on established SOC at screening. For future Pyridorin studies, the FDA has agreed that all patients will need to be on stable SOC for at least 6 months prior to screening.

When the subgroup of patients that will be studied in the Phase 3 trials was examined (the RENAAL patient population with bSCr < 3.0 mg/dL on stable SOC @ screening) a dose dependent statistically significant treatment effect of 57% at 300 mg BID was observed.

In addition to the primary efficacy endpoint of change from baseline in SCr, the changes in serum cystatin C were also measured based on the demonstration of a 50% reduction in serum cystatin C by Pyridorin relative to placebo in all patients in Study PYR-205/207. The cystatin C results in PYR-210 followed similar trends to what was observed in the subgroups analyzed for SCr changes. A 26% treatment effect was observed in both treated arms (300 mg BID and 150 mg BID) of patients on SOC at screening in the RENAAL population (bSCr < 3.0 mg/dL).

Changes in urinary TGF-β1 were measured based on the demonstration of a reduction in TGF-β1 in PYR 206 and PYR 205/207. The mean change from baseline to endpoint in urinary TGF-β1 levels was -5.8 pg/mg for the Pyridorin 300 mg BID group, +21.4 pg/mg for the Pyridorin 150 mg BID group and +264 pg/mg for the placebo group. Although a dose dependent trend of decreasing TGF-β1 was observed in treated patients, the differences did not reach statistical significance.

Changes in 24 hour urinary protein creatinine ratio (PCR) were also measured. The mean change from baseline to endpoint in urinary PCR was -118 mg/g for the Pyridorin 300 mg BID group, +182 mg/g for the Pyridorin 150 mg BID group and +179 mg/g for the placebo group. Although there was evidence of a possible reduction in the 300 mg BID group relative to the placebo group, the difference was not statistically significant. The average baseline PCR was extremely high in this patient population (~3000 mg/gm) making the likelihood of observing significant effects within one year very low. It is possible that Pyridorin would further reduce urinary PCR with exposures longer than those in the PYR-210 study. Shorter term effects on proteinuria are usually only seen with anti-hypertensive drugs that improve renal hemodynamics. Pyridorin treatment did not affect blood pressure.

In summary, treatment with Pyridorin up to 300 mg BID was well tolerated. No safety signals were observed in this study. Treatment with Pyridorin for 1 year demonstrated a statistically significant treatment effect of 57% for the Pyridorin 300 mg dose (p=0.0094) and 45% for the Pyridorin 150 mg dose (p=0.0414) in the subgroup of patients with a baseline SCr < 3.0 that were on established SOC at screening. The more robust treatment effect observed in the Pyridorin 300 mg BID group over the Pyridorin 150 mg BID group indicates evidence for a dose response in this patient population. Pyridorin also demonstrated evidence of a reduction in serum cystatin C and urinary TGF-β1.

The efficacy data from PYR-210 was consistent with the previous Phase 2 trials PYR-206 and PYR-205/207. These results support the use of the 300 mg BID dose for pivotal studies, as all doses were well tolerated and there was a suggestion of a better treatment effect with the highest dose.

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We have reached agreement with the FDA in a Special Protocol Assessment (SPA) on the patient population to be studied in the pivotal Phase 3 studies: type 2 diabetic patients with overt nephropathy and a bSCr < 3.0 mg/dL that are on an established and stable SOC regimen at screening. In this specific patient population, Pyridorin dosed at 300 mg BID demonstrated a 57% treatment effect in PYR-210 in the endpoint of SCr change from baseline relative to placebo.

Clinical Development Strategy

The clinical development path for a drug to treat diabetic nephropathy has traditionally been very long and associated with significant risk. In the past few years there have been four drug candidates that failed in Phase 3 clinical trials: Pimagedine, Sulonex, Avosantan and Bardoxalone. These drug candidates all looked promising in their respective Phase 2 studies, but all four failed in pivotal trials. A close examination of these clinical development programs reveals that in each case the Phase 3 studies were conducted in a different patient population using a different endpoint than was studied in their respective Phase 2 programs. This unusual circumstance arose because of the very challenging regulatory pathway that previously existed in this field. The long term endpoint that the FDA previously required in Phase 3 (time to SCr doubling or ESRD) made it nearly impossible to evaluate the drug against a similar endpoint in a Phase 2 trial. For example, the recruitment and patient follow-up time for the IDNT study totaled 60 months or 5 years. Bearing in mind trial costs and patent lifetime, this is very long and expensive for a Phase 2 study. Companies chose to use Phase 2 trials to study surrogate endpoints. They also chose patient populations where a treatment effect on the surrogate endpoint would be the most pronounced. Since the FDA did not accept these surrogate endpoints and narrow patient populations for the Phase 3 program, the transition to a Phase 3 trial was quite risky. All four companies ended up evaluating a significant number of types of patients in Phase 3 that they had never evaluated before, using an endpoint for which they had relatively little data.

We took a different approach in our clinical development strategy for Pyridorin. Specifically, during the Phase 2 program, working closely with the FDA, we examined broader patient populations under different conditions of standard of care to identify those patients most appropriate for the Phase 3 program. The pre-specified subgroup analyses of the Phase 2b study indicate that the appropriate diabetic nephropathy patient population to study in Phase 3 is patients on long term establish standard of care at screening with a baseline SCr >1.3 and < 3.0 mg/dL. In this patient population, Pyridorin therapy produced a greater than a 50% treatment effect that was statistically significant (P = 0.009) at the 300 mg bid dose. The Phase 2b study also indicated that patients that would not be appropriate to include in the Phase 3 pivotal study are those not on a stable regimen of standard of care at screening. These patients did not demonstrate a Pyridorin treatment effect and very likely did not reach a stable blood pressure and stable SCr baseline prior to the start of the study which would confound the treatment effect analysis.

We also used a SCr increase-based endpoint that would correlate with a potentially approvable endpoint. Simultaneously, we provided the FDA with analyses from previously completed Phase 3 clinical studies in diabetic nephropathy that supported a new, lower SCr increase-based endpoint. As a result, we potentially significantly reduced the cost of the Phase 3 trials and made our Phase 2b endpoint even closer to the Phase 3 endpoint.

As agreed to in the SPA, the Pyridorin Phase 3 study will be conducted in the specific patient population where Pyridorin has previously shown greater than a 50% treatment effect on a year-1 SCr endpoint (PYR-210).

Phase 3 Development Plan

Based on these clinical results and the SPA agreement with the FDA, we intend to commence the first of two Pyridorin Phase 3 diabetic nephropathy clinical trials (PYR-311) in the first half of 2014.

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We intend to commence the second of the Phase 3 trials (PYR-312) during the first half of 2016. These two clinical trials (PYR-311 and PYR-312), if successful, will serve as the basis for the product registration application.

PYR-311 and PYR-312 are identical Phase 3 randomized, double-blind, placebo-controlled, international multi-center studies to evaluate the efficacy of Pyridorin 300 mg twice daily (BID) compared to placebo in reducing the rate of progression of renal disease due to type 2 diabetes. Each study will provide approximately 90% power to detect a 28% treatment effect. This progression rate will be estimated by the time to the composite endpoint consisting of the earliest event amongst:

A SCr increase of ≥ 50% from baseline that occurs during follow-up; or

End Stage Renal Disease (ESRD).

The FDA has agreed to the SCr increase of ≥ 50% from baseline endpoint as indicated in our SPA agreement with the FDA which covers the design of the Pyridorin Phase 3 program and the endpoint to be used for drug approval. This endpoint was previously validated by an FDA-NKF (National Kidney Foundation) Workshop held in December of 2012 that included leading nephrology clinical investigators and extensive analyses of completed kidney disease clinical studies demonstrating a highly significant correlation between time to a 50% SCr increase and time to ESRD.

The key secondary objective of the studies is to determine the safety of Pyridorin compared to placebo, as assessed by adverse events, 12-lead ECGs, vital signs, physical examination, clinical chemistries, glycosylated hemoglobin (HbA1c), and hematology.

Each study will enroll approximately 600 patients with a history of overt diabetic nephropathy defined by a SCr measurement of ≥ 1.3 mg/dL for female patients or ≥ 1.5 mg/dL for male patients, < 3.0 mg/dL for all patients, and a urine PCR ≥ 1200 mg/g at screening. Patients must be on stable standard of care (SOC) regimen which is defined as an ACE-I or ARB at a constant dose for at least 26 weeks prior to randomization.

PYR-311 will include one interim analysis that will be conducted approximately 18 months following study initiation. At that time, an independent Data and Safety Monitoring Board (DSMB) will assess the general safety of Pyridorin and will perform an analysis of its effect on the rate of SCr progression. If the DSMB determines that Pyridorin is not safe or that it is futile to continue the trial because of lack of efficacy, the trial will be terminated. On the other hand, if the DSMB determines Pyridorin is safe and it is not futile to continue the study, the study will be continued until the necessary number of events have accrued per the study design.

We have had extensive discussions with the FDA regarding this new clinical endpoint as well as the protocol design, inclusion-exclusion criteria, and the trial population. These discussions culminated in an agreement with the FDA on a SPA. The new primary endpoint for this study has the potential to provide for a significantly shorter clinical development path at a substantially reduced cost as compared to the previous clinical endpoint of SCr doubling or ESRD. We believe that we will be the first company to conduct a Phase 3 clinical trial for diabetic nephropathy using this new endpoint.

Acute Kidney Injury (AKI)

Pyridorin targets specific pathogenic oxidative chemistries that emerge in diabetes. These same pathogenic oxidative chemistries emerge with the onset of AKI and are believed to contribute to the severity of the AKI. An intravenous formulation of Pyridorin could provide significant benefit in this acute setting. Because of its benign safety profile, Pyridorin could also be used as preventative therapy in patients at high risk.

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AKI constitutes a very significant market opportunity for Pyridorin. Since this would be an intravenous product used in an acute setting, it would not compete with an oral Pyridorin product used for the chronic treatment of diabetic nephropathy.

AKI is characterized by a rapid reduction in kidney function resulting in a failure to maintain fluid, electrolyte and acid-base homoeostasis. It covers a wide spectrum of disease ranging from less severe forms of injury to more advanced injury when acute kidney failure may require renal replacement therapy (RRT). The incidence of AKI varies from 20% to 40% in critical care patients. In the U.S., 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%. If RRT is required, the mortality rate rises to as high as 80%.

The most common causes of AKI include:

- Sepsis
- Cardiovascular surgery
- Ischemic reperfusion injury
- Contrast dye induced AKI
- Chemotherapy induced AKI
- Trauma
- Serious Burns

Severe AKI is characterized by surge in pathogenic oxidative chemistries. These oxidative chemistries can lead to further damage to the kidneys and ultimately result in acute renal failure (ARF). Even if ARF does not occur, there is evidence that patients who experience AKI have a much higher incidence of subsequent chronic kidney disease.

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New biomarkers have been identified that allow for earlier detection of AKI. One such biomarker is neutrophil gelatinase-associated lipocalin (NGAL). Early detection of AKI would allow therapeutic intervention with an agent like Pyridorin that could inhibit these pathogenic oxidative chemistries and prevent further damage to the kidneys. Because of its benign safety profile, Pyridorin is an attractive candidate for early intervention (e.g. elevated NGAL). Pyridorin may also have application as a preventative therapy in patients at high risk such as those patient undergoing cardiovascular surgery, receiving contrast dye or undergoing chemotherapy.

We will conduct additional preclinical studies to identify those indications where Pyridorin would be most effective. This will form the basis for our clinical development plan.

Commercialization

Given our stage of development, we have not yet established a commercial organization or distribution capabilities. Pyridorin, if approved, is intended to be prescribed to patients with diabetic nephropathy. These patients are normally under the care of a nephrologist, an endocrinologist, and/or a primary care physician (PCP). All of these specialties prescribe therapy for diabetic nephropathy, with the endocrinologist or the PCP typically treating patients in the earlier stage of the disease and the nephrologist typically treating patients in the later stages of the disease (overt diabetic nephropathy). Our current plan is to evaluate a possible partnership to commercialize Pyridorin for the treatment of diabetic nephropathy in patients with type 2 diabetes in the United States and Europe if it is approved. We may also build our own commercial infrastructure or utilize contract reimbursement specialists, sales people and medical education specialists, and take other steps to establish the necessary commercial infrastructure at such time as we believe that Pyridorin is approaching marketing approval. Outside of the United States and Europe, subject to obtaining necessary marketing approvals, we will likely seek to commercialize Pyridorin through distribution or other collaboration arrangements for kidney disease in patients with type 2 diabetes. As a result of our ongoing clinical work, we have been engaged in dialogue with specialists who treat patients with kidney disease. We believe that these activities have provided us with a growing knowledge of the physicians we plan to target for commercial launch of Pyridorin for the treatment of diabetic nephropathy in patients with type 2 diabetes, subject to marketing approval in the United States and Europe.

Competition

The biopharmaceutical industry is characterized by intense competition and rapid innovation. Although we believe that Pyridorin is one of the few drug candidates in advanced clinical trials for diabetic kidney disease, our competitors may be able to develop other compounds or drugs that are able to achieve similar or better results. Our potential competitors include major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies and universities and other research institutions. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. We believe the key competitive factors that will affect the development and commercial success of our product candidates are efficacy, safety and tolerability profile, reliability, convenience of dosing, price and reimbursement.

Diabetic Nephropathy

As of 2010, the Center for Disease Control and U.S. Census data estimate the prevalence of diabetic nephropathy across all stages of disease to be approximately 6 million patients in the U.S. 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.

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While the market opportunity for drugs to treat diabetic nephropathy is large and growing, the availability of drugs to treat this condition is very limited. There are two classes of drugs currently approved to slow the progression of diabetic nephropathy: ACE-Inhibitors and ARBs. These agents target the renin-angiotensin system. Approved initially as anti-hypertension drugs, these agents are now considered standard of care (SOC) for patients with diabetic nephropathy. Pyridorin is intended to be given in conjunction with these therapies; therefore, actual competition will not come from drugs targeting the renin-angiotensin system. Instead, it may come from companies seeking to treat diabetic nephropathy through some other mechanism of action. The table below summarizes the competitive landscape.

COMPANIES WITH CLINICAL PROGRAMS IN DIABETIC NEPHROPATHY

Company	Agent	Phase	Program Status
AbbVie	Endothelin receptor antagonist	3	Active
Bayer Healthcare	Mineralcorticoid Receptor Antagonist	2	Active
Pfizer	Chemokine CCR2/5 Receptor Antagonist	2	Active
	Phosphodiesterase type 5 inhibitor	2	Active
ChemoCentryx	Chemokine CCR2 Receptor Antagonist	2	Active
Eli Lilly	Transforming Growth Factor B Monoclonal Antibody (IV)	2	Active
	MR Antagonist	2	Active
Mitsubishi Tanabe Pharma	Unknown	1	Active

Competition for Phase 3 Recruitment

AbbVie's Phase 3 trial is actively recruiting over 4,100 patients worldwide. While the eligible patient population is not identical, it is similar enough to potentially affect enrollment goals set by our Pyridorin Phase 3 program.

Acute Kidney Injury

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%. If RRT is required, the mortality rate rises to as high as 80%.

The current treatment for AKI is mainly supportive in nature; no therapeutic modalities to date have shown efficacy in treating the condition.

The market opportunity for effective treatments for AKI is large. There are a small number of industry drug trials in later stage development. Companies with an active AKI agent or program include AbbVie, Novartis, Thrasos Innovation, and AlloCure.

Sales of Pyridoxamine as a Dietary Supplement

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. We believe this decline was in response to the FDA ruling, and not a result of subsequent specific FDA letters to these vendors.

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In the case of Pyridorin, we believe that illegal sales of pyridoxamine will have little if any effect on Pyridorin sales for the following reasons:

1. The FDA has a track record of enforcing the regulations against dietary supplement companies that attempt to sell the active ingredient of an FDA approved drug. Since pyridoxamine will be approved for diabetic patients with substantial kidney disease, it is likely the FDA will continue this policy for pyridoxamine.

2. NephroGenex has issued patents covering pyridoxamine as an agent to treat diabetic nephropathy patients and other diabetic complications, and also as an agent to inhibit pathogenic oxidative chemistries that emerge in diabetes. This intellectual property makes it difficult to effectively market pyridoxamine as a dietary supplement without infringing on these issued patents.

3. A significant investment in pyridoxamine production capacity would be required by the dietary supplement industry just to impact a small percentage of Pyridorin drug sales. Furthermore, a non-oxidative method of pyridoxamine production would have to be developed, since the commonly used oxidative method cannot be scaled up due to safety and environmental concerns. We have already developed and patented a non-oxidative method of pyridoxamine production (used in the Phase 2b study), thus making the task of developing a new, non-infringing, non-oxidative method of pyridoxamine production that much more difficult and expensive.

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 this directive. Pyridoxamine is not included on either list, and therefore the sale of pyridoxamine in foods and supplements in Europe is not permitted. We have kept the European Commission Health and Consumers Protection Directorate-General up to date on the clinical status of Pyridorin, and plans for Phase 3 trials.

This office has indicated to NephroGenex as recently as 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.

Intellectual Property

The proprietary nature of, and protection for, our product candidates and our discovery programs, processes and know-how are important to our business. We have sought patent protection in the United States and internationally for Pyridorin and our discovery programs, and any other inventions to which we have rights, where available and when appropriate. Our policy is to pursue, maintain and defend patent rights, whether developed internally or licensed from third parties, and to protect the technology, inventions and improvements that are commercially important to the development of our business. We also rely on trade secrets that may be important to the development of our business. However, we do not have composition of matter patent protection for Pyridorin which may result in competitors being 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.

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

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be commercially useful in protecting our product candidates, discovery programs and processes. For this and more comprehensive risks related to our intellectual property, please see "Risk Factors Risks Relating to Our Intellectual Property."

Patents and Proprietary Rights Covering Our Drug Candidates

We strive to protect our product candidates and exclusivity rights, as well as both maintain and fortify our position in the field of kidney disease therapeutics. We believe our intellectual property portfolio consists of early and broad filings in the area. We have focused on patents and patent applications covering, where possible, use of our products in disease treatment. We have sought and continue to seek the strongest possible intellectual property protection available to us in order to prevent others from directly competing with us, as well as to exclude competition around our products where possible, their manufacture, and methods for use of the products in disease treatment. Our intellectual property portfolio contains 28 issued patents and at least 8 pending patent applications in the U.S. and worldwide of both in-licensed and NephroGenex-owned inventions. This portfolio includes patents and proprietary rights around:

(i) Methods for using Pyridorin (pyridoxamine dihydrochoride) as a therapeutic agent to treat diabetic nephropathy;

(ii) Methods for manufacture of Pyridorin;

(iii) Methods for using Pyridorin as a therapeutic agent to treat a variety of other kidney diseases and other disorders; and

(iv) Pyridorin analog drug candidates, and their use for treating kidney disease.

We own patents covering methods for using Pyridorin to treat diabetic nephropathy in patients with type 2 diabetes and elevated levels of SCr, and thus closely track the anticipated drug label for an approved Pyridorin drug. These patents consist of an issued U.S. patent (U.S. Patent 8067444) and corresponding issued patents in Canada and Europe, which will expire in 2024 absent any extension to the patent term. As discussed in more detail herein, if and when our pharmaceutical products receive FDA approval, we expect to apply for patent term extensions on patents covering those products.

