AEGIS CAPITAL CORP

Pharmaceuticals
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Initiating Coverage

June 17, 2014

NephroGenex, Inc.

Rating: Buy

Knocking Down Nephropathy

Key Metrics

NRX - NASDAQ	$5.77
Pricing Date	Jun 16 2014
Price Target	$25.00
52-Week Range	$13.00 - $5.00
Shares Outstanding (mm)	8.6
Market Capitalization ($mm)	$49.6
3-Mo Average Daily Volume	14,948
Institutional Ownership	NM
Debt/Total Capital	NM
ROE	NM
Book Value/Share	$3.77
Price/Book	1.5x
Dividend Yield	NM
LTM EBITDA Margin	NM

EPS ($) FY: December

	2013A	Prior 2014E	Curr. 2014E	Prior 2015E	Curr. 2015E
1Q-Mar	--	--	(0.37)A	--	(0.42)E
2Q-Jun	--	--	(0.24)E	--	(0.39)E
3Q-Sep	--	--	(0.30)E	--	(0.37)E
4Q-Dec	--	--	(0.38)E	--	(0.40)E
FY	(19.71)	--	(1.26)E	--	(1.58)E
P/E	NM		NM		NM

Source: BigCharts.com

Company Description:
NephroGenex, Inc. (http://www.nephrogenex.com/) is an emerging pharmaceutical company developing therapeutics for kidney diseases.

Investment Highlights:

- **Initiating Coverage.** We are initiating coverage of NephroGenex, Inc., an emerging pharmaceutical company developing a novel small molecule, Pyridorin™, for the treatment of nephropathy (kidney disease) in patients with Type 2 diabetes. The firm is expected to imminently begin dosing patients in a Phase 3 trial of Pyridorin™ for diabetic nephropathy, which is likely to complete enrollment early next year and report interim data before the end of 2015. In our view, positive results could catalyze a transformative licensing agreement or an acquisition of NephroGenex by an established pharmaceutical company. Our rating is Buy with an 18-month price target of $25.00 per share.
- **Significant Market Opportunity.** In our view, diabetic nephropathy constitutes an appealing market niche, since this represents a significant unmet medical need that constitutes a prevalent condition among individuals suffering from diabetes. It is estimated that there are roughly 25mm individuals in the U.S. with diabetes, with an additional 60mm diabetics across Europe. The incidence of diabetes is increasing as the prevalence of poor diet and sedentary habits continues to rise. We note that there are currently no therapies available to address the oxidative damage to the kidney caused by the accumulation of advanced glycation end-products (AGEs). Pyridorin™ has been shown to selectively block pathways that induce the formation of such harmful compounds. We believe that the target market for Pyridorin™ could be as high as 10mm subjects in the U.S. alone. Peak sales for the drug could easily exceed $1bn in only the U.S. market.
- **Attractive Valuation.** NephroGenex, which went public in February 2014 in an IPO underwritten by Aegis Capital Corp. as sole book runner, currently trades at a market cap of under $50mm, with an enterprise value of under $17mm. We believe that in late 2015 the company could trade at a market cap of >$320mm, assuming that positive interim data is released from the Phase 3 PIONEER trial of Pyridorin™.

The Disclosure section may be found on pages 33 - 34 of this report.

Investment Thesis

NephroGenex, Inc. is a specialty pharmaceuticals firm focusing on the clinical development of a novel drug for diabetic nephropathy. The company's lead drug candidate, Pyridorin™ (pyridoxamine hydrochloride, or pyridoxamine HCl), is a derivative of vitamin B6 (pyridoxine), although it possesses a distinct chemical structure. Pyridorin™ is aimed at the inhibition of the pathogenic oxidative chemistries that are known to be elevated in diabetic patients, and that play a key role in the mediation of processes that lead to kidney disease in these individuals. In 2006 and 2007, NephroGenex in-licensed various patents covering the worldwide rights to Pyridorin™ use and synthesis. BioStratum had previously conducted a total of 36 preclinical safety trials, four Phase 1 studies, and five Phase 2 studies with Pyridorin™. NephroGenex subsequently conducted a multi-center, randomized, placebo-controlled Phase 2b study with Pyridorin™, designated PYR-210, which defined a patient population that preferentially responded to the drug. Using the data gleaned from PYR-210, NephroGenex finalized the design of a pivotal Phase 3 study aimed at assessing the safety and efficacy of Pyridorin™ for the treatment of nephropathy in patients with Type 2 diabetes. This study is slated to begin imminently, and is scheduled to complete enrollment within roughly nine months, with interim data expected prior to the end of next year. In our view, positive data could lead to a transformative licensing agreement with an established pharmaceutical firm or the acquisition of NephroGenex, which intends to develop Pyridorin™ to the point at which a clear regulatory path to approval can be established with clear proof-of-concept pivotal data, and then enlist an established firm with existing sales and marketing infrastructure in order to optimally commercialize the drug. We note that the nephropathy indication currently has few treatment options available, and that Pyridorin™ represents a unique approach with what we believe is a substantially superior safety profile to