We also have a worldwide, exclusive license from Kansas University Medical Center to an earlier set of patents covering methods for using Pyridorin to treat diabetic nephropathy. These patents include an issued patent in the U.S. (US Patent 5985857) and corresponding patents in Europe and Japan, which will expire in 2016 absent any extension to the patent term. 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 also own patents covering Methods for manufacture of Pyridorin; these patents consist of two issued U.S. patents (U.S. Patents 7214799 and 8431712), which will expire in 2025.

We also have worldwide, exclusive licenses from Kansas University Medical Center, the University of South Carolina, and Vanderbilt University to patents covering methods for using Pyridorin to treat a variety of other disorders. These patents include patents for treating urinary stone disease (US Patent 6521645), proteinuria (U.S. Patent 6472400), retinopathy (U.S. Patent 6750209), neuropathy (U.S. Patents 6750209 and 7030146), oxidative protein modification (U.S. Patent No. 6730686),

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oxidative stress-related disorders (U.S. Patent No. 6716858), hypercholesterolemia (U.S. Patent No. 6740668), and some corresponding foreign patents. The term of these patents will expire at various times, but all would expire by 2021. These patents further include pending applications in the United States for treating symptoms of kidney disorders, and inflammatory disorders. If granted, patents issuing from these patent applications would expire at different times, but all would expire by 2032.

We own pending patent 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.

Intellectual Property Strategy

We continually assess our intellectual property strategy in order to fortify our position in our market space. To that end, we are prepared to file additional patent applications in any of the above families should our intellectual property strategy require such filings and/or where we seek to adapt to competition or seize business opportunities. Further, we are prepared to file patent applications relating to the other products in our pipeline soon after the experimental data necessary for a strong application become available and our cost-benefit analyses justify filing such applications. In addition to filing and prosecuting patent applications in the United States, we typically file counterpart patent applications in Europe and additional countries where we think such foreign filing is likely to be beneficial.

We do not know if patents will be issued for all of the patent applications in our portfolio. Furthermore, for patent claims now issued and for claims to be issued in the future, we do not know if such claims will provide significant proprietary protection to our drug candidates and proprietary technologies or if they will be challenged, circumvented, or invalidated. Our success will in part depend on our ability to obtain and maintain patents protecting our drug candidates, technologies and inventions, to operate without infringing the proprietary rights of third parties, and to enforce and defend our patents and ensure others do not infringe on our proprietary rights.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, a patent's term may be shortened if a patent is terminally disclaimed over another patent or as a result of delays in patent prosecution by the patentee, and a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in granting a patent.

The patent term of a patent that covers an FDA-approved drug or biologic may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug or biologic is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug or biologic may be extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug or biologic. In the future, if and when our pharmaceutical products receive FDA approval we expect to apply for patent term extensions on patents covering those products. We anticipate that some of our issued patents may be eligible for patent term extensions. For more information regarding U.S. patent laws, see "Business Government Regulation."

In addition to the patent term extension rights described above, any of our product candidates that receive FDA approval may also be eligible for market exclusivity protection under the Federal Food,

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Drug and Cosmetic Act or the Biologics Price Competition and Innovation Act of 2009. For more information regarding market exclusivity laws, see "Business Government Regulation."

Many pharmaceutical companies, biotechnology companies and academic institutions are competing with us in the field of diabetic nephropathy and filing patent applications potentially relevant to our business. In order to contend with the inevitable possibility of third party intellectual property conflicts, from time to time, we review and assess the third-party intellectual property landscape for competitive and other developments that may inform or impact our intellectual property development and commercialization strategies. From time to time, we may find it necessary or prudent to obtain licenses from third party intellectual property holders. Where licenses are readily available at reasonable cost, such licenses are considered a normal cost of doing business. In other instances, however, where a third party holds relevant intellectual property and is a direct competitor, a license might not be available on commercially reasonable terms or available at all. Accordingly, we attempt to manage the risk that such third party intellectual property may pose by conducting, among other measures, freedom-to-operate studies to guide our early-stage research away from areas where we are likely to encounter obstacles in the form of third party intellectual property. As our programs advance, we continue to monitor the intellectual property landscape in an effort to assess the advisability of licensing third party intellectual property or taking other appropriate steps to address such freedom-to-operate or development issues in the manner we deem in the best interests of the Company.

With respect to third party intellectual property, it is impossible to establish with certainty that our product candidates will be free of claims by third party intellectual property holders or whether we will require licenses from such third parties. Even with modern databases and on-line search engines, literature searches are imperfect and may fail to identify relevant patents and published applications. Even when a third party patent is identified, we may conclude upon a thorough analysis, that we do not infringe the patent or that the patent is invalid. If the third party patent owner disagrees with our conclusion and we continue with the business activity in question, we might have patent litigation thrust upon us. Alternatively, we might decide to initiate litigation in an attempt to have a court declare the third party patent invalid or not infringed by our activity. In either scenario, patent litigation typically is costly and time-consuming, and the outcome is uncertain. The outcome of patent litigation is subject to uncertainties that cannot be quantified in advance, for example, the credibility of expert witnesses who may disagree on technical interpretation of scientific data. Ultimately, in the case of an adverse outcome in litigation, we could be prevented from commercializing a product or using certain aspects of our discovery platform as a result of patent infringement claims asserted against us. This could have a material adverse effect on our business.

To protect our competitive position, it may be necessary to enforce our patent rights through litigation against infringing third parties. Litigation to enforce our own patent rights is subject to the same uncertainties discussed above. In addition, however, litigation involving our patents carries the risk that one or more of our patents will be held invalid (in whole or in part, on a claim-by-claim basis) or held unenforceable. Such an adverse court ruling could allow third parties to commercialize our products, and then compete directly with us, without payment to us.

Trade Secrets

In addition to patents, we rely on trade secrets and know-how to develop and maintain our competitive position. Trade secrets and know-how can be difficult to protect. We seek to protect our proprietary processes, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and commercial partners. These agreements are designed to protect our proprietary information. We also seek to preserve the integrity and confidentiality of our data, trade secrets and know-how by maintaining physical security of our premises and physical and electronic security of our information technology systems.

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License Agreements

Licensing Payments

Set forth below is a summary chart outlining various potential license payments due under our license agreements referenced below:

Indication	Diabetic Nephropathy *Phase III*	Acute Kidney Injury, Chemotherapy Protection, or Radiation Damage *Pre-clinical AKI*	Diabetic Neuropathy or Hyperlipedemia *Not in current pipeline*
Institution	Kansas University Medical Center	Vanderbilt University	South Carolina Research Foundation
FDA Approval of SPA	$25,000		
Filing of IND		$75,000	
Commencement of first Phase 1		$100,000	
Commencement of first Phase 2		$150,000	$325,000
Commencement of first Phase 3		$250,000	$500,000
File NDA or foreign equivalent			$750,000
FDA Approval of NDA	$200,000	$500,000 ($250,000 credited against royalty)	$2,000,000
First commercial sale			$2,500,000
Royalty on Net Sales	None	5% (minus $250,000 credit)	None
Licensing Fee	None	None	$112,000 due 3/31/14 $30,000 per quarter thereafter (credited against milestone payments & upfront sublicense fees)
Upon execution of a sublicense		25% of any sublicense fees or milestone payments	$35,000 plus 25% of upfront sublicense fees

License Agreements

Kansas University Medical Center (KUMC) Exclusive License Agreement

In May 2007, we entered into an amended license agreement with KUMC. Under the agreement, KUMC grants us an exclusive, royalty-free, worldwide license, with a right to grant sublicenses, to make, have made, use, distribute, sell, have sold, have distributed, offer to sell, market, import, have imported or otherwise dispose of licensed products for diagnostic testing and palliative, prophylactic and therapeutic treatments which incorporate the use of the technology relating to the licensed patents and improvements. The patents licensed from KUMC include claims reciting methods for using Pyridorin to: (a) treat diabetic nephropathy (expires by 2016 absent any extension); (b) treat proteinuria or albuminuria associated with elevated blood sugar levels (expires by 2016 absent any extension); (c) treat retinopathy or neurodegenerative disease (expires by 2016 absent any extension); (d) inhibiting oxidative modification of proteins or treating atherosclerosis in a non-hyperglycemic mammal (expires by 2016 in the U.S. and 2019 outside the U.S. absent any extension); (e) treat a condition associated with oxidative stress in a hyperglycemic mammal (expires by 2016 absent any extension); (f) treat diabetes-associated increases in hypercholesterolemia or hypertriglyceridemia in a diabetic mammal; (expires by 2016 in the U.S. and 2019 outside the U.S. absent any extension);

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(g) treat diabetic neuropathy (expires by 2016 absent any extension); (h) decrease dialysis-related amyloidosis or dialysis-related increases in permeability of the peritoneal membrane in a dialysis patient (expires by 2016 absent any extension); and (i) urinary stone disease (expires by 2021 absent any extension).

The patents licensed from KUMC also include patents with claims reciting novel Pyridorin analogues, and methods for using them to treat AGE-related pathologies, diabetic nephropathy, proteinuria, albuminuria; diabetes-associated increases in hypercholesterolemia or hypertriglyceridemia in a diabetic mammal; and for inhibiting oxidative modification of proteins or treating atherosclerosis in a non-hyperglycemic mammal (expire by 2016 in the U.S. and 2019 outside the U.S. absent any extension). The granted license is subject to certain rights and license granted to the United States and to foreign governments pursuant to U.S. government patent laws and regulations.

We must pay KUMC milestone payments related to milestones met in the FDA regulatory approval process. These milestone payments include $25,000 upon receipt of FDA approval of our SPA for our first licensed product and $200,000 upon receipt of FDA approval of our submitted NDA for our first licensed product in respect to the first primary indication. We must exercise commercially reasonable efforts to seek regulatory approval for the marketing of a licensed product for at least one primary indication, effect the introduction of a licensed product for at least one primary indication into the commercial market and to maximize these sales. Primary indications are the diagnosis, treatment, palliation or prophylaxis of diabetic nephropathy, diabetic retinopathy and diabetic neuropathy.

The agreement survives until expiration of the last to expire licensed patent, or in November 2018, whichever occurs last. We may terminate the license for any reason upon 90 days written notice. If either we or KUMC breach a material obligation under the agreement the non-breaching party may terminate the agreement upon an additional written notice.

The South Carolina Research Foundation (SCRF) Exclusive License Agreement

In April 2012, we entered into an amended license agreement with SCRF. Under the agreement, SCRF grants us an exclusive, royalty-free, worldwide license, under certain patent rights and related technology (including know-how) with a right to sub-license to utilize the patent rights and the technology during the term of the agreement and to practice under the patent rights to make, have made, use, sell, have sold, offer to sell, market, import, lease, or otherwise dispose of licensed products for all uses covered under the patent rights. The licensed product is Pyridorin or any other pharmaceutical compound labeled for an FDA-approved indication that would infringe a valid claim of the patent rights in the absence of the license.

The patents licensed from SCRF include claims reciting methods for using Pyridorin to: (a) inhibit oxidative modification of proteins or treating atherosclerosis in a non-hyperglycemic mammal (expires by 2016 in the U.S. and 2019 outside the U.S. absent any extension); (b) treat diabetes-associated increases in hypercholesterolemia or hypertriglyceridemia in a diabetic mammal; (expires by 2016 in the U.S. and 2019 outside the U.S. absent any extension); and (c) treat diabetic neuropathy (expires by 2016 in the U.S. and 2019 outside the U.S. absent any extension). The patents licensed from SCRF also include patents with claims reciting novel Pyridorin analogues, and methods for using them to treat diabetes-associated increases in hypercholesterolemia or hypertriglyceridemia in a diabetic mammal, and for inhibiting oxidative modification of proteins or treating atherosclerosis in a non-hyperglycemic mammal; (expire in 2016 in the U.S. and 2019 outside the U.S. absent any extension).

Under the license, SCRF retains the right to practice under the patents in the field solely for non-profit, educational, research, and academic purposes. The license also is subject to any U.S. government rights in the patent rights, if the technology or patent rights were developed with the support of the U.S. government or an agency thereof.

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We must exercise commercially reasonable efforts to develop and commercialize one or more licensed products. If we fail to comply with our diligence obligations with respect to at least one licensed product, then SCRF may terminate the license. If we develop Pyridorin for the treatment of hyperlipidemia or diabetic *neuro*pathy, we must pay SCRF milestone payments related to milestones met in the FDA regulatory approval process in the aggregate amount of $6,075,000. We must pay SCRF an annual license fee each year that we are actively marketing Pyridorin or have an active sublicense for Pyridorin for the treatment of hyperlipidemia or diabetic *neuro*pathy, which are creditable only against Licensed Product Sublicense upfront fees and milestone payments earned and payable in the same calendar year. We must pay SCRF an annual fee of $122,000 for 2013 and $120,000 for 2014 and the years thereafter. We must pay SCRF a one-time fee of $35,000 upon execution of a sub-license between NephroGenex and a third party, and must pay to SCRF 25% of any non-royalty sublicense payments made by such sub-licensee to NephroGenex. The planned phase 3 program for Pyridorin is for the treatment of diabetic nephropathy. Hyperlipidemia and diabetic neuropathy are not being evaluated in the current trial.

The agreement survives until the expiration or other disposition of the licensed patent rights. We may terminate the license at any time on three months prior written notice to SCRF. If we breach a material obligation under the agreement, and such obligation is not cured within 90 days after we receive written notice of the breach, then SCRF may terminate the agreement upon an additional written notice. SCRF may also terminate the license if (i) we cease operations and have not assigned the license to a third party; (ii) we become insolvent or make a general assignment of substantially all of our assets for the benefit of creditors, or if a petition of bankruptcy or any reorganization shall be commenced by, against, or in respect of us; or (iii) we fail to make a payment due under the license and the default is not cured within 30 days after written notice of such default, and SCRF has provided additional written notice.

Vanderbilt University (VU) Exclusive License Agreement

In connection with our additional pipeline opportunities for specific types of acute kidney injury, in July 2012, we entered into a license agreement with VU, which was amended on November 6, 2013. Under the agreement, VU grants us an exclusive, royalty-bearing, worldwide license, under certain patent rights, and a corresponding nonexclusive license under related know-how, with a right to sub-license, to make, have made, use, offer to sell, sell, and import licensed products incorporating the technology embodied in the licensed VU patent rights for use of pyridoxamine in the field of use, which is defined as treatment of acute renal failure or acute renal injury, use for radiation protection, and use for chemotherapy protection. The patent applications licensed from VU include claims reciting methods for using Pyridorin to: (a) ameliorate at least one symptom of a kidney disorder associated with oxidative stress, carbonyl stress, or combinations thereof (if issued, would expire by 2026); (b) treat or prevent acute renal injury or acute renal failure (if issued, would expire by 2026); and (c) treat an inflammatory disorder (if issued, would expire by 2032).

The patent applications licensed from VU also include claims reciting intravenous formulations of Pyridorin (if issued, would expire by 2026). Federal government rights in the licensed patents are reserved, as are VU's right to use the subject matter of the licensed patents for academic research or other not-for-profit scholarly purposes, and to grant to other academic, governmental, or not-for-profit organizations a non-exclusive right, non-transferable, non-sublicensable right to practice the licensed patent rights for academic research or other not-for-profit scholarly research purposes, expressly excluding any human use.

We must pay VU milestone payments related to milestones met in the FDA regulatory approval process in the aggregate amount of $1,075,000. We must also pay VU a 5% royalty on net sales of licensed products in the field of use. We must also pay VU 25% of non-royalty sublicense payments to us such as milestone payments we recoup from sub licensees. We must exercise commercially

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reasonable efforts to develop and commercialize a licensed product for at least one indication. Our diligence obligations include a series of patent prosecution and clinical trial milestones. If we fail to comply with our diligence obligations with respect to at least one licensed product, then VU may terminate the license.

The agreement survives until the last to expire of the licensed patent rights. We may terminate the agreement upon 60 days written notice to VU. If either we or VU breach a material obligation under the agreement, and such obligation, then the non-breaching party may terminate the agreement upon an additional written notice. VU may also terminate the license if we become insolvent or suspend business, or file a voluntary petition or an answer admitting the jurisdiction of the court, or consent to an involuntary petition pursuant to any reorganization or insolvency law of any jurisdiction, or make an assignment for the benefit of creditors, or apply for or consent to the appointment of a receiver or trustee of a substantial part of our property.

BioStratum, Inc. (BioStratum) Grant Back License Agreement

In May 2007, we entered into a grant-back license agreement with BioStratum as part of our acquisition of certain of BioStratum's assets, including certain patent rights. The licensed patent rights include all patents and patent applications licensed by NephroGenex from BioStratum under an earlier, terminated license agreement between the parties. These rights include all patents owned or licensed by us with the exception of the patent applications that we license from VU. Under this agreement, we grant BioStratum an exclusive, sublicensable license and sublicense under those patent rights to make, have made, use, sell, offer for sale and import licensed products solely in Japan, Taiwan, Korea and China. The licensed products are Pyridorin or AGE inhibitor products that are covered by the licensed patents. As this license has been fully paid, there are no milestone payments under this agreement. In this agreement, we also agreed not to modify the Kansas or USC license agreements in a manner that would adversely affect BioStratum's rights.

The license grant to BioStratum was made solely to enable BioStratum to exercise its rights and perform its obligations pursuant to a license agreement with Kowa Company, Ltd. (Kowa) pursuant to which BioStratum granted Kowa an exclusive license (the Kowa Agreement) to manufacture and use licensed products in Japan, Taiwan, Korea, and China. The Kowa Agreement was terminated by Kowa on December 5, 2007.

After termination of the BioStratum grant-back license agreement for any reason other than assignment or transfer of the Kowa Agreement to NephroGenex, we are required to obtain the written consent of BioStratum to grant a license to any third party to develop, make, have made, use, sell, offer for sale, or import Licensed Products in Japan, Taiwan, Korea or China.

Manufacturing

We do not own or operate manufacturing facilities for the production of any of our product candidates, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We currently rely on third-party contract manufacturers for all of our required raw materials, active pharmaceutical ingredient (API) and finished product for our preclinical research and clinical trials, including the Phase 3 trials for Pyridorin for the treatment of diabetic nephropathy in patients with type 2 diabetes. In December 2013, we entered into a manufacturing agreement with Patheon Pharmaceuticals Inc. to manufacture pyridoxamine dihydrochloride, the API in Pyridorin. At our direction, Patheon will manufacture clinical trial material batches of pyridoxamine dihydrochloride capsules and placebo for our clinical supply. We do not have any current contractual relationships for the manufacture of commercial supplies of any of our product candidates if they are approved. If any of our products are approved by any regulatory agency, we intend to enter into agreements with a third-party contract manufacturer and one or more back-up manufacturers for the commercial

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production of those products. Development and commercial quantities of any products that we develop will need to be manufactured in facilities, and by processes, that comply with the requirements of the FDA and the regulatory agencies of other jurisdictions in which we are seeking approval. We currently employ internal resources to manage our manufacturing contractors.

The typical route for the chemical synthesis of Pyridorin (pyridoxamine) uses oxidative methods where the starting material is the readily and economically available pyridoxine (vitamin B6). Although such oxidative manufacturing methods are usable at a small scale, oxidative methods are not viable for large-scale production and commercialization. For example, the first step in the metabolism of pyridoxine is an enzymatic oxidation of the alcohol group to an aldehyde, thus converting pyridoxine to pyridoxal. The oxidative chemical synthetic parallels this by utilizing oxidizing agents such as manganese dioxide to convert pyridoxine to pyridoxal. However, the oxidation of pyridoxine is problematic at the scale required for commercial manufacturing for several reasons, including the need to rapidly remove large amounts of solid oxidants to minimize the potential for continuing oxidation reactions. Such overoxidation not only can convert pyridoxal to pyridoxic acid but can also lead to non-selective oxidation of the second hydroxymethyl group at the 5-position. Other difficulties can be encountered subsequent to the formation of pyridoxal. For example, in order to form the desired amine, pyridoxal is conveniently reacted with hydroxylamine to form an intermediate oxime that must be subsequently reduced. Hydroxylamine is a dangerous reagent to handle on an industrial scale due to its instability, its high reactivity and its toxicity. Reduction of the oxime is known and can be performed by methods such as using zinc. However, this is also an unfavorable reagent for large scale manufacturing. Reduction with hydrogen catalysts such as platinum or palladium is possible, but this route is expensive, difficult to control, and difficult to scale up. Over-reduction can lead to the generation of deoxy impurities that may be toxic anti-metabolites contaminating the API.

To overcome this barrier to commercialization, we have developed and patented a non-oxidative method for the synthesis of pyridoxamine and all of its intermediate compounds and salts. This method provides for large scale synthesis at a fraction of the price required using traditional oxidative methods. It also eliminates the safety and environmental hazards associated with these oxidative methods.

Government Regulation and Product Approval

Governmental authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, labeling, packaging, promotion, storage, advertising, distribution, marketing and export and import of products such as those we are developing. Our product candidates must be approved by the FDA through the NDA process before they may be legally marketed in the United States and by the EMA through the MAA process before they may be legally marketed in Europe. Our product candidates will be subject to similar requirements in other countries prior to marketing in those countries. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

United States Government Regulation

NDA Approval Processes

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act (the FDCA) and implementing regulations. Failure to comply with the applicable U.S. requirements at any time during the product development process or approval process, or after approval, may subject an applicant to administrative or judicial sanctions, any of which could have a material adverse effect on us. These sanctions could include:

- refusal to approve pending applications;

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withdrawal of an approval;

imposition of a clinical hold;

warning letters;

product seizures;

total or partial suspension of production or distribution; or

injunctions, fines, disgorgement, or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

completion of nonclinical laboratory tests, animal studies and formulation studies conducted according to Good Laboratory Practices (GLPs) or other applicable regulations;

submission to the FDA of an IND, which must become effective before human clinical trials may begin;

performance of adequate and well-controlled human clinical trials according to Good Clinical Practices (GCPs) to establish the safety and efficacy of the proposed drug for its intended use;

submission to the FDA of a NDA;

satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current Good Manufacturing Practices (cGMPs) to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and

FDA review and approval of the NDA.

Once a pharmaceutical candidate is identified for development, it enters the preclinical or nonclinical testing stage. Nonclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. An IND sponsor must submit the results of the nonclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. Some nonclinical testing may continue even after the IND is submitted. In addition to including the results of the nonclinical studies, the IND will also include a protocol detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the first phase lends itself to an efficacy determination. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the IND on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin. A clinical hold may occur at any time during the life of an IND, and may affect one or more specific studies or all studies conducted under the IND.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCPs. They must be conducted under protocols detailing the objectives of the trial, dosing procedures, research subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND, and progress reports detailing the status of the clinical trials must be submitted to the FDA annually. Sponsors also must timely report to FDA serious and unexpected adverse reactions, any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigation

brochure, or any findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the drug. An institutional review board, or IRB, at each institution participating in the clinical trial must review and approve the protocol before a clinical trial commences at that institution and must also approve the information regarding the trial and the consent form that must be

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provided to each research subject or the subject's legal representative, monitor the study until completed and otherwise comply with IRB regulations.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

Phase 1. The drug is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and elimination. In the case of some products for severe or life-threatening diseases, such as cancer, especially when the product may be inherently too toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.

Phase 2. Clinical trials are performed on a limited patient population intended to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These studies are intended to establish the overall risk-benefit ratio of the product and provide an adequate basis for product labeling.

Human clinical trials are inherently uncertain and Phase 1, Phase 2 and Phase 3 testing may not be successfully completed. The FDA or the sponsor may suspend a clinical trial at any time for a variety of reasons, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to the submission of an IND, at the end of Phase 2 and before a NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date and for the FDA to provide advice on the next phase of development. Sponsors typically use the meeting at the end of Phase 2 to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trial that they believe will support the approval of the new drug. If a Phase 2 clinical trial is the subject of discussion at the end of Phase 2 meeting with the FDA, a sponsor may be able to request a Special Protocol Assessment, or SPA, the purpose of which is to reach agreement with the FDA on the Phase 3 clinical trial protocol design and analysis that will form the primary basis of an efficacy claim.

According to published guidance on the SPA process, a sponsor which meets the prerequisites may make a specific request for a SPA and provide information regarding the design and size of the proposed clinical trial. The FDA is supposed to evaluate the protocol within 45 days of the request to assess whether the proposed trial is adequate, and that evaluation may result in discussions and a request for additional information. A SPA request must be made before the proposed trial begins, and all open issues must be resolved before the trial begins. If a written agreement is reached, it will be documented and made part of the record. The agreement will be binding on the FDA and may not be changed by the sponsor or the FDA after the trial begins except with the written agreement of the sponsor and the FDA or if the FDA determines that a substantial scientific issue essential to determining the safety or efficacy of the drug was identified after the testing began.

Concurrent with clinical trials, sponsors usually complete additional animal safety studies and also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing commercial quantities of the product in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug and the manufacturer must develop methods for testing the quality, purity and potency of the

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drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its proposed shelf-life.

The results of product development, nonclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests and other control mechanisms, proposed labeling and other relevant information are submitted to the FDA as part of a NDA requesting approval to market the product. The submission of a NDA is subject to the payment of user fees, but a waiver of such fees may be obtained under specified circumstances. The FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. It may request additional information rather than accept a NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing.

Once the submission is accepted for filing, the FDA begins an in-depth review. NDAs receive either standard or priority review. A drug representing a significant improvement in treatment, prevention or diagnosis of disease may receive priority review. The FDA may refuse to approve a NDA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data. Even if such data are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. The FDA reviews a NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant. The FDA may refer the NDA to an advisory committee for review and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving a NDA, the FDA will inspect the facility or facilities where the product is manufactured and tested.

Expedited Review and Approval

The FDA has various programs, including Fast Track, priority review, and accelerated approval, which are intended to expedite or simplify the process for reviewing drugs, and/or provide for the approval of a drug on the basis of a surrogate endpoint. Even if a drug qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or that the time period for FDA review or approval will be shortened. Generally, drugs that are eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs and those that offer meaningful benefits over existing treatments. For example, Fast Track is a process designed to facilitate the development and expedite the review of drugs to treat serious or life-threatening diseases or conditions and fill unmet medical needs. Priority review is designed to give drugs that offer major advances in treatment or provide a treatment where no adequate therapy exists an initial review within six months as compared to a standard review time of ten months.

Although Fast Track and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track designated drug and expedite review of the application for a drug designated for priority review. Accelerated approval, which is described in Subpart H of 21 CFR Part 314, provides for an earlier approval for a new drug that is intended to treat a serious or life-threatening disease or condition and that fills an unmet medical need based on a surrogate endpoint. A surrogate endpoint is a laboratory measurement or physical sign used as an indirect or substitute measurement representing a clinically meaningful outcome. As a condition of approval, the FDA may require that a sponsor of a product candidate receiving accelerated approval perform post-marketing clinical trials.

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In the Food and Drug Administration Safety and Innovation Act, or FDASIA, which was signed into law in July 2012, Congress encouraged the FDA to utilize innovative and flexible approaches to the assessment of products under accelerated approval. The law required the FDA to issue related draft guidance within a year after the law's enactment and also promulgate confirming regulatory changes. In June 2013, the FDA published a draft Guidance for Industry entitled, "Expedited Programs for Serious Conditions Drugs and Biologics" which provides guidance on FDA programs that are intended to facilitate and expedite development and review of new drugs as well as threshold criteria generally applicable to concluding that a drug is a candidate for these expedited development and review programs. In addition to the Fast Track, accelerated approval and priority review programs discussed above, the FDA also provided guidance on a new program for Breakthrough Therapy designation. A request for Breakthrough Therapy designation should be submitted concurrently with, or as an amendment to an IND. FDA has already granted this designation to around 30 new drugs and recently approved the first Breakthrough Therapy designated drug.

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of the use of our drug candidates, some of our U.S. patents may be eligible for limited patent term extension 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, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND, and the submission date of a NDA, plus the time between the submission date of a NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the application for extension must be made prior to expiration of the patent. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restorations of patent term for some of our currently owned or licensed patents to add patent life beyond their current expiration date, depending on the expected length of clinical trials and other factors involved in the submission of the relevant NDA.

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of a NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for a NDA, 505(b)(2) NDA or supplement to an approved NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

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Pediatric Exclusivity and Pediatric Use

Under the Best Pharmaceuticals for Children Act (BPCA) certain drugs may obtain an additional six months of exclusivity, if the sponsor submits information requested in writing by the FDA (a Written Request) relating to the use of the active moiety of the drug in children. The FDA may not issue a Written Request for studies on unapproved or approved indications or where it determines that information relating to the use of a drug in a pediatric population, or part of the pediatric population, may not produce health benefits in that population.

We have not received a Written Request for such pediatric studies, although we may ask the FDA to issue a Written Request for such studies in the future. To receive the six-month pediatric market exclusivity, we would have to receive a Written Request from the FDA, conduct the requested studies in accordance with a written agreement with the FDA or, if there is no written agreement, in accordance with commonly accepted scientific principles, and submit reports of the studies. A Written Request may include studies for indications that are not currently in the labeling if the FDA determines that such information will benefit the public health. The FDA will accept the reports upon its determination that the studies were conducted in accordance with and are responsive to the original Written Request or commonly accepted scientific principles, as appropriate, and that the reports comply with the FDA's filing requirements.

In addition, the Pediatric Research Equity Act (PREA) requires all applications (or supplements to an application) submitted under section 505 of the FDCA (21 U.S.C. Section 355) for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration to contain a pediatric assessment unless the applicant has obtained a waiver or deferral. It also authorizes the FDA to require holders of approved NDAs for marketed drugs to conduct pediatric studies under certain circumstances. In general, PREA applies only to those drugs developed for diseases and/or conditions that occur in both the adult and pediatric populations. Products intended for pediatric-specific indications will be subject to the requirements of PREA only if they are initially developed for a subset of the relevant pediatric population.

As part of the FDASIA, Congress reauthorized both BPCA and PREA, which were slated to expire on September 30, 2012, and made both laws permanent.

Post-approval Requirements

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further FDA review and approval. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved products that have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs.

Any drug products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things:

- record-keeping requirements;
- reporting of adverse experiences with the drug;
- providing the FDA with updated safety and efficacy information;
- drug sampling and distribution requirements;
- notifying the FDA and gaining its approval of specified manufacturing or labeling changes; and

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complying with FDA promotion and advertising requirements.

Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and some state agencies for compliance with cGMP and other laws.

We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products. Future FDA and state inspections may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct.

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. In addition, FDA regulations and guidance are often revised or reinterpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether legislative changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be.

Regulation Outside of the United States

In addition to regulations in the United States, we will be subject to regulations of other countries governing clinical trials and commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of countries outside of the United States before we can commence clinical trials in such countries and approval of the regulators of such countries or economic areas, such as the European Union, before we may market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Under European Union regulatory systems, a company may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure, which is compulsory for medicines produced by biotechnology or those medicines intended to treat AIDS, cancer, neurodegenerative disorders or diabetes and optional for those medicines which are highly innovative, provides for the grant of a single marketing authorization that is valid for all European Union member states. The decentralized procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization may submit an application to the remaining member states. Within 90 days of receiving the applications and assessments report, each member state must decide whether to recognize approval. If a member state does not recognize the marketing authorization, the disputed points are eventually referred to the European Commission, whose decision is binding on all member states.

Reimbursement

Sales of our products will depend, in part, on the extent to which the costs of our products will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly challenging the prices charged for medical products and services. Additionally, the containment of healthcare costs has become a priority of federal and state governments and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. If these third-party payors do not consider our products

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to be cost-effective compared to other therapies, they may not cover our products after approved as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (the MMA) imposed new requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities which will provide coverage of outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for our products for which we receive marketing approval. However, 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. 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 American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. A plan for the research will be developed by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures will be made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of any product, if any such product or the condition that it is intended to treat is the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's product could adversely affect the sales of our product candidates. If third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010 (collectively, the ACA), enacted in March 2010, is expected to have a significant impact on the health care industry. ACA is expected to expand coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, among other things, ACA is expected to expand and increase industry rebates for drugs covered under Medicaid programs and make changes to the coverage requirements under the Medicare Part D program. We cannot predict the impact of ACA on pharmaceutical companies, as many of the ACA reforms require the promulgation of detailed regulations implementing the statutory provisions which has not yet occurred. 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. Any legal challenges to ACA, as well as Congressional efforts to repeal ACA, add to the uncertainty of the legislative changes enacted as part of ACA.

In addition, in some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country

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to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally tend to be significantly lower.

Legal Proceedings

From time to time, we are involved in various legal proceedings arising in the ordinary course of our business. We are not presently a party to any legal proceedings the outcome of which, if determined adversely to us, would individually or in the aggregate have a material adverse effect on our business, operating results or financial condition.

Facilities

Our corporate headquarters and clinical development operations are located in Research Triangle Park, North Carolina where we lease and occupy approximately 3,100 square feet of space. The lease for our office expired in December 2013 and is currently leased on a month-to-month basis. We intend to enter into a long-term lease in the near future. We believe that our facility is suitable and adequate for our current needs.

Employees

As of March 17, 2014, we had 6 employees, of which all are involved in our drug development operations and in general and administrative functions. None of our employees are represented by a labor union and we consider our employee relations to be good. In addition, we are or have engaged with a sizable number of consultants and companies that provide expertise in each of the key functions involved with the development of Pyridorin, including in the fields of regulatory, non-clinical, clinical and CMC. In addition, from time to time, we consult with scientific and clinical advisors.

The Company's Internet address is www.nephrogenex.com. The Company's annual reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to reports filed pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, are available free of charge through the Investor Relations section of our website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission, or the SEC. The SEC maintains an internet site that contains our public filings with the SEC and other information regarding the Company, at www.sec.gov. These reports and other information concerning the Company may also be accessed at the SEC's Public Reference Room at 100 F Street, NE, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The contents of these websites are not incorporated into this Annual Report. Further, our references to the URLs for these websites are intended to be inactive textual reference only.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012. 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 Securities and Exchange Commission. We refer to the Jumpstart Our Business Startups Act of 2012 herein as the "JOBS Act," and references herein to "emerging growth company" shall have the meaning associated with it in the JOBS Act.

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Item 1A. RISK FACTORS

Except for the historical information contained herein or incorporated by reference, this report and the information incorporated by reference contains forward-looking statements that involve risks and uncertainties. These statements include projections about our accounting and finances, plans and objectives for the future, future operating and economic performance and other statements regarding future performance. These statements are not guarantees of future performance or events. Our actual results could differ materially from those discussed in this report. Factors that could cause or contribute to these differences include, but are not limited to, those discussed in the following section, as well as those discussed in Part II, Item 7 entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere throughout this report and in any documents incorporated in this report by reference.

You should consider carefully the following risk factors, together with all of the other information included or incorporated in this report. If any of the following risks, either alone or taken together, or other risks not presently known to us or that we currently believe to not be significant, develop into actual events, then our business, financial condition, results of operations or prospects could be materially adversely affected. If that happens, the market price of our common stock could decline, and stockholders may lose all or part of their investment.

Risks Relating to Our Financial Position and Need for Additional Capital

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 $6.3 million and $2.9 million for the years ended December 31, 2013 and 2012, respectively. We had an accumulated deficit of approximately $41.0 million as of December 31, 2013. Our working capital and cash and cash equivalents as of December 31, 2013 were $(14.7) million and $2.1 million, respectively.

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, which is our lead product candidate, and our other product candidates, prepare for and begin the commercialization of any approved products, and add infrastructure and personnel to support our product development efforts and operations as a public company. We anticipate that any such losses could be significant for the next several years as we begin our Phase 3 clinical program of Pyridorin for the treatment of diabetic nephropathy in patients with type 2 diabetes, which we call the Pyridorin 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,

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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 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.

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, and to conduct the research and development and clinical and regulatory activities necessary to bring other product candidates to market. 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 New Drug Application (NDA) or Marketing Authorization Application (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 will not increase.

We intend to use substantially all of the net proceeds from our recently completed initial public offering to fund (i) the continued clinical development of Pyridorin for the treatment of diabetic nephropathy in patients with type 2 diabetes, including our anticipated Phase 3 trial and (ii) further development of an intravenous formulation of Pyridorin for AKI. Any remaining amounts will be used for general corporate purposes, general and administrative expenses, capital expenditures, working capital and prosecution and maintenance of our intellectual property. As such, our net proceeds from our recently completed initial public offering will not be sufficient to complete clinical development of any of our product candidates. Accordingly, 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 program for the treatment of diabetic nephropathy in patients with type 2 diabetes, and the clinical development of an intravenous formulation of Pyridorin for AKI;
- the willingness of the EMA or other regulatory agencies outside the U.S. to accept our Phase 3 Pyridorin program, as well as our other completed and planned clinical and nonclinical studies and other work, as the basis for review and approval of Pyridorin in the European Union for the treatment of diabetic nephropathy in patients with type 2 diabetes;
- 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, including our product candidates in preclinical development;
- the ability of our product candidates to progress through clinical development successfully;
- our need to expand our research and development activities;

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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 defend 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 technological and market developments;

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 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 of our 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 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

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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 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;

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

- 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 candidates 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 our 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 may emerge;

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

- our ability to adhere to clinical study 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

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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 of 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 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. 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 and clinical studies, such as a thorough QT interval (TQT) clinical study, 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.

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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.

Although the FDA has agreed to our endpoint for approval, other regulatory agencies outside the United States, such as the EMA, 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 an additional clinical trial in order to seek approval outside the United States.

The EMA and 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 the EMA and other regulatory authorities may require us to perform. As such, any requirement by the EMA or 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.

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, 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 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, the age and condition of the patients, the stage and severity of disease, the nature of the protocol, the proximity of patients to clinical sites and the availability of effective treatments 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;

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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 participants 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;

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;

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;

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.

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 study (PYR-210). However, in a subgroup of patients on stable long term standard of care, Pyridorin showed a dose dependent treatment effect of approximately 50%. This subgroup is the

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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 trial will utilize a new 50% SCr increase event endpoint. 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 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.

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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 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

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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.

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.

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

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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 approve the manufacturing facilities of our future contract manufacturers 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 contract manufacturers for the production of the active pharmaceutical ingredients and the formulation of sufficient quantities 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 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 current good manufacturing practice 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

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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 current Good Manufacturing Practices (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.

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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 illegal 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; and

potential product liability claims.

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,

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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 contrast-dye-induced

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acute renal failure and ischemia-reperfusion 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 beyond the net proceeds of our recently completed initial public offering 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 assure you 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 our clinical trials for 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. We cannot assure you that additional or more severe adverse side effects with respect to Pyridorin will not 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, 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,

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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:

- the results of our and our potential strategic collaborators' clinical trials and preclinical studies;
- our ability to recruit and enroll 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 than our future products, if any, 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.

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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 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.

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

As of March 17, 2014, we had 6 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 will 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;
- 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.

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; J. Wesley Fox, our president and chief scientific officer; Bob Peterson, our vice president of product development and regulatory affairs; Pepper Landson, our vice president of clinical operations; 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

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addition, our advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours.

Failure to build our finance infrastructure and improve 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 Securities and Exchange Commission, 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 begun implementing our 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 anticipate that we will 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 retention of additional financial and accounting capabilities, 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 Securities and Exchange Commission. 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 Securities and Exchange Commission.

Until we are able to expand our finance and administrative capabilities and establish necessary financial reporting infrastructure, we may not be able to prepare and disclose, in a timely manner, our financial statements and other required disclosures or comply with the Sarbanes-Oxley Act or existing or new reporting requirements. 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

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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:

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 ($10 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 provided 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 ($1 million coverage), umbrella liability

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($2 million coverage), employment practices liability, property, auto, workers' compensation, and directors' and officers' insurance. We currently maintain products liability insurance ($10 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;
- reprioritize our development programs and even cease development and commercialization of our product candidates; or
- 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

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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 31, 2013, we were the owner of record or the licensee of 28 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 31, 2013, we were the owner of record of 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 2032. We own pending applications in the United States and Europe covering Pyridorin

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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 particular 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 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.

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

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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, the U.S. Supreme Court has recently 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:

- 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

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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

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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. 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.

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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 extremely limited and substantially less liquid than the average trading market for companies quoted on the NASDAQ Capital Market. 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 March 17, 2014, approximately 69.0% of our outstanding shares of common stock was 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. In addition, as of March 17, 2014, 6,624,907 shares of common stock, or 74.8% of our outstanding shares, were restricted from resale under securities laws or as a result of lock-up agreements, further limiting the liquidity of our common stock; however, such lock-up agreements will expire at the close of business on August 10, 2014.

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. Since our initial public offering which occurred in February 2014 until March 26, 2014, the price of our common stock on the NASDAQ Capital Market has ranged from $7.26 per share to $12.88 per share. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this Annual Report on Form 10-K, these factors include:

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;

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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.

Care Capital III LLC, together with its affiliates (collectively, Care Capital) is our largest stockholder. As of March 17, Care Capital beneficially owned 4,241,097 shares of our common stock. The shares of common stock beneficially owned by Care Capital represent approximately 47.9% 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

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the number of directors on our board from time to time. Richard Markham and Robert R. Seltzer, partners at Care Capital, were elected to our board of directors as nominees of Care Capital.

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 that we did not incur as a private company. In addition, our administrative staff is required to perform additional tasks and 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 Securities and Exchange Commission 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 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

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three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission.

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, 2014, 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 begin 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 or internal controls

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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.

A significant portion of our total outstanding shares of common stock is restricted from immediate resale but may be sold into the market in the near future. This could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur in the future. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock.

As of March 17, 2014, we had 8,855,114 shares of common stock outstanding. Of these shares, 2,389,787 shares may be resold in the public market immediately and the remaining 6,465,333 shares are currently restricted under securities laws or as a result of lock-up agreements entered into in connection with our initial public offering but will be able to be resold on August 10, 2014, the first day after the lock-up expires, subject to Rule 144. Sales of stock by these stockholders could have a material adverse effect on the trading price of our common stock.

Moreover, holders of an aggregate of 5,747,951 shares of our common stock will have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also intend to register all 676,923 shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance and once vested, subject to the 180 day lock-up periods under the lock-up agreements entered into in connection with our initial public offering.

Future sales and issuances of our common stock or rights to purchase common stock pursuant to our equity incentive plans could result in additional dilution of the percentage ownership of our stockholders and could cause our share price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

In connection with our initial public offering, we agreed, subject to limited exceptions, not to issue, sell or transfer any shares of common stock for 180 days after the date of the prospectus without the consent of Aegis Capital Corp. Our officers, directors and certain stockholders agreed prior to the commencement of our initial public offering, subject to limited exceptions, not to sell or transfer any shares of common stock for 180 days after the date of the prospectus without the consent of Aegis Capital Corp. However, Aegis Capital Corp. may release these shares from any restrictions at any time. We cannot predict what effect, if any, market sales of shares held by any stockholder or the availability of shares for future sale will have on the market price of our common stock.

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As of December 31, 2013, we had 563,855 options outstanding under our 2005 Plan. Sales of shares granted under our equity incentive plans may result in material dilution to our existing stockholders, which could cause our share price to fall.

As of December 31, 2013, we had 24,000 restricted stock units outstanding that were approved by our stockholders. In addition, we registered shares of our common stock underlying the warrants issued to the representative of the underwriters in connection with our initial public offering.

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 Global 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:

a 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;

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

a 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

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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 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

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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, 2013, we had federal net operating loss carryforwards (NOLs) of $23.9 million which expire from 2024 through 2033. 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.

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Item 1B. UNRESOLVED STAFF COMMENTS

None.

Item 2. PROPERTIES

Our corporate headquarters and clinical development operations are located in Research Triangle Park, North Carolina where we lease and occupy approximately 3,100 square feet of space. The lease for our office expired in December 2013 and is currently leased on a month-to-month basis. We intend to enter into a long-term lease in the near future. We believe that our facility is suitable and adequate for our current needs.

Item 3. LEGAL PROCEEDINGS

We are not a party to any legal proceedings and we are not aware of any claims or actions pending or threatened against us. In the future, we might from time to time become involved in litigation relating to claims arising from our ordinary course of business.

Item 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

Item 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our Common Stock began trading on the NASDAQ Capital Market on February 11, 2014 under the symbol "NRX". Prior to that there was no public market for our common stock. Shares sold in our initial public offering on February 10, 2014 were priced at $12.00 per share.

On March 17, 2014, the trading price for the common stock as reported on the NASDAQ Capital Market was $9.16. The following table sets forth the high and low sales prices for the Common Stock, as reported on the NASDAQ Capital Market since our common stock commenced public trading on February 11, 2014:

Year Ended December 31, 2014	High	Low
First Quarter (beginning February 11, 2014)	$ 12.88	$ 7.26

Stockholders

As of March 17, 2014, there were approximately 47 stockholders of record of the 8,855,114 outstanding shares of our common stock which excludes stockholders whose shares were held in nominee or street name by brokers.

Dividends

We have not paid dividends to our stockholders since our inception and we do not plan to pay cash dividends in the foreseeable future. We currently intend to retain earnings, if any, to finance the growth of our Company.

Equity Compensation Plans

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report.

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Unregistered Sales of Securities

Issuances of Convertible Notes

Between 2011 and 2013, the Company sold convertible promissory notes for approximately $7.9 million in aggregate to shareholders of the Company, pursuant to exemptions from registration provided by Section 4(2) of the Securities Act and/or Rule 506 of Regulation D promulgated under the Securities Act. These convertible promissory notes converted into common stock upon the closing of our initial public offering.

Stock option and other equity awards

On May 2, 2013, we granted stock options to purchase 91,261 shares of common stock with an exercise price of $2.02 per share pursuant to our 2005 Stock Option Plan, as amended and restated, to Pierre Legault, our Chief Executive Officer. The issuance of such options were exempt either pursuant to Rule 701 under the Securities Act, as a transaction pursuant to a compensatory benefit plan, or pursuant to Section 4(2) of the Securities Act, as a transaction by an issuer not involving a public offering.

In addition, on November 7, 2013, we agreed to grant Pierre Legault restricted stock units which represent the right to receive 24,000 shares of our common stock, subject to the terms and conditions of a restricted stock unit agreement and grant notice connected therewith. The grant of such restricted stock units was exempt either pursuant to Rule 701 under the Securities Act, as a transaction pursuant to a compensatory benefit plan, or pursuant to Section 4(2) of the Securities Act, as a transaction by an issuer not involving a public offering.

Issuer Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

Use of Proceeds from Registered Securities

On February 14, 2014, we completed our initial public offering of 3,100,000 shares of our common stock at a price of $12.00 per share for aggregate gross proceeds of approximately $37.2 million. The offer and sale of all of the shares in the offering were registered under the Securities Act pursuant to a registration statement on Form S-1, which was declared effective on February 10, 2014 (File No. 333-193023). Aegis Capital Corp. acted as sole book-running manager and underwriter for the. The offering commenced on February 10, 2014 and did not terminate until the sale of all of the shares offered.

We received aggregate net proceeds from the offering of approximately $33.4 million, after deducting approximately $2.6 million of underwriting discounts and commissions, and approximately $1.2 million of estimated offering expenses payable by us. None of the underwriting discounts and commissions or other offering expenses were incurred or paid to directors or officers of ours or their associates or to persons owning 10 percent or more of our common stock or to any affiliates of ours.

We have invested the net proceeds from the offering in a variety of capital preservation investments, including short-term, investment grade, interest bearing instruments such as commercial paper and corporate debt securities and U.S. government securities. There has been no material change in our planned use of the net proceeds from the offering as described in our final prospectus filed with the Securities and Exchange Commission pursuant to Rule 424(b) under the Securities Act on February 11, 2014. We have broad discretion in the use of the net proceeds from our initial public offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our stock.

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Item 6. SELECTED FINANCIAL DATA

Not required as we are a smaller reporting company.

Item 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in the forward-looking statements as a result of certain factors. We discuss factors that we believe could cause or contribute to these differences below and elsewhere in this report including those set forth under Item 1A."Risk Factors" in this Annual Report on Form 10-K.

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.

We have devoted substantially all of our resources to development efforts relating to our product candidate, including conducting clinical trials of our product candidate, providing general and administrative support for these operations and protecting our intellectual property. We do not have any products approved for sale and have not generated any revenue from product sales. From our inception until December 31, 2013, we have funded our operations primarily through the private placement of preferred stock, common stock and convertible notes totaling $32.0 million.

We have incurred net losses in each year since our inception in 2004. Our net losses were approximately $6.3 million and $2.9 million for the years ended December 31, 2013 and 2012, respectively. As of December 31, 2013, we had an accumulated deficit of approximately $41.0 million. Substantially all of our net losses resulted from costs incurred in connection with our research and development programs, from general and administrative costs associated with our operations and as a result of a change in value of preferred stock warrants.

We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We anticipate that our expenses will increase substantially as we:

- complete the development of our lead product candidate, Pyridorin, for the treatment of diabetic nephropathy in patients with type 2 diabetes;
- complete the development of an intravenous formulation of Pyridorin for the treatment of AKI;
- seek to obtain regulatory approvals for Pyridorin;
- outsource the commercial manufacturing of Pyridorin for any indications for which we receive regulatory approval;
- contract with third parties for the sales, marketing and distribution of Pyridorin for any indications for which we receive regulatory approval;

maintain, expand and protect our intellectual property portfolio;

continue our research and development efforts;

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add operational, financial and management information systems and personnel, including personnel to support our product development and commercialization efforts; and

operate as a public company.

We do not expect to generate revenue from product sales unless and until we successfully complete development and obtain marketing approval for one or more of our product candidates, which we expect will take a number of years and is subject to significant uncertainty. Accordingly, we anticipate that we will need to raise additional capital prior to the commercialization of Pyridorin or any other product candidate. Until such time, if ever, as we can generate substantial revenue from product sales, we expect to finance our operating activities 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. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and our ability to develop our product candidates.

Financial Overview

Revenue

We did not have any revenue during the period from May 25, 2004 (inception) through December 31, 2013. Our ability to generate revenue in the future will depend almost entirely on our ability to successfully develop, obtain regulatory approval for and then successfully commercialize Pyridorin in the United States. In the event we choose to pursue a partnering arrangement to commercialize Pyridorin or other products outside the United States, we would expect to initiate additional research and development and clinical trial activities in the future.

Research and Development Expenses

Since our inception, we have focused our resources on our research and development activities, including conducting nonclinical studies and clinical trials, manufacturing development efforts and activities related to regulatory filings for Pyridorin. We recognize research and development expenses as they are incurred. Our research and development expenses consist primarily of:

salaries and related overhead expenses for personnel in research and development functions;

fees paid to consultants and CROs, including in connection with our nonclinical and clinical trials, and other related clinical trial fees, such as for investigator grants, patient screening, laboratory work, clinical trial database management, clinical trial material management and statistical compilation and analysis;

costs related to acquiring and manufacturing clinical trial materials;

depreciation of leasehold improvements, laboratory equipment and computers;

costs related to compliance with regulatory requirements; and

costs related to stock options or other stock-based compensation granted to personnel in research and development functions.

From inception through December 31, 2013, we have incurred approximately $28.9 million in research and development expenses. We plan to increase our research and development expenses for the foreseeable future as we continue the development of Pyridorin for the treatment of diabetic nephropathy in patients with type 2 diabetes and other indications, subject to the availability of additional funding.

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The table below summarizes our direct research and development expenses by program for the periods indicated. Our direct research and development expenses consist principally of external costs, such as fees paid to investigators, consultants, central laboratories and CROs, in connection with our clinical trials, and costs related to acquiring and manufacturing clinical trial materials. We do not allocate salaries, stock-based compensation, employee benefit or other indirect costs related to our research and development function to specific product candidates. Those expenses are included in "Indirect research and development expense" in the table below.

	Years Ended December 31,	
	2013	2012
Direct research and development expense	$	$ 757,934
Personnel costs	940,632	955,100
Indirect research and development expense	538,841	639,147
Total research and development expense	$ 1,479,473	$ 2,352,181

The successful development of our clinical and preclinical product candidates is highly uncertain. At this time, we cannot reasonably estimate the nature, timing or costs of the efforts that will be necessary to complete the remainder of the development of any of our clinical or preclinical product candidates or the period, if any, in which material net cash inflows from these product candidates may commence. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- the scope, rate of progress and expense of our ongoing, as well as any additional, clinical trials and other research and development activities;
- future clinical trial results; and
- the timing and receipt of any regulatory approvals.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development of a product candidate or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

Pyridorin

The majority of our research and development resources are focused on the Phase 3 Pyridorin program and our other planned clinical and nonclinical studies and other work needed to submit Pyridorin for the treatment of diabetic nephropathy in patients with type 2 diabetes for regulatory approval in the United States and Europe. We have incurred and expect to continue to incur expense in connection with these efforts, including:

- working with our CRO to prepare for launch of the Phase 3 trial;
- working with our third-party drug formulator to produce sufficient drug product for the Phase 3 program and other contemplated trials; and
- working with our CRO to conduct a thorough QT interval (TQT) trial.

In addition, we are evaluating the application of an intravenous formulation of Pyridorin to specific types of acute renal failure in which pathogenic oxidative chemistries have been identified as likely causative factors in the onset, severity and progression of this condition. These include

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contrast-dye-induced acute renal failure and ischemia-reperfusion acute renal injury, which can arise in cardiac and vascular surgeries. In connection with these efforts, we have incurred and expect to incur significant expenses relating to:

- working with research institutions with expertise using animal models of various types of acute renal injury to conduct studies to determine where Pyridorin would have the most beneficial effect in ameliorating the severity and progression of the induced acute renal injury; and

- working with a third-party drug formulator to produce intravenous Pyridorin solutions for preclinical and clinical studies.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs for employees in executive, operational, finance and human resources functions. Other significant general and administrative expenses include allocation of facilities costs, professional fees for directors, accounting and legal services and expenses associated with obtaining and maintaining patents.

We expect that our general and administrative expenses will increase as we operate as a public company and due to the potential commercialization of Pyridorin. We believe that these increases will likely include increased costs for director and officer liability insurance, costs related to the hiring of additional personnel and increased fees for outside consultants, lawyers and accountants. We also expect to incur increased costs to comply with corporate governance, internal controls and similar requirements applicable to public companies.

Other Income

Other income consists of interest income earned on our cash and cash equivalents, interest expense pertaining to interest accrued on our convertible notes and the change in value of our preferred stock warrants. Each of the noteholders has converted their notes into common stock and the preferred stock warrants were settled in 2014.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with generally accepted accounting principles in the United States (GAAP). The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenues and expenses during the reporting periods. We evaluate these estimates and judgments on an ongoing basis. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in note B to our financial statements appearing elsewhere in the prospectus, we believe that the following accounting policies are the most critical for fully understanding and evaluating our financial condition and results of operations.

Fair Value of Financial Instruments

FASB ASC 820 *Fair Value Measurements and Disclosures*, defines fair value as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between

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market participants at the measurement date. FASB ASC 820 requires disclosures about the fair value of all financial instruments, whether or not recognized, for financial statement purposes. The estimates presented in these financial statements are not necessarily indicative of the amounts that could be realized on disposition of the financial instruments.

FASB ASC 820 specifies a hierarchy of valuation techniques based on whether the inputs to those valuation techniques are observable or unobservable. Observable inputs reflect market data obtained from independent sources, while unobservable inputs reflect market assumptions. The hierarchy gives the highest priority to unadjusted quoted prices in active markets for identical assets or liabilities (Level 1 measurement) and the lowest priority to unobservable inputs (Level 3 measurement).

The three levels of the fair value hierarchy are as follows:

Level 1 Quoted prices in active markets for identical assets or liabilities that the reporting entity has the ability to access at the measurement date. Level 1 primarily consists of financial instruments whose value is based on quoted market prices such as exchange-traded instruments and listed equities.

Level 2 Inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly. Level 2includes financial instruments that are valued using models or other valuation methodologies. These models consider various assumptions, including volatility factors, current market prices and contractual prices for the underlying financial instruments. Substantially all of these assumptions are observable in the marketplace, can be derived from observable data or are supported by observable levels at which transactions are executed in the marketplace.

Level 3 Unobservable inputs for the asset or liability. Financial instruments are considered Level 3 when their fair values are determined using pricing models, discounted cash flows or similar techniques and at least one significant model assumption or input is unobservable.

The carrying amounts reported in the balance sheet for cash and cash equivalents, accounts payable and accrued expenses approximate their fair value based on the short-term maturity of these instruments. The carrying amounts reported in the balance sheet for notes payable approximate their fair value based on market rates of interest and the terms of the notes. We recognize all derivative financial instruments as assets or liabilities in the financial statements and measures them at fair value with changes in fair value reflected as current period income or loss unless the derivatives qualify as hedges.

Research and development costs

Costs incurred in connection with research and development activities are expensed as incurred. These costs include licensing fees to use certain technology in our research and development projects as well as fees paid to consultants and various entities that perform certain research and testing on our behalf.

Stock based compensation

We recognize compensation cost relating to share-based payment transactions in net loss using a fair-value measurement method, in accordance with Financial Accounting Standards Board Accounting Standards Codification (ASC)-718 "Compensation-Stock Compensation". ASC-718 requires all share based payments to employees, including grants of employee stock option, to be recognized in operating results as compensation expense based on fair value over the requisite service period of the awards. We determine the fair value of share-based awards using the Black-Scholes option-pricing model which uses both historical and current market data to estimate fair value. The method incorporates various assumptions such as the risk-free interest rate, expected volatility, expected dividend yield, expected

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forfeiture rate and expected life of the options. We have also granted stock options to nonemployees. Grants to non-employees are accounted for in accordance with ASC-505-50 Equity-Based Payments to Non-Employees. We determine the fair value of share based awards granted to nonemployees similar to the way fair value of awards are determined for employees except that certain assumptions used in the Black-Scholes option-pricing model, such as expected life of the option, maybe different and the fair value of each award is adjusted at the end of each period for any change in fair value from the previous valuation until the award vests.

In December 2013, we engaged an independent third-party to conduct a valuation of our common stock as of December 15, 2013, and the common stock was valued at $5.79 per share as of such date.

The appreciation in stock value from $5.79 per share as of December 31, 2013 to $12.00 per share in the initial public offering principally reflects the successful initial public offering and the increase in the likelihood of bringing an approved drug to the market increased.

Specifically, the difference between the fair value of $2.02 per common share used to value stock options granted during the year ended December 31, 2013 and the initial public offering price is primarily the result of the following company specific and external factors:

Key business milestones:

On November 7, 2013 and December 12, 2013, we hired Pierre Legault as Chief Executive Officer and John Hamill as Chief Financial Officer, respectively. Each of Mr. Legault and Mr. Hamill are experienced executives with extensive experience in the biotechnology sector.

In October 2013, we hired the underwriter for our initial public offering and conducted an organizational meeting.

In November 2013, we made an initial confidential submission of a draft registration statement on Form S-1 for our initial public offering.

Based upon preliminary discussions with our investors and potential investors, we believed that there would be interest in investing in a company with our profile and at our stage of development.

In December 2013, we entered into a Manufacturing Agreement with Patheon to formulate adequate drug product to initiate our Phase 3 trial.

In November and December 2013, we raised $1.0 million and $1.65 million, respectively, of additional funding through the issuance of convertible notes.

While we entered into an SPA with the FDA in April 2013, until we begin our Phase 3 trial and know that we have the funds to proceed, it is our view that the values of the SPA will not have been realized.

The proceeds from our initial public offering greatly enhanced our ability to conduct the clinical trials contemplated by the SPA referenced above.

Market and other external factors:

Since December 2013, the market conditions specific to the biotechnology industry continued to perform well and demonstrated receptivity to investing in earlier stage biotechnology companies, as evidenced by the NASDAQ Biotechnology Index, which was up approximately 28% during the second half of 2013.

Our initial public offering price took into account that the initial public offering had occurred, a public market for our common stock had been created and that our preferred stock and outstanding convertible notes each converted into common stock in connection with the initial

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public offering, and, therefore excluded any discount for lack of marketability of our common stock, which was factored into our estimated value in December 2013.

Upon closing of our initial public offering, all outstanding shares of preferred stock converted into common stock, thus eliminating the superior rights and preferences of our preferred stock as compared to our common stock.

JOBS Act

On April 5, 2012, the JOBS Act was enacted. Section 107 of the JOBS Act provides that an "emerging growth company" can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended (the Securities Act), for complying with new or revised accounting standards. In other words, an "emerging growth company" can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to use the extended transition period for complying with new or revised accounting standards under Section 102(b)(1) of the JOBS Act. This election allows us to delay the adoption of new or revised accounting standards that have different effective dates for public and private companies until those standards apply to private companies. As a result of this election, our financial statements may not be comparable to companies that comply with public company effective dates.

We are in the process of evaluating the benefits of relying on other exemptions and reduced reporting requirements provided by the JOBS Act. Subject to certain conditions set forth in the JOBS Act, as an "emerging growth company," we intend to rely on certain of these exemptions, including without limitation, (i) providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and (ii) complying with any requirement that may be adopted by the PCAOB regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis. 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 Securities and Exchange Commission.

Results of Operations

Comparison of the Year Ended December 31, 2013 and the Year Ended December 31, 2012

The following table summarizes our results of operations for each of the years ended December 31, 2013 and 2012, together with the changes in those items in dollars and as a percentage:

	Years Ended December 31,		Dollar	
	2013	2012	Change	% Change
Expenses:				
Research and development	$ 1,479,473	$ 2,352,181	$ (872,708)	(37.1)%
General and administrative	1,026,238	349,686	$ 676,552	193.5%
Loss from operations	(2,505,711)	(2,701,867)	$ 196,156	(7.3)%
Other Income (expense):				
Change in value of preferred stock warrants	(3,416,838)	(1,800)	(3,415,038)	189,724.3%
Interest expense	(382,986)	(201,554)	(181,432)	90.0%
Interest income	872	1,057	(185)	(17.5)%
Net loss	$ (6,304,663)	$ (2,904,164)	$ (3,400,499)	117.1%

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Research and Development Expenses

Research and development expenses were $1.5 million and $2.4 million for the years ended December 31, 2013 and 2012, respectively, representing a decrease of approximately $1.0 million, or 37.1%. This decrease in research and development expense primarily reflects our work with the FDA to obtain a new endpoint for the Pyridorin Phase 3 study including the assistance of clinical, medical and biostatistician consultants in data analyses and meetings and correspondence with the FDA. This work was largely completed in 2012, and therefore the observed decrease in research and development expense reflects the discontinuation of their services.

General and Administrative Expenses

General and administrative expenses were approximately $1.0 million and $350,000 for the years ended December 31, 2013 and 2012, respectively, representing an increase of approximately $677,000, or 193.5%. This increase in general and administrative expenses was primarily a result of meetings with numerous pharmaceutical companies and potential investors to initiate and build interest in our product opportunity after reaching agreement with the FDA on a SPA for the required clinical trials necessary for Pyridorin approval and registration. This effort resulted in an increase in travel and business consulting expenses over the corresponding period from the previous year.

Interest Expense, Net

Interest expense, net was approximately $382,000 and $200,000 for the years ended December 31, 2013 and 2012, respectively, representing an increase of approximately $182,000, or 91.0%. This increase in interest expense, net was primarily a result of increased interest costs associated with convertible promissory notes we have used to finance our operations since the conclusion of the Pyridorin Phase 2b study.

Liquidity and Capital Resources

Sources of Liquidity

We have incurred losses and cumulative negative cash flows from operations since our inception in May 2004 and, as of December 31, 2013, we had an accumulated deficit of $41.0 million. We anticipate that we will continue to incur losses for at least the next several years. We expect that our research and development and general and administrative expenses will continue to increase and, as a result, we will need additional capital to fund our operations, which we may seek to obtain 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.

Since our inception through December 31, 2013, we have funded our operations principally with $32.0 million from the sale of common stock, preferred stock and convertible notes and approximately $244,000 from a government grant. As of December 31, 2013, we had cash and cash equivalents of approximately $2.1 million. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation. Currently, our funds are held in cash and money market bank accounts.

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The gross proceeds we have received from the issuance and sale of common stock, convertible notes and preferred stock, as of December 31, 2013, are as follows:

Securities Issued	Year	Number of Shares	Gross Proceeds
Convertible notes	2004 - 2013		$ 9,471,870
Common stock	2004 - 2010	12,169	$ 6,136
Series A preferred stock	2007/2008/2010	20,255,126	$ 22,500,000
Total		20,267,295	$ 31,978,006

On February 14, 2014, we closed our initial public offering of 3,100,000 shares of common stock at a price of $12.00 per share for total gross proceeds of $37,200,000, less underwriting discounts and commissions.

Cash Flows

The following table sets forth the significant sources and uses of cash for the periods set forth below:

	Years Ended December 31,	
	2013	2012
Net cash provided by (used in):		
Operating activities	$ (2,712,297)	$ (2,170,701)
Investing activities	(11,810)	
Financing activities	4,532,419	1,254,822
Net increase (decrease) in cash and cash equivalents	$ 1,808,312	$ (915,879)

Operating Activities.

Net cash used in operating activities of $2.7 million during the year ended December 31, 2013 was primarily a result of our net loss, offset by the add-back of non-cash items of approximately $3.4 million for the change in fair value of preferred stock warrants and $471,000 for non-cash stock-based compensation and interest expense.

Investing Activities. Net cash used in investing activities during the year ended December 31, 2013 primarily reflected our use of cash to purchase equipment.

Financing Activities. Net cash provided by financing activities in the years ended December 31, 2013 and 2012 consisted of approximately $4.5 million and $1.3 million, respectively, of net proceeds from the sale of convertible notes.

Future Funding Requirements

To date, we have not generated any revenue. We do not know when, or if, we will generate any revenue from product sales. We do not expect to generate significant revenue from product sales unless and until we obtain regulatory approval of and commercialize Pyridorin or any of our other product candidates. At the same time, we expect our expenses to increase in connection with our ongoing development activities, particularly as we continue the research, development and clinical trials of, and seek regulatory approval for, our product candidates. We expect to incur additional costs associated with operating as a public company. In addition, subject to obtaining regulatory approval of any of our

product candidates, we expect to incur significant commercialization expenses for product sales,

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marketing, manufacturing and distribution. We anticipate that we will need substantial additional funding in connection with our continuing operations.

Based upon our current operating plan and after receiving the proceeds from our initial public offering in February 2014, we believe that our existing cash, cash equivalents and short-term investments, will enable us to fund our operating expenses and capital expenditure requirements into 2016. We intend to devote our cash to fund our Phase 3 Pyridorin program and our planned clinical trials and nonclinical studies and other work needed to submit applications for Pyridorin for the treatment of diabetic nephropathy in patients with type 2 diabetes for regulatory approval in the United States and Europe; to fund further preclinical and Phase 1 & 2 development work on an intravenous formulation of Pyridorin for AKI in which pathogenic oxidative chemistries have been identified as a possible contributing factor in the severity of this condition; and for general corporate purposes, general and administrative expenses, capital expenditures, working capital and prosecution and maintenance of our intellectual property. We have based our estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures necessary to complete the development of our product candidates.

Our future capital requirements will depend on many factors, including:

- the progress, costs, results of and timing of our Phase 3 Pyridorin program for the treatment of diabetic nephropathy in patients with type 2 diabetes, and the clinical development of an intravenous formulation of Pyridorin for AKI;
- the willingness of the EMA or other regulatory agencies outside the U.S. to accept our Phase 3 Pyridorin program, as well as our other completed and planned clinical and nonclinical studies and other work, as the basis for review and approval of Pyridorin in the European Union for the treatment of diabetic nephropathy in patients with type 2 diabetes;
- 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, including our product candidates in preclinical development;
- 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 defend 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 technological and market developments;

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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.

Until such time, if ever, as we can generate substantial revenue from product sales, we expect to finance our cash needs 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. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our common stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through government or other third-party funding, commercialization, marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us.

Contractual Obligations and Commitments

As of December 31, 2013, we had contractual obligations of approximately $650,000 relating to interest on our outstanding convertible notes.

We are a party to license agreements with universities and other third parties, as well as patent assignment agreements, under which we have obtained rights to patents, patent applications and know-how. These license agreements are subject to various milestone payments related to milestones met in the FDA regulatory approval process. In July 2008, we made a $25,000 payment to the University of Kansas Medical Center Research Institute, Inc. (University of Kansas) upon the completion and FDA acceptance of our Phase I clinical trials.

We have employment agreements with certain employees which require the funding of specific levels of payments, if certain events, such as a change in control or termination without cause, occur. We enter into contracts in the normal course of business with CROs for clinical trials and clinical supply manufacturing and with vendors for preclinical research studies and other services and products for operating purposes, which generally provide for termination within 30 days of notice or less, and therefore are cancelable contracts and not included as contractual obligations and commitments.

Net Operating Losses

As of December 31, 2013, we had federal net operating loss carryforwards, or NOLs, of approximately $23.9 million which expire from 2024 through 2033. 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.

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Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements as defined under Securities and Exchange Commission rules.

Recent Accounting Pronouncements

In June 2011, the FASB issued ASU 2011-05, "Comprehensive Income (Topic 220) Presentation of Comprehensive Income" which amends ASC 220, "Comprehensive Income". ASU 2011-05 gives an entity the option to present the total comprehensive income, the components of net income, and the components of other comprehensive income either in a single continuous statement of comprehensive income or in two separate but consecutive statements. ASU 2011-05 is effective for fiscal years, and interim periods within those years, beginning after December 15, 2011. We did not have any other comprehensive income related transactions during the years ended December 31, 2013 or 2012 and as such did not present required statements.

In December 2011, the FASB issued ASU 2011-12 "Deferral of the Effective Date for Amendments to the Presentation of Reclassifications of Items out of Accumulated Other Comprehensive Income in Accounting Standards Update No. 2011-05." This update stated that the specific requirement to present items that are reclassified from other comprehensive income to net income alongside their respective components of net income and other comprehensive income will be deferred. In February 2013, the FASB issued ASU 2013-02 "Reporting of Amounts Reclassified Out of Accumulated Other Comprehensive Income". This update requires companies to present the effects on the line items of net income of significant reclassifications out of accumulated other comprehensive income if the amount being reclassified is required under GAAP to be reclassified in its entirety to net income in the same reporting period. ASU 2013-02 is effective prospectively for the Company for fiscal years, and interim periods within those years, beginning after December 15, 2013. The Company does not expect its adoption to have a material impact on our financial statements.

Basic and Diluted Net Loss Attributable to Common Stockholders per Common Share

Our Series A preferred stock represent participating securities. However, since we operate at a loss, and losses are not allocated to the preferred stock, the two class method does not affect our calculation of earnings per share. We had a net loss for all periods presented; accordingly, the inclusion of common stock options would be anti-dilutive.

Dilutive common stock equivalents would include the dilutive effect of convertible securities, common stock and options for common stock. Potentially dilutive common stock equivalents totaled approximately 563,855 common stock options and 24,000 restricted stock units for the year ended December 31, 2013. Potentially dilutive common stock equivalents were excluded from the diluted earnings per share denominator for all periods because of their anti-dilutive effect. Therefore, the weighted average shares used to calculate both basic and diluted earnings per share are the same.

Quantitative and Qualitative Disclosure About Market Risk

Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates.

Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10.0% change in interest rates would not have a material effect on the fair market value of our portfolio. Accordingly, we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a sudden change in market interest rates on our investment portfolio.

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We do not believe that our cash and cash equivalents have significant risk of default or illiquidity. While we believe our cash and cash equivalents do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. In addition, at times we maintain significant amounts of cash and cash equivalents at one or more financial institutions that are in excess of federally insured limits.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material effect on our results of operations during 2012 or 2013.

Item 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Not required as we are a smaller reporting company.

Item 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The financial statements required to be filed pursuant to this Item 8 are appended to this report. An index of those financial statements is found in Item 15.

Item 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

Item 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our principal executive officer and principal financial officer, after evaluating the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended) as of the end of the period covered by this Annual Report on Form 10-K, have concluded that, based on such evaluation, our disclosure controls and procedures were adequate and effective. In designing and evaluating our disclosure controls and procedures, our management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and our management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Management's Report on Internal Control over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by rules of the SEC for newly public companies.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting, identified in connection with the evaluation of such internal control, that occurred during the last fiscal quarter that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. OTHER INFORMATION

Not applicable.

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PART III

Item 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this Item concerning our directors is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2014 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

Item 11. EXECUTIVE COMPENSATION

The information required by this Item concerning our directors is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2014 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

Item 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this Item concerning our directors is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2014 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

Item 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this Item concerning our directors is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2014 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

Item 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this Item concerning our directors is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2014 Annual Meeting of Stockholders, which we intend to file with the SEC within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

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PART IV

Item 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

Financial Statements and Schedules

(a)

The following documents are filed as part of this report:

(1) Financial Statements:

(2) Financial Statement Schedules:

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(3) Exhibits. The exhibits filed as part of this Annual Report on Form 10-K are set forth on the Exhibit Index immediately following our consolidated financial statements. The Exhibit Index is incorporated herein by reference.

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SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: March 31, 2014

NephroGenex, Inc.

By: /s/ PIERRE LEGAULT

Pierre Legault

Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities indicated below and on the dates indicated.

Signature	Title	Date
/s/ PIERRE LEGAULT Pierre Legault	Chief Executive Officer and Director (Principal Executive Officer)	March 31, 2014
/s/ JOHN P. HAMILL John P. Hamill	Chief Financial Officer (Principal Financial and Accounting Officer)	March 31, 2014
/s/ RICHARD MARKHAM Richard Markham	Chairman of the Board of Directors	March 31, 2014
/s/ J. WESLEY FOX J. Wesley Fox, Ph.D.	Director	March 31, 2014
/s/ JAMES MITCHUM James Mitchum	Director	March 31, 2014
/s/ ROBERT R. SELTZER Robert R. Seltzer	Director	March 31, 2014
/s/ EUGEN STEINER, M.D. Eugen Steiner, M.D.	Director	March 31, 2014
/s/ MARTIN VOGELBAUM Martin Vogelbaum	Director	March 31, 2014

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders
NephroGenex, Inc.

We have audited the accompanying balance sheets of NephroGenex, Inc., a Development Stage Company, (the "Company") as of December 31, 2013 and 2012, and the related statements of operations, stockholders' deficiency, and cash flows for each of the years in the two-year period ended December 31, 2013 and the cumulative period from May 25, 2004 (inception) to December 31, 2013. The financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of NephroGenex, Inc. as of December 31, 2013 and 2012, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2013 and the cumulative period from May 25, 2004 (inception) to December 31, 2013, in conformity with accounting principles generally accepted in the United States of America.

Jenkintown, Pennsylvania
March 31, 2014

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NEPHROGENEX, INC.

(A Development Stage Company)

Balance Sheets

	December 31, 2013	December 31, 2012
Assets		
Current assets		
Cash and cash equivalents	**$ 2,131,990**	$ 323,678
Prepaid expenses and other assets	**11,711**	24,022
Total current assets	**2,143,701**	347,700
Property and equipment, net	**10,826**	3,143
Deferred initial public offering costs	**461,079**	
Other assets	**4,097**	13,586
Total assets	**$ 2,619,703**	$ 364,429
Liabilities and Stockholders' Deficiency		
Current liabilities		
Accounts payable	**$ 47,865**	$ 77,920
Accrued and other liabilities	**1,858,061**	1,334,972
Preferred stock warrant liability	**6,982,640**	3,565,802
Convertible notes payable	**7,916,870**	3,354,822
Total current liabilities	**16,805,436**	8,333,516
Stockholders' deficiency		
Series A preferred stock: $.001 par value; 32,690,676 shares authorized; 23,688,396 shares issued and outstanding as of December 31, 2013 and 2012	**23,688**	23,688
Common stock; $.001 par value; 39,751,707 shares authorized; 319,896 shares issued and outstanding as of December 31, 2013 and 2012	**320**	320
Additional paid-in capital	**26,789,465**	26,701,448
Deficit accumulated during the development stage	**(40,999,206)**	(34,694,543)
Total stockholders' deficiency	**(14,185,733)**	(7,969,087)
Total liabilities and stockholders' deficiency	**$ 2,619,703**	$ 364,429

See accompanying notes to financial statements

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NEPHROGENEX, INC.

(A Development Stage Company)

Statements of Operations

	Year Ended December 31, 2013	Year Ended December 31, 2012	Cumulative Period From May 25, 2004 (inception) to December 31, 2013
Expenses			
Research and development	**$ 1,479,473**	$ 2,352,181	$ 29,007,865
General and administrative	**1,026,238**	349,686	4,451,044
Total expenses	**2,505,711**	2,701,867	33,458,909
Loss from operations	**(2,505,711)**	(2,701,867)	(33,458,909)
Other income (expense):			
Change in value of preferred stock warrants	**(3,416,838)**	(1,800)	(7,037,734)
Interest expense	**(382,986)**	(201,554)	(1,432,765)
Interest income	**872**	1,057	685,723
Qualifying Therapeutic Discovery Program grant			244,479
Net loss and comprehensive loss	**$ (6,304,663)**	$ (2,904,164)	$ (40,999,206)
Net loss per share, basic and diluted	**$ (19.71)**	$ (9.08)	$ (211.37)
Weighted average shares outstanding, basic and diluted	**319,896**	319,896	193,967

See accompanying notes to financial statements

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NEPHROGENEX, INC.

(A Developmental Stage Company)

Statement of Stockholders' Deficiency

	Series A Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated During the Development Stage	Total
	Shares	Amount	Shares	Amount			
Balance at May 25, 2004 (inception)		$		$	$	$	$
Sale of common stock for cash in May 2004 at $0.05 per share			1,692	2	548		550
Net loss						(129,923)	(129,923)
Balance at December 31, 2004			1,692	2	548	(129,923)	(129,373)
Net loss						(688,915)	(688,915)
Balance at December 31, 2005			1,692	2	548	(818,838)	(818,288)
Issuance of shares to BioStratum, Inc. (Note G)			12,708	13	4,948		4,961
Issuance of shares and warrant to Vanderbilt University (Note G)			462		6,910		6,910
Issuance of shares to Tryggvason Biotech AB (Note G)			154		60		60
Net loss						(1,337,715)	(1,337,715)
Balance at December 31, 2006			15,016	15	12,466	(2,156,553)	(2,144,072)
Issuance of Series A preferred stock for cash, licensed technology and the conversion of debt in May 2007 (Note E)	4,783,612	4,784			2,498,539		2,503,323
Issuance of shares to FibroStatin, SL (Note G)			154		5,000		5,000
Exercise of warrant by Vanderbilt University (Note G)			17,257	17	(17)		
Sale of Series A preferred stock for cash in December 2007	1,800,456	1,800			2,243,602		2,245,402
Net loss						(7,570,642)	(7,570,642)
Balance at December 31, 2007	6,584,068	6,584	32,427	32	4,759,590	(9,727,195)	(4,960,989)
Issuance of Series A preferred stock and common stock in March 2008 (Note E)	16,204,100	16,204	45,234	45	20,214,872		20,231,121
Issuance of common stock to BioStratum, Inc. (Note G)			207,744	208	80,813		81,021
Issuance of common stock to Vanderbilt University (Note G)			24,014	24	9,341		9,365
Stock based compensation					115,347		115,347
Net loss						(6,740,834)	(6,740,834)
Balance at December 31, 2008	22,788,168	22,788	309,419	309	25,179,963	(16,468,029)	8,735,031
Stock based compensation					126,725		126,725
Net loss						(7,549,788)	(7,549,788)
Balance at December 31, 2009	22,788,168	22,788	309,419	309	25,306,688	(24,017,817)	1,311,968
Issuance of common stock upon exercise of stock options			10,477	11	5,575		5,586
Sale of Series A preferred stock in July 2010	900,228	900			999,100		1,000,000
Stock based compensation					139,209		139,209
Net loss						(5,920,765)	(5,920,765)
Balance at December 31, 2010	23,688,396	23,688	319,896	320	26,450,572	(29,938,582)	(3,464,002)

Stock based compensation					125,370		125,370
Net loss						(1,851,797)	(1,851,797)
Balance at December 31, 2011	23,688,396	23,688	319,896	320	26,575,942	(31,790,379)	(5,190,429)
Stock based compensation					125,506		125,506
Net loss						(2,904,164)	(2,904,164)
Balance at December 31, 2012	23,688,396	23,688	319,896	320	26,701,448	(34,694,543)	(7,969,087)
Stock based compensation					88,017		88,017
Net loss						(6,304,663)	(6,304,663)
Balance at December 31, 2013	23,688,396	$ 23,688	319,896	$ 320	$ 26,789,465	$ (40,999,206)	$ (14,185,733)

See accompanying notes to financial statements

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NEPHROGENEX, INC.

(A Developmental Stage Company)

Statements of Cash Flows

	Year Ended December 31, 2013	Year Ended December 31, 2012	Cumulative Period from May 25, 2004 (Inception) to December 31, 2013
Cash flows from operating activities			
Net loss	**$ (6,304,663)**	$ (2,904,164)	$ (40,999,206)
Adjustments to reconcile net loss to net cash and cash equivalents used in operating activities			
Depreciation and amortization	**4,127**	20,803	106,179
Common stock issued in consideration for research and development			1,218,297
Change in fair value of preferred stock warrants	**3,416,838**	1,800	7,037,734
Non-cash interest expense	**382,986**	201,554	1,408,868
Stock based compensation expense	**88,017**	125,506	720,174
Changes in operating assets and liabilities Prepaid expenses and other assets	**21,800**	5,283	(15,808)
Accounts payable, accrued and other liabilities	**(321,402)**	378,517	824,380
Net cash and cash equivalents used in operating activities	**(2,712,297)**	(2,170,701)	(29,699,382)
Cash flows from investing activities			
Property and equipment purchases	**(11,810)**		(117,005)
Net cash and cash equivalents used in investing activities	**(11,810)**		(117,005)
Cash flows from financing activities			
Proceeds from issuance of notes payable			1,655,000
Payment of note payable			(100,000)
Proceeds from issuance of convertible notes payable	**4,562,048**	1,254,822	7,916,870
Payment of deferred initial public offering costs	**(29,629)**		(29,629)
Proceeds from issuance of common stock, Series A preferred stock and warrants			22,500,550
Proceeds from exercise of common stock options			5,586
Net cash and cash equivalents provided by financing activities	**4,532,419**	1,254,822	31,948,377
Net increase (decrease) in cash and cash equivalents	**1,808,312**	(915,879)	2,131,990
Cash and cash equivalents			
Beginning of period	**$ 323,678**	1,239,557	
End of period	**$ 2,131,990**	$ 323,678	$ 2,131,990

Supplemental disclosure of cash flow information				
Cash paid for interest	**$**		$	$ 4,690
Supplemental disclosure of noncash financing activities				
Conversion of notes payable into Series A preferred stock and warrants	**$**		$	$ 1,555,000
Conversion of accrued interest into Series A preferred stock and warrants	**$**		$	$ 758,772
Increase in paid-in capital resulting from exercise of warrant	**$**		$	$ 2,458,882
Deferred initial public offering costs included in accrued and other liabilities	**$**	**431,450**	$	$ 431,450

See accompanying notes to financial statements

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NEPHROGENEX, INC.

(A Development Stage Company)

Notes to Financial Statements

December 31, 2013 and 2012 and the period from May 25, 2004 (inception) to December 31, 2013

NOTE A ORGANIZATION, HISTORY AND NATURE OF OPERATIONS

NephroGenex, Inc. (the "Company") was incorporated in Delaware on May 25, 2004. The Company is a drug development company focused on developing novel therapies for kidney disease. The Company acquired commercial rights to Pyridorin and conducted a Phase 2b clinical study in diabetic nephropathy patients.

As a development stage enterprise, the Company's primary efforts to date have been devoted to raising capital, recruiting senior management and staff and performing research and development. The Company has had limited capital resources and has experienced recurring net losses and negative cash flows from operations since inception. Operations have been financed to date by debt and equity financings as discussed in Note E. On February 14, 2014, the Company closed its initial public offering of 3,100,000 shares of common stock at a price of $12.00 per share for total gross proceeds of $37,200,000, less underwriting discounts and commissions as discussed in Note M.

In addition to the normal risks associated with a new business venture, the Company currently has no commercially approved products and there can be no assurance that the Company's research and development will be successfully commercialized. Developing and commercializing a product requires significant time and capital and is subject to regulatory review and approval as well as competition from other biotechnology and pharmaceutical companies. The Company operates in an environment of rapid change and is dependent upon the continued services of its employees and consultants and obtaining and protecting intellectual property.

NOTE B SIGNIFICANT ACCOUNTING POLICIES

[1] Basis of presentation:

The financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP").

From its inception the Company has devoted substantially all of its efforts to business planning, engaging regulatory, manufacturing and other technical consultants, acquiring operating assets, planning clinical trials and raising capital. Accordingly, the Company is considered to be in the development stage as defined in Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") 915: *Development Stage Entities.*

[2] Use of estimates:

The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosures of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

[3] Cash and cash equivalents:

The Company considers all highly liquid investments with original maturities of three months or less to be cash equivalents.

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NEPHROGENEX, INC.

(A Development Stage Company)

Notes to Financial Statements (Continued)

December 31, 2013 and 2012 and the period from May 25, 2004 (inception) to December 31, 2013

NOTE B SIGNIFICANT ACCOUNTING POLICIES (CONTINUED)

[4] Property and equipment:

Property and equipment consists of furniture, fixtures and computers. Property and equipment are carried at cost less accumulated depreciation. Depreciation is calculated using the straight-line method over the respective asset's useful life. Maintenance and repairs that do not improve or extend the life of assets are expensed as incurred. When an asset is retired or disposed of, the cost and related accumulated depreciation are removed from the accounts and any resulting gains or losses are reflected within the statement of operations.

[5] Fair value of financial instruments:

FASB ASC 820 *Fair Value Measurements and Disclosures,* defines fair value as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. FASB ASC 820 requires disclosures about the fair value of all financial instruments, whether or not recognized, for financial statement purposes. The estimates presented in these financial statements are not necessarily indicative of the amounts that could be realized on disposition of the financial instruments.

FASB ASC 820 specifies a hierarchy of valuation techniques based on whether the inputs to those valuation techniques are observable or unobservable. Observable inputs reflect market data obtained from independent sources, while unobservable inputs reflect market assumptions. The hierarchy gives the highest priority to unadjusted quoted prices in active markets for identical assets or liabilities (Level 1 measurement) and the lowest priority to unobservable inputs (Level 3 measurement).

The three levels of the fair value hierarchy are as follows:

Level 1 Quoted prices in active markets for identical assets or liabilities that the reporting entity has the ability to access at the measurement date. Level 1 primarily consists of financial instruments whose value is based on quoted market prices such as exchange-traded instruments and listed equities.

Level 2 Inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly (e.g. quoted prices of similar assets or liabilities in active markets, or quoted prices for identical or similar assets or liabilities in markets that are not active). Level 2 includes financial instruments that are valued using models or other valuation methodologies. These models consider various assumptions, including volatility factors, current market prices and contractual prices for the underlying financial instruments. Substantially all of these assumptions are observable in the marketplace, can be derived from observable data or are supported by observable levels at which transactions are executed in the marketplace.

Level 3 Unobservable inputs for the asset or liability. Financial instruments are considered Level 3 when their fair values are determined using pricing models, discounted cash flows or similar techniques and at least one significant model assumption or input is unobservable.

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NEPHROGENEX, INC.

(A Development Stage Company)

Notes to Financial Statements (Continued)

December 31, 2013 and 2012 and the period from May 25, 2004 (inception) to December 31, 2013

NOTE B SIGNIFICANT ACCOUNTING POLICIES (CONTINUED)

The carrying amounts reported in the balance sheet for cash and cash equivalents, accounts payable and accrued expenses approximate their fair value based on the short-term maturity of these instruments. The carrying amounts reported in the balance sheet for notes payable approximate their fair value based on market rates of interest and the terms of the notes. The Company recognizes all derivative financial instruments as assets or liabilities in the financial statements and measures them at fair value with changes in fair value reflected as current period income or loss unless the derivatives qualify as hedges. Certain terms of the May 4, 2007 Stock Purchase Agreement were accounted for as derivatives, which are valued under Level 3 of the fair value hierarchy. See Note E, Stockholders' Deficiency.

[6] Research and development costs:

Costs incurred in connection with research and development activities are expensed as incurred. These costs include licensing fees to use certain technology in the Company's research and development projects as well as fees paid to consultants and various entities that perform certain research and testing on behalf of the Company.

[7] Income taxes:

The Company utilizes the liability method of accounting for income taxes as required by FASB ASC Topic 740 Income Taxes. Under this method, deferred tax assets and liabilities are determined based on differences between financial reporting and tax reporting bases of assets and liabilities and are measured using enacted tax rates and laws that are expected to be in effect when the differences are expected to reverse. Uncertain tax positions are evaluated in accordance with this topic and if appropriate, the amount of unrecognized tax benefits are recorded within deferred tax assets. Valuation allowances are established when necessary to reduce deferred tax assets to the amounts expected to be realized.

ASC Topic 740 also clarifies the accounting for uncertainty in income taxes recognized in the financial statements. The interpretation prescribes a recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken, or expected to be taken, in a tax return. There were no significant matters determined to be unrecognized tax benefits taken or expected to be taken in a tax return that have been recorded in the Company's financial statements through December 31, 2013. ASC Topic 740 provides guidance on the recognition of interest and penalties related to income taxes. There were no interest or penalties related to income taxes that have been accrued or recognized as of December 31, 2013 or 2012 for the years then ended or for the period from May 25, 2004 (inception) to December 31, 2013. The Company has elected to treat interest and penalties, to the extent they arise, as a component of income taxes. Tax years beginning in 2010 for federal purposes are generally subject to examination by taxing authorities, although net operating losses from all prior years are subject to examinations and adjustments for at least three years following the year in which the tax attributes are utilized.

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NEPHROGENEX, INC.

(A Development Stage Company)

Notes to Financial Statements (Continued)

December 31, 2013 and 2012 and the period from May 25, 2004 (inception) to December 31, 2013

NOTE B SIGNIFICANT ACCOUNTING POLICIES (CONTINUED)

[8] Stock based compensation:

The Company recognizes compensation cost relating to share-based payment transactions in net loss using a fair-value measurement method, in accordance with ASC-718 *Compensation-Stock Compensation*. ASC-718 requires all share based payments to employees, including grants of employee stock option, to be recognized in operating results as compensation expense based on fair value over the requisite service period of the awards. The Company determines the fair value of share-based awards using the Black-Scholes option-pricing model which uses both historical and current market data to estimate fair value. The method incorporates various assumptions such as the risk-free interest rate, expected volatility, expected dividend yield, expected forfeiture rate and expected life of the options. The Company has also granted stock options to nonemployees. Grants to non employees are accounted for in accordance with ASC-505-50 *Equity Based Payments to Non-Employees*. The Company determines the fair value of share based awards granted to nonemployees similar to the way fair value of awards are determined for employees except that certain assumptions used in the Black-Scholes option-pricing model, such as expected life of the option, maybe different and the fair value of each award is adjusted at the end of each period for any change in fair value from the previous valuation until the award vests.

[9] Earnings Per Share:

Basic earnings per share ("EPS") excludes dilution and is computed by dividing income (loss) available to common stockholders by the weighted-average number of common shares outstanding for the period. Diluted EPS reflects the potential dilution that could occur if securities or other contracts to issue common stock were exercised or converted into common stock or resulted in the issuance of common stock that shared in the earnings of the entity. Since there are a significant number of common stock options outstanding, fluctuations in the actual market price could have a variety of results for each period presented. No potentially dilutive equity instruments were included in the computations of diluted earnings per share for the years ended December 31, 2013 or 2012 or for the period from May 25, 2004 (inception) to December 31, 2013 because their effect would be anti-dilutive as a result of losses incurred during those periods. Shares issuable upon the exercise of options outstanding at December 31, 2013 and 2012 were 563,855 and 474,209, respectively. As of December 31, 2013, the Company had also issued 24,000 Restricted Stock Units (RSU).

NOTE C PROPERTY AND EQUIPMENT

Property and equipment as of December 31, 2013 and 2012 consisted of:

	Useful Life	2013	2012
Computer equipment	3 years	$ 50,730	$ 38,920
Furniture and fixtures	7 years	66,275	66,275
		117,005	105,195
Less accumulated depreciation		(106,179)	(102,052)
Property and equipment, net		$ 10,826	$ 3,143

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NEPHROGENEX, INC.

(A Development Stage Company)

Notes to Financial Statements (Continued)

December 31, 2013 and 2012 and the period from May 25, 2004 (inception) to December 31, 2013

NOTE C PROPERTY AND EQUIPMENT (CONTINUED)

For the years ended December 31, 2013 and 2012 depreciation expense was approximately $4,100 and $20,800, respectively. Depreciation expense for the period from May 25, 2004 (inception) to December 31, 2013 was approximately $106,200.

NOTE D NOTES PAYABLE

During the period from May 25, 2004 (inception) to December 31, 2006 certain stockholders lent the Company an aggregate of approximately $1.7 million dollars. In connection therewith, the Company executed numerous agreements ("Notes") that provided the lenders with various rights and preferences including interest at rates ranging from 7.75% to 11.25%, security interest in all the assets of the Company and conversion rights into preferred stock. Certain Notes issued in 2006 contained beneficial conversion features ("BCF") whereby upon conversion of the convertible note into preferred stock, the holder received a favorable exchange rate that was accounted for as additional interest expense. The BCF totaled $560,000 and was recognized as additional interest expense amortized over the life of the Notes.

On May 4, 2007, all the Notes, and the related accrued and unpaid interest was converted into shares of Series A Preferred Stock (Note E).

During 2011, the Company sold convertible promissory notes for approximately $2,100,000 in aggregate to shareholders of the Company, which are payable on April 1, 2014, the maturity date of the Notes.

During 2012, the Company sold convertible promissory notes for approximately $1,255,000 in aggregate to shareholders of the Company, which are payable on April 1, 2014, the maturity date of the Notes.

During 2013, the Company sold convertible promissory notes for approximately $4,562,000 in aggregate to shareholders of the Company, which are payable on April 1, 2014, the maturity date of the Notes.

At December 31, 2013, the Company had outstanding promissory notes in an aggregate amount of approximately $7,917,000. All issuers of the promissory notes are also investors in Company. Each of the notes has a stated interest rate of 8% per annum. Further, each of the notes automatically convert into preferred stock on or before April 1, 2014 upon an equity raise of at least $7.5 million with the approval of the majority of the note holders at a price of 90% of the price per share of such equity raise. This contingent beneficial conversion will only be recorded if it is probable that the contingency will occur. The notes are also convertible into shares of Series A preferred stock at the election of the holder, at a price of $1.11083 per share. The notes provide that if the Company has a liquidation event prior to the maturity date of the notes and the notes are not converted, the Company will be obligated to pay the holders of the notes an amount equal to twice the amount of the unpaid principal amount of the notes plus accrued interest. Liquidation events would include (1) the closing of the sale, transfer, exclusive license or other disposition of all or substantially all of the Company's assets, (2) the consummation of the merger or consolidation of the Company with or into another entity, (3) the closing of the transfer in one transaction or a series of related transactions, to a person or group of

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(A Development Stage Company)

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NOTE D NOTES PAYABLE (CONTINUED)

affiliated persons other than an underwriter of the Company's securities, of the Company's securities if, after such closing, such person or group of affiliated persons would hold 50% or more of the outstanding voting stock of the Company (or the surviving or acquiring entity), or (4) liquidation, dissolution or winding up of the Company.

The Company has accrued interest of approximately $650,000 and $267,000 as of December 31, 2013 and 2012, respectively, which is included in accrued and other liabilities on the accompanying balance sheets. Interest expense relating to the notes amounted to approximately $383,000 and $202,000 for the years ended December 31, 2013 and 2012, respectively, and $1,433,000 for the period from May 25, 2004 (inception) to December 31, 2013.

On February 14, 2014, in connection with the closing of the Company's initial public offering, the convertible promissory notes and accrued interest were converted into shares of common stock (see Note M).

NOTE E STOCKHOLDERS' DEFICIENCY

Series A Preferred Stock

The Series A Preferred Stock ("Series A") has the following rights, preferences and restrictions:

Dividends

Series A stockholders are entitled to receive dividends prior to and in preference to common stockholders. Series A dividends are cumulative at an annual rate of $.08887 per share payable in the event of a liquidation as defined or when and if declared by the Company's Board of Directors (the "Board").

Liquidation

In the event of a liquidation of the Company as defined, Series A stockholders are entitled to receive two times the applicable issuance price (adjusted for stock splits, stock dividends and other recapitalization events) plus accrued and unpaid dividends. In the event proceeds available for distribution to Series A stockholders at liquidation are insufficient to pay the full obligation, then the proceeds available for distribution will be prorated among the Series A stockholders. The definition of a liquidating event includes a change in control. As of December 31, 2013, the applicable issuance price per share was approximately $1.11. The aggregate liquidation value of the Series A stock, including accrued and unpaid dividends, at December 31, 2013 was approximately $65.0 million.

Conversion

A Series A stockholder can elect to convert their Series A stock on a one-for-6.5 basis (adjusted for stock splits, stock dividends and other recapitalization events) into shares of common stock at any time. Conversion is automatic in the event of an underwritten public offering that meets certain defined per share and aggregate proceeds. Series A stockholders also have anti-dilution rights in the event the Company were to issue capital stock at price below the per share price paid by the Series A

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NOTE E STOCKHOLDERS' DEFICIENCY (CONTINUED)

stockholders as defined. As of December 31, 2013, the Series A stock converts into common stock on a one-for-one basis.

Voting

Series A stockholders vote on an as if converted to common stock basis. In addition, the Series A stockholders are entitled to elect three directors to the Board while common stockholders are entitled to elect one director to the Board. Series A stockholders also have certain defined protective rights that require approval by the Series A stockholder before certain actions can be taken by the Company.

May 2007 Stock Purchase Agreement

On May 4, 2007, the Company entered into a Stock Purchase Agreement (the "Agreement") with new and existing stockholders. The terms of the agreement provided for the initial issuance of approximately 4.8 million shares of Series A stock (the "First Close") in exchange for cash of $1.5 million, conversion of the Notes, including accrued interest, of $2.3 million, and the acquisition of certain technology from BioStratum, Inc ("Bio"). The Agreement also provided for a second and third close (referred to individually as "Warrant 1" and "Warrant 2", respectively, or collectively as "Warrants") whereby certain investors in the First Close were given a right, but not the obligation, to purchase additional shares of Series A and common stock at defined prices. The value assigned to the acquired technology from Bio was approximately $1.1 million. Such amount was expensed as research and development expense at the time the First Close was completed since the acquired technology will be used in the Company's research efforts and had no alternative future use. For financial reporting purposes, the First Close was accounted for as the issuance of 4.8 million shares of Series A stock and two warrants (Warrant 1 and 2) in consideration for cash, conversion of the Notes and acquired technology.

The table below summarizes the allocation of the consideration received to the financial instruments issued in the First Close.

Consideration received	
Cash	$ 1,500,000
Conversion of the Notes and accrued interest (See Note D)	2,313,772
Acquired technology	1,093,339
	$ 4,907,111
Allocation to financial instruments	
Series A stock	$ 2,503,323
Preferred stock warrant liability	2,403,788
	$ 4,907,111

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NOTE E STOCKHOLDERS' DEFICIENCY (CONTINUED)

Warrant 1 and 2

Warrant 1, as amended, gives the holder the right, but not the obligation, to purchase up to an additional 18 million shares of Series A stock and 45,234 shares of common stock in consideration for $20 million. Warrant 1 was exercised in part during December 2007 and fully exercised during March 2008. In connection with the partial exercise of Warrant 1 in December 2007, the Company issued approximately 1.8 million shares of Series A stock in exchange for $2 million. In March 2008, the holders of Warrant 1 exercised their remaining right to acquire 16 million shares of Series A stock and 45,234 common shares in consideration for approximately $18 million. As discussed in more detail below, the deemed fair value of Warrant 1 at the date of issuance through the date of exercise was accounted for as a preferred stock warrant liability.

Accordingly, upon the partial exercise of Warrant 1 in December 2007, the prorated share of the deemed fair value of Warrant 1 at the time of exercise attributable to the Series A stock issued was reclassified from the preferred stock warrant liability to paid-in capital and accounted for as additional consideration received in connection with the partial exercise of Warrant 1. Such amount was $245,402. In March 2008, the balance of the liability for Warrant 1, of $2,213,480, was reclassified from preferred stock warrant liability to paid-in capital and accounted for as additional consideration received.

Warrant 2 gives the holder the right, but not the obligation, to purchase up to an additional 9 million shares of Series A stock at a per share price of approximately $1.11. Warrant 2 can be exercised at any time upon the election of the majority of certain Series A stockholders or upon the achievement of the development milestone, as defined. In addition, in the event that the Company enters into an agreement that results, or will result in a liquidation event, as defined, then in lieu of purchasing the number of shares in Warrant 2, the holders would be entitled to sell their right to acquire the Warrant 2 shares in connection with, and simultaneously with the closing of, such a liquidation event, for consideration equal to the difference between (1) the consideration per share that would be received for each issued and outstanding share in connection with such liquidation event, assuming the issuance of all Warrant 2 shares prior to the liquidation event and (2) the Series A purchase price ($1.11083 as of December 31, 2013) multiplied by the number of Warrant 2 shares available to be purchased by the holder.

The fair value of the Warrants was estimated on the date of issuance using the Black-Scholes option pricing model. The Company accounts for the Warrants in accordance with the provisions of ASC-480 and other accounting standards. The Company will record the fair value of the Warrants as a liability on its balance sheet until the Warrants expire or are exercised. The Warrants are revalued to their then estimated fair value, using the Black-Scholes model, at each reporting period end through December 31, 2012, and the Probability Weighted Expected Return Method calculated with the assistance of a third party valuation firm as of December 31, 2013, and any change in the fair value of the Warrants is reflected in operating results. The assumptions used in the Black-Scholes model to value the Warrants from their May 4, 2007 date of issuance through December 31, 2012 was a term ranging from 1 to 4 years, a risk free interest rate of approximately 0.185% to 3.36%, volatility of 60%, and the fair value of the Series A stock ranging from $1.11 to $1.39.

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NOTE E STOCKHOLDERS' DEFICIENCY (CONTINUED)

The table below summarizes the changes in the fair value measurements of the Warrants, which used significant unobservable inputs (Level 3), from their issuance date (May 4, 2007) to December 31, 2013:

Warrants deemed fair value at issuance	$	**2,403,788**
Reclassification to additional paid-in capital upon partial Warrant 1 exercise		**(245,402)**
Change in deemed fair value of the Warrants during 2007		**4,463,509**
Deemed fair value of warrants at December 31, 2007		**6,621,895**
Reclassification to additional paid-in capital upon remaining Warrant 1 exercise		**(2,213,480)**
Change in deemed fair value of the Warrants during 2008		**941,639**
Deemed fair value of warrants at December 31, 2008		**5,350,054**
Change in deemed fair value of the Warrants during 2009		**(950,641)**
Deemed fair value of warrants at December 31, 2009		**4,399,413**
Change in deemed fair value of the Warrants during 2010		
Deemed fair value of warrants at December 31, 2010		**4,399,413**
Change in deemed fair value of the Warrants during 2011		**(835,411)**
Deemed fair value of warrants at December 31, 2011		**3,564,002**
Change in deemed fair value of the Warrants during 2012		**1,800**
Deemed fair value of warrants at December 31, 2012		**3,565,802**
Change in deemed fair value of the Warrants during 2013		**3,416,838**
Deemed fair value of warrants at December 31, 2013	$	**6,982,640**

As of December 31, 2013, Warrant 2 was exercisable into approximately 9 million shares of Series A stock at an aggregate exercise price of $10 million.

As discussed in more detail in Note G, the Company issued shares of Series A stock and/or shares of common stock to BioStratum, Inc., Vanderbilt University, Tryggvason Biotech AB, and FibroStatin, SL.

On February 14, 2014, in connection with the closing of the Company's initial public offering, the Series A stock was converted into shares of common stock and Warrant 2 was settled (see Note M).

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NOTE F STOCK OPTION PLAN

In 2005, the Company adopted the NephroGenex, Inc. 2005 Stock Option Plan (the "Plan"). The Plan, as amended, provides for the granting of up to 609,303 shares of common stock to employees and consultants of the Company in the form of incentive and nonqualified stock options and shares of restricted stock. Options and restricted stock vest over various periods ranging from eight months to four years. Options expire ten years from grant date. Shares available for future grant at December 31, 2013 total 35,355. The table below summarizes stock option activity from the Plan's inception through December 31, 2013.

	Number of Shares	Weighted Average Exercise Price	Exercisable At December 31, 2013
Granted	2,492	$ 32.50	1,262
Outstanding as of December 31, 2005	2,492	32.50	
Granted	52,663	0.65	53,540
Exercised			
Cancelled			
Outstanding as of December 31, 2007	55,155	2.08	
Granted	284,923	0.39	303,166
Exercised			
Cancelled	(2,000)	0.39	
Outstanding as of December 31, 2008	338,078	0.65	
Granted	114,504	1.95	389,882
Exercised			
Cancelled	(18,964)	0.98	
Outstanding as of December 31, 2009	433,618	0.98	
Granted			389,882
Exercised	(10,477)	0.39	
Cancelled			
Outstanding as of December 31, 2010	423,141	0.98	
Granted	90,308	1.82	442,212
Exercised			
Cancelled	(1,538)	0.39	
Outstanding as of December 31, 2011	511,911	1.17	
Granted			

Exercised			
Cancelled	(37,702)	1.50	442,212
Outstanding as of December 31, 2012	474,209	1.11	
Granted	91,261	2.02	
Exercised			
Cancelled	(1,615)	32.50	
Outstanding as of December 31, 2013	563,855	$ 1.17	466,928

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NOTE F STOCK OPTION PLAN (CONTINUED)

As of December 31, 2013, there were 466,928 options exercisable with a weighted average exercise price of $0.98 and a weighted average remaining term of 4.7 years.

The Company determines the fair value of stock options using the Black-Scholes option pricing model. The assumptions used to value stock options from the Company's inception to December 31, 2013 included expected terms ranging 4 to 10 years, risk free interest rate of approximately 2%, volatility of 60%, zero dividend yield and an estimated fair value of a share of common stock ranging from $0.39 to $2.02. Total unrecognized compensation costs related to nonvested awards at December 31, 2013 was approximately $125,000 and is expected to be recognized within future operating results over a weighted average period of approximately 1.8 years. Stock based compensation expense for the years ended December 31, 2013 and 2012 was approximately $84,000 and $126,000, respectively. Stock based compensation expense for the period from May 25, 2004 (inception) to December 31, 2013 was approximately $716,000.

In November 2013, the Company issued 24,000 Restricted Stock Units (RSU) to its CEO in connection with his employment agreement (see Note J). These RSUs were not issued under the Plan. The RSU represent the right to receive shares of common stock, subject to the terms and conditions of a restricted stock unit agreement and grant notice.

As of December 31, 2013, none of the RSU had vested. The fair value of the RSU was estimated to be $109,200, on the date of grant, which is being recognized over the four year vesting period of the RSU. For the year ended December 31, 2013 and for the period from May 25, 2004 (Inception) to December 31, 2013, the Company recognized $4,550 of stock based compensation. Total unrecognized compensation costs related to the RSU at December 31, 2013 was approximately $105,000, which is expected to be recognized within future operating results over a period of approximately 3.8 years.

NOTE G LICENSE AGREEMENTS

[1] BioStratum, Inc.

On May 8, 2006, the Company entered into a licensing agreement with Bio Stratum Incorporated ("Bio") for exclusive rights to use certain technology. The agreement was amended on September 13, 2006 (the "2006 Bio Agreement") and was superseded on May 4, 2007 by the Termination, Assignment, Assumption and Participation Agreement (the "2007 Bio Agreement"). In consideration for obtaining the licensed technology in 2006, the 2006 Bio Agreement provided for the issuance of 12,708 shares of common stock as defined and the payment of an upfront licensing fee of $500,000. The licensing fee was expensed during 2006 as research and development as the licensed technology will be used in the Company's research efforts and had no alternative future use. The fair value of the 12,708 shares of common stock issued to Bio totaled approximately $5,000. The 2006 Bio Agreement contained numerous other terms and conditions substantially all of which were superseded by the 2007 Bio Agreement. The 2007 Bio Agreement provided for the Company to issue approximately 1.8 million shares of Series A stock and to issue approximately 208,000 shares of common stock contingent on the exercise of Warrant 1 (Note E). The estimated fair value of the 1.8 million shares of Series A stock totaled approximately $1.1 million and was expensed upon issuance as research and development as the licensed technology will be used in the Company's research efforts and had no alternative future use.

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NOTE G LICENSE AGREEMENTS (CONTINUED)

As discussed in Note E, during March 2008, the balance of Warrant 1 was fully exercised and Bio received approximately 208,000 shares of common stock as additional consideration for the licensed technology. The estimated fair value of the shares of common stock issued totaled approximately $81,000 and was expensed in 2008 upon issuance as research and development as the licensed technology will be used in the Company's research efforts and had no alternative future use.

For each of the years ended December 31, 2013 and 2012, the total expense recognized in operating results from the Bio Agreements was $0. For the cumulative period from May 25, 2004 (inception) to December 31, 2013, the total expense recognized in operating results from the Bio Agreements was approximately $1.1 million. As of December 31, 2013, Bio owned approximately 1.8 million shares of the Company's Series A stock and approximately 221,000 shares of the Company's common stock.

[2] Vanderbilt University

During 2006, the Company entered into a licensing agreement with Vanderbilt University ("Vanderbilt") for the rights to use certain technology. The agreement, as amended, requires the Company to make milestone payments totaling approximately $1.1 million in the event certain defined events occur. Should the Company successfully develop a product using the licensed technology, Vanderbilt will be due royalties based on net sales at a rate of 5%. The Company must also pay Vanderbilt 25% of non-royalty sub-licensee payments received from a sub-licensee. Certain milestones can be paid in stock or are creditable against future royalties due based on net sales. As of December 31, 2013, no milestone or royalty payments have been paid or accrued.

Annual minimum royalties due under the licensing agreement are $10,000 and will increase to $25,000 when a claim in the licensed patent rights is issued in a major market country, as defined. The licensing agreement expires when the underlying patents to the licensed technology expire. The Company may terminate the agreement upon 60 days written notice to Vanderbilt. In consideration for the license, the Company issued 462 shares of common stock and granted Vanderbilt the right to maintain their ownership interest at 2.5% (the "Right") for the period to a private financing, as defined. The estimated value of the 462 shares of common stock and the Right totaled approximately $7,000, which was expensed as research and development as the licensed technology will be used in the Company's research efforts and has no alternative future use. The licensing agreement was amended in 2007 and provided for the settlement of the Right in exchange for 17,257 shares of common stock. The amendment also obligated the Company to issue an additional 24,014 shares of common stock contingent on the exercise of Warrant 1.

As discussed in Note E, during March 2008, the balance of Warrant 1 was fully exercised, and accordingly, Vanderbilt received 24,014 shares of common stock as additional consideration for the licensed technology. The estimated fair value of the shares of common stock totaled approximately $9,000, which was expensed upon issuance as research and development as the licensed technology will be used in the Company's research efforts and had no alternative future use. For all periods presented, expenses recognized in connection with Vanderbilt were not material.

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NOTE G LICENSE AGREEMENTS (CONTINUED)

[3] Tryggvason Biotech AB:

During 2005, the Company entered into a licensing agreement with Tryggvason Biotech AB and Handelsbolaget Christer Betsholtz (collectively "Tryggvason") for the exclusive commercial rights to use their proprietary glomerular profiling technology. The agreement included an upfront payment of $5,000 and a commitment to issue 154 shares of common stock. The licensing fee was expensed as research and development as the licensed technology will be used in the Company's research efforts and has no alternative future use. The fair value of the 154 shares of common stock issued was insignificant at the time of issuance. These shares of common stock were issued on April 12, 2005. Tryggvason will be due royalties based on 2% of net sales, as defined. No royalties have been paid or accrued through December 31, 2013. The licensing agreement expires upon the expiration of the underlying patents.

[4] FibroStatin SL:

During 2005, the Company entered into a licensing agreement with FibroStatin SL, for exclusive commercial rights to their proprietary technology. The agreement included an upfront payment of $5,000 and a commitment to issue FibroStatin 154 shares of common stock. The licensing fee was expensed as research and development as the licensed technology will be used in the Company's research efforts and has no alternative future use. The common stock was issued during 2006. The fair value of the 154 shares of common stock issued was insignificant at the time of issuance. This licensing agreement was terminated on April 12, 2007.

[5] The University of Kansas Medical Center Research Institute, Inc.:

During 2007, Bio assigned their rights to certain technology licensed from the University of Kansas Medical Center Research Institute, Inc. ("KUMC") to the Company. The license gives the Company worldwide royalty free rights to use certain technology. Upon the achievement of certain defined product development milestones, the Company would be obligated to make up to $225,000 of payments to KUMC. As of December 31, 2013, no milestones have been paid or accrued. The term of the agreement expires on the expiration of the underlying KUMC patents or November 2018, whichever occurs last. The Company can terminate the agreement with 90 days notice.

[6] The University of South Carolina Research Foundation, Corp.:

During 2007, Bio assigned their rights to certain technology licensed from the University of South Carolina Research Foundation, Corp. ("USCRF") to the Company. The license gives the Company worldwide rights to use certain technology. The agreement was amended during August 2013. The Company is obligated to pay an annual licensing fee of $30,000 through 2008, $60,000 from 2009 through 2010, $62,000 from 2011 through 2012, $122,000 in 2013 and $120,000 thereafter. Upon the achievement of certain defined product development milestones, the Company would be obligated to make up to $6.1 million of payments to USCRF. The Company will be obligated to pay USCRF a one-time fee of $35,000 upon execution of a sublicense and would pay to USCRF 25% of any non-royalty sublicense payments received from a sub-licensee. As of December 31, 2013, no

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NEPHROGENEX, INC.

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NOTE G LICENSE AGREEMENTS (CONTINUED)

development milestones have been paid or accrued nor does the Company expect to achieve any development milestones during the next few years. The term of the agreement expires on the expiration of the underlying USCRF patents. The Company can terminate the license at any time upon three months prior written notice to USCRF.

NOTE H INCOME TAXES

The Company recognized deferred tax liabilities and assets for the expected future tax consequences of events that have been recognized differently between the financial statements and tax returns. Under this method, deferred tax liabilities and assets are determined based on the difference between the financial statement carrying amounts and tax basis of liabilities and assets using enacted tax rates and laws in effect in the years in which the differences are expected to reverse. Deferred tax assets are evaluated for realization based on a more-likely-than-not criteria in determining if a valuation allowance should be provided.

There was no income tax provision for the years ended December 31, 2013 and 2012.

The components of the Company's deferred tax assets at December 31, 2013 and 2012 are as follows:

		2013	2012
Net operating loss carry forwards	$	9,293,775	8,354,190
Stock based compensation		57,181	55,364
Tax credits		1,070,690	964,280
Depreciation		4,649	7,409
Amortization		3,399,809	3,202,551
Accrued bonus		139,311	84,293
Accrued expenses		121,788	188,349
Accrued interest		33,357	67,091
Deferred tax asset		14,120,560	12,923,527
Less: valuation allowance		(14,120,560)	(12,923,527)
Net deferred tax asset	$		$

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NOTE H INCOME TAXES (CONTINUED)

The Company's valuation allowance increased by $1,197,033 and $1,114,635 during the years ended December 31, 2013 and 2012, respectively. The reconciliation between the Company's effective tax rate and the federal statutory rate for the year ended December 31, 2013 and 2012 are as follows:

	2013	2012
Federal statutory rate	(34.00)%	(34.00)%
State income taxes	(6.00)%	(6.00)%
Preferred stock warrant expense	18.60%	
Other	0.53%	1.30%
Valuation allowance	20.87%	38.70%
Effective tax rate	%	%

As of December 31, 2013, the Company had approximately $23,900,000 of Federal net operating losses that will begin to expire in 2024 and approximately $19,500,000 of New Jersey net operating losses that will begin to expire in 2015. As of December 31, 2013, the Company has research and development credit carryovers for Federal and New Jersey of approximately $826,000 and $243,000, respectively; these will begin to expire in 2024 for federal and 2015 for New Jersey tax purposes. The Internal Revenue Code ("IRC") limits the amounts of net operating loss carryforwards that a company may use in any one year in the event of certain cumulative changes in ownership over a three-year period as described in Section 382 of the IRC. The Company has not performed a detailed analysis to determine whether an ownership change has occurred. Such a change of ownership could limit the utilization of the net operating losses, and could be triggered by subsequent sales of securities by the Company or its stockholders.

The Company did not have a liability related to unrecognized tax benefits as of December 31, 2013 or 2012.

The Company records interest accrued and penalties related to unrecognized tax benefits within the income tax expense. The Company had not accrued any interest or penalties related to unrecognized benefits. The Company is no longer subject to federal income tax assessment for years before 2010 and for years before 2009 for New Jersey income tax purposes. However, since the Company has incurred net operating losses in every year since inception, all of its income tax returns are subject to examination and adjustments by the Internal Revenue Service for at least three years following the year in which the tax attributes are utilized. The Company does not believe that there will be a material change in its unrecognized tax positions over the next twelve months. There is no amount of unrecognized tax benefit that, if recognized, would affect the effective tax rate.

NOTE I RECENT ACCOUNTING PRONOUNCEMENTS

In June 2011, the FASB issued ASU 2011-05, "Comprehensive Income (Topic 220) Presentation of Comprehensive Income" which amends ASC 220, "Comprehensive Income". ASU 2011-05 gives an entity the option to present the total comprehensive income, the components of net income, and the components of other comprehensive income either in a single continuous statement of comprehensive

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NOTE I RECENT ACCOUNTING PRONOUNCEMENTS (CONTINUED)

income or in two separate but consecutive statements. ASU 2011-05 is effective for fiscal years, and interim periods within those years, beginning after December 15, 2011. The Company did not have any other comprehensive income related transactions during the years ended December 31, 2013 or 2012 and as such did not present required statements.

In December 2011, the FASB issued ASU 2011-12 "Deferral of the Effective Date for Amendments to the Presentation of Reclassifications of Items out of Accumulated Other Comprehensive Income in Accounting Standards Update No. 2011-05". This update stated that the specific requirement to present items that are reclassified from other comprehensive income to net income alongside their respective components of net income and other comprehensive income will be deferred. In February 2013, the FASB issued ASU 2013-02 "Reporting of Amounts Reclassified Out of Accumulated Other Comprehensive Income". This update requires companies to present the effects on the line items of net income of significant reclassifications out of accumulated other comprehensive income if the amount being reclassified is required under GAAP to be reclassified in its entirety to net income in the same reporting period. ASU 2013-02 is effective prospectively for the Company for fiscal years, and interim periods within those years, beginning after December 15, 2013. The Company does not expect its adoption to have a material impact on our financial statements.

NOTE J COMMITMENTS

Lease

On May 18, 2008, the Company entered into an operating lease agreement in Princeton, New Jersey. This lease was terminated during 2011. During June 2011, the Company entered into an operating lease agreement in Research Triangle Park, North Carolina. The North Carolina lease expired in December 2013, and the Company is currently leasing the space on a month-to-month basis.

For the years ended December 31, 2013 and 2012 and for the cumulative period from May 25, 2004 (inception) to December 31, 2013, rent expense was approximately $52,000, $51,000, and $538,000, respectively.

Employment Agreements

On November 7, 2013, the Company entered into an employment agreement with a Chief Executive Officer ("CEO") whose employment commenced on October 18, 2013 (the "Commencement Date"). The employment agreement provides for an annual salary, bonus and company benefits.

In addition, the CEO received a grant of restricted stock units which represent the right to receive 24,000 shares of the Company's common stock, subject to the terms and conditions of a restricted stock unit agreement and grant notice connected therewith (the "RSU Award"). The Company will also make special cash bonus payments to the CEO on each date that restricted stock units are delivered to the CEO in an amount equal to the product of the number of shares of common stock underlying the restricted stock units delivered on such date and $16.12, less applicable taxes and withholdings; but in no event shall this bonus amount exceed $387,000 in the aggregate, before adjustment for applicable taxes and withholdings. The per share bonus amount shall be equitably adjusted in the event of any capitalization adjustment of the Company.

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NEPHROGENEX, INC.

(A Development Stage Company)

Notes to Financial Statements (Continued)

December 31, 2013 and 2012 and the period from May 25, 2004 (inception) to December 31, 2013

NOTE J COMMITMENTS (CONTINUED)

The employment agreement further provides that during the CEO's continuing service to the Company, if the number of issued and outstanding shares of the Company's capital stock increases, without limitation, in connection with an initial public offering of the Company's common stock or a stock dividend with respect to the Company's preferred stock, but not including the conversion of convertible debt or convertible promissory notes issued prior to the one year anniversary of the Commencement Date (the "Additional Shares"), the Company shall grant the CEO an option under the 2005 Plan or any successor plan of the Company (the "True Up Option") covering the number of shares of common stock equal to three ninety-sevenths of the Additional Shares, rounded to the nearest whole share. In connection with the Company's initial public offering in February 2014, the True Up Option was granted (see Note M). The Company has no obligation to grant any True Up Option with respect to the issuance or authorization of additional shares after the completion of the initial public offering of the Company's common stock.

On December 12, 2013, the Company entered into an employment agreement with a Chief Financial Officer ("CFO"), whose service as the CFO commenced on January 21, 2014 (the "Commencement Date"). The employment agreement provides the CFO with an annual salary, bonus and company benefits.

In addition, the CFO became entitled to a stock option award to acquire up to 30,769 shares of the Company's common stock upon the successful completion of the Company's initial public offering in February 2014 (see Note M). The Options will have an exercise price equal to the fair market value of a share of the Company's common stock on the date of grant. The options will vest in accordance with the following schedule: 25% of the options will vest on the first anniversary of the Commencement Date and 2.0833% of the options will vest on the monthly anniversary of the Commencement Date in each of the following 36 months; provided that the options will become 100% vested upon (i) a change of control, provided the CFO remains in service through the date of such transaction, or (ii) a cessation of the CFO's employment due to death, disability, termination by the Company or resignation by the CFO.

NOTE K RELATED PARTY TRANSACTIONS

From time to time, the Company reimbursed Care Capital, LLC ("Care"), an affiliate of the majority shareholder of the Company, for certain expenses paid by Care on behalf of the Company. During 2007, the Company reimbursed Care approximately $80,000 for expenses incurred by Care in connection with the May 2007 Stock Purchase Agreement (Note E).

The Company uses the services of a Care employee and reimburses Care for such personnel services incurred by Care on behalf of the Company. For the years ended December 31, 2013 and 2012 and the cumulative period from May 25, 2004 (inception) to December 31, 2013, the total expense recognized in operating results in connection with services provided by Care was $124,000, $106,000 and $664,000, respectively.

As discussed in Note G, the Company has entered into license and royalty agreements with certain shareholders of the Company.

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NEPHROGENEX, INC.

(A Development Stage Company)

Notes to Financial Statements (Continued)

December 31, 2013 and 2012 and the period from May 25, 2004 (inception) to December 31, 2013

NOTE L QUALIFIED THERAPEUTIC DISCOVERY PROGRAM AWARD

The Company was awarded approximately $244,000 under the Federal government Qualifying Therapeutic Discovery Program ("QTDP") initiative, all of which is related to qualified expenditures in 2010. Notification of the award was in October 2010, and receipt of the cash was in December 2010. The award is included in other income in the accompanying statement of operations for the period from May 25, 2004 (inception) through December 31, 2013.

NOTE M SUBSEQUENT EVENTS

On January 16, 2014, an agreement was reached among the Company's significant shareholders to cancel Warrant 2 (see Note E). Pursuant to the agreement, an aggregate of 593,589 shares of common stock were issued to the holders of Warrant 2 concurrently with the completion of the Company's initial public offering, as described below, in return for cancelling Warrant 2.

On February 6, 2014, the Company effected a 1-for-6.5 reverse stock split of its issued and outstanding shares of common stock and a proportional adjustment to the conversion ratio for each series of Series A Preferred Stock (see Note E). Accordingly, all share and per share amounts for all periods presented in these financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect the reverse stock split and adjustment of the preferred share conversion ratios.

On February 10, 2014, the Company entered into an underwriting agreement pursuant to which the Company agreed to sell to the underwriter at the public offering price per share less underwriting discounts 3,100,000 shares of common stock. In addition, the Company granted the underwriter an over-allotment option, which is exercisable for up to 45 days after February 11, 2014, that permits the underwriters to purchase a maximum of 465,000 additional shares from the Company. If the underwriters exercise all or part of this option, they will purchase shares covered by the option at the public offering price per share, less the underwriting discount. The Company also agreed to issue to the underwriter warrants to purchase up to 62,000 shares of common stock. The warrants will be exercisable at any time, in whole or in part, during the four-year period commencing one year from the effective date of the Company's initial public offering. The warrants are exercisable at a per share price of $15.00 per share. The exercise price and number of shares issuable upon exercise of the warrants may be adjusted in certain circumstances including in the event of a stock dividend or the Company's recapitalization, reorganization, merger or consolidation. However, the warrant exercise price or underlying shares will not be adjusted for issuances of shares of common stock at a price below the warrant exercise price.

On February 14, 2014, the Company filed a restated certificate of incorporation (the "Restated Certificate") with the Secretary of State of the state of Delaware in connection with the closing of the Company's initial public offering of shares of its common stock. The Restated Certificate amends and restates in its entirety the Company's restated certificate of incorporation, as amended to, among other things:

(1) authorize 100,000,000 shares of common stock,

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NEPHROGENEX, INC.

(A Development Stage Company)

Notes to Financial Statements (Continued)

December 31, 2013 and 2012 and the period from May 25, 2004 (inception) to December 31, 2013

NOTE M SUBSEQUENT EVENTS (CONTINUED)

(2) eliminate all references to the previously existing Series A Preferred stock and authorize 5,000,000 shares of undesignated preferred stock that may be issued from time to time by the board of directors without further stockholder authorization in one or more series upon the terms, limitations, voting rights, relative rights and preferences and variations designated by the board of directors,

(3) establish a classified board of directors in which directors will be divided into three classes, with the term of office of the first class to expire at the first annual meeting of stockholders following the initial classification of directors, the term of office of the second class to expire at the second annual meeting of stockholders following the initial classification of directors, and the term of office of the third class to expire at the third annual meeting of stockholders following the initial classification of directors,

(4) permit the board of directors to alter, amend or repeal the bylaws without obtaining stockholder approval,

(5) require the approval of at least 80% of the shares entitled to vote at an election of directors to adopt, amend or repeal the bylaws or repeal the provisions of the Restated Certificate regarding the inability of stockholders to call a special meeting of stockholders, among other provisions;

On February 14, 2014, the Company closed its initial public offering of 3,100,000 shares of common stock at a price of $12.00 per share for total gross proceeds of $37,200,000, less underwriting discounts and commissions. In connection with the completion of the offering, 3,644,354 shares of common stock were issued for the conversion of all outstanding shares of Series A Preferred stock, the convertible notes and accrued interest outstanding as of December 31, 2013 were converted into 1,186,475 shares of common stock, and 593,589 aggregate shares of common stock were issued in connection with the settlement of Warrant 2 as described above.

On February 14, 2014, an individual was appointed to the Company's board of directors whose term will expire at the annual meeting of stockholders to be held in 2015. In connection with the appointment as a director, subject to an increase in the amount of available options at the next annual meeting, the individual was granted an option to purchase 3,076 shares of the Company's common stock, at fair market value, under the Company's 2005 Stock Option Plan.

On February 14, 2014, pursuant to an employment agreement (see Note J) and subject to shareholder approval to increase the number of shares in the Plan, the Company granted the CEO 242,524 stock options in the Company's common stock. In accordance with the employment agreement, 114,234 of these options were granted with an exercise price of $12.00 and 37,029 were granted with an exercise price of $2.02. All of these options will vest over 4 years pursuant to the terms in the employment agreement.

On February 14, 2014, pursuant to an employment agreement (see Note J) and subject to shareholder approval to increase the number of shares in the Plan, the Company granted the CFO 30,769 stock options in the Company's common stock at an exercise price of $11.90. These options will vest over 4 years pursuant to the terms in the employment agreement.

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Exhibit List

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/Reg. Number
3.1	Restated Certificate of Incorporation of the Registrant.		Form 8-K (Exhibit 3.1)	02/14/14	001-36303
3.2	Restated Bylaws of the Registrant.		Form 8-K (Exhibit 3.2)	02/14/14	001-36303
4.1	Form of Common Stock Certificate.		Form S-1 (Exhibit 4.1)	01/10/14	333-193023
4.2	Form of Representative's Warrant.		Form S-1 (Exhibit 4.2)	01/29/14	333-193023
4.3	Amended and Restated Investors' Rights Agreement, dated February 28, 2008, as amended February 14, 2014	**X**			
10.1*	Executive Employment Agreement by and between the Registrant and Pierre Legault, dated November 7, 2013.		Form S-1 (Exhibit 10.1)	12/23/13	333-193023
10.1.1*	Restricted Stock Unit Grant Notice and Agreement by and between the Registrant and Pierre Legault, dated November 7, 2013.	X			
10.2*	Offer of Employment Letter by and between the Registrant and Bob Peterson, dated August 8, 2009.		Form S-1 (Exhibit 10.2)	12/23/13	333-193023
10.3*	Employment Agreement by and between J. Wesley Fox and the Registrant, dated April 30, 2007.		Form S-1 (Exhibit 10.3)	12/23/13	333-193023
10.4*	Form of Indemnification Agreement by and between the Registrant and its directors and officers.		Form S-1 (Exhibit 10.4)	12/23/13	333-193023
10.5	Lease Agreement, by and between Highwoods Realty Limited Partnership and the Registrant dated June 15 2011.		Form S-1 (Exhibit 10.5)	12/23/13	333-193023
10.6.1	Amended and Restated License Agreement between University of Kansas Medical Center Research Institute, Inc. and BioStratum Incorporated (assigned to the Registrant), effective as of November 19, 1998.		Form S-1 (Exhibit 10.6.1)	12/23/13	333-193023
10.6.2	First Amendment to Amended and Restated License Agreement between University of Kansas Medical Center Research Institute, Inc. and the Registrant, effective as of May 4, 2007.		Form S-1 (Exhibit 10.6.2)	12/23/13	333-193023

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Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/Reg. Number
10.6.3	Second Amendment to Amended and Restated License Agreement between University of Kansas Medical Center Research Institute, Inc. and the Registrant, effective as of June 25, 2008.		Form S-1 (Exhibit 10.6.3)	12/23/13	333-193023
10.7.1	License Agreement between the University of South Carolina Research Foundation and BioStratum Incorporated (assigned to the Registrant), dated August 27, 2004.		Form S-1 (Exhibit 10.7.1)	12/23/13	333-193023
10.7.2	Amendment to License Agreement between The South Carolina Research Foundation and the Registrant, effective as of June 20, 2011.		Form S-1 (Exhibit 10.7.2)	12/23/13	333-193023
10.7.3	Second Amendment to License Agreement between The South Carolina Research Foundation and the Registrant, effective as of April 2, 2012.		Form S-1 (Exhibit 10.7.3)	12/23/13	333-193023
10.7.4	Third Amendment to License Agreement between The South Carolina Research Foundation and the Registrant, effective as of August 9, 2013.		Form S-1 (Exhibit 10.7.4)	12/23/13	333-193023
10.7.5	Fourth Amendment to License Agreement between The University of South Carolina Research Foundation and the Registrant, effective as of January 14, 2014.		Form S-1 (Exhibit 10.7.5)	01/17/14	333-193023
10.8.1	License Agreement between Vanderbilt University and the Registrant, effective as of January 11, 2006.		Form S-1 (Exhibit 10.8.1)	12/23/13	333-193023
10.8.2	First Amendment to License Agreement between Vanderbilt University and the Registrant, effective as of April 30, 2007.		Form S-1 (Exhibit 10.8.2)	12/23/13	333-193023
10.8.3	Restated and Amended License Agreement between Vanderbilt University and the Registrant, effective as of July 1, 2012.		Form S-1 (Exhibit 10.8.3)	12/23/13	333-193023
10.8.4	First Amendment to Restated and Amended License Agreement between Vanderbilt University and the Registrant, effective as of November 6, 2013.		Form S-1 (Exhibit 10.8.4)	12/23/13	333-193023

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Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/Reg. Number
10.9.1	License Agreement between BioStratum, Incorporated and the Registrant, effective as of May 8, 2006.		Form S-1 (Exhibit 10.9.1)	12/23/13	333-193023
10.9.2	Amendment to License Agreement between BioStratum, Incorporated and the Registrant, effective September 13, 2006.		Form S-1 (Exhibit 10.9.2)	12/23/13	333-193023
10.9.3	Grant Back License Agreement by and between the Registrant and BioStratum, Incorporated, dated May 4, 2007.		Form S-1 (Exhibit 10.9.3)	12/23/13	333-193023
10.10.1*	NephroGenex, Inc. 2005 Stock Option Plan, as amended and restated.		Form S-1 (Exhibit 10.10.1)	12/23/13	333-193023
10.10.2*	Form of Stock Option Grant Notice under the 2005 Stock Option Plan of the Registrant.		Form S-1 (Exhibit 10.10.2)	12/23/13	333-193023
10.10.3*	Form of Stock Option Grant Notice (With Acceleration) under the 2005 Stock Option Plan of the Registrant.		Form S-1 (Exhibit 10.10.3)	12/23/13	333-193023
10.11*	Executive Employment Agreement between the Registrant and John P. Hamill, dated December 12, 2013.		Form S-1 (Exhibit 10.11)	12/23/13	333-193023
10.12	Form of Omnibus Agreement and Consent among the Registrant, Care Capital Investments III, LP, Care Capital Offshore Investments III, LP, Rho Ventures V, L.P., Rho Ventures V Affiliates, L.L.C., Biostratum, Incorporated, Vanderbilt University, Vanderbilt University Medical Center, Vanderbilt University, by and through its Medical Center and John B. Mazur.		Form S-1 (Exhibit 10.12)	01/10/14	333-193023
31.1	Certification of the Chief Executive Officer	**X**			
31.2	Certification of the Chief Financial Officer	**X**			
32	Certification pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	**X**			

* Management contract or compensatory plan or arrangement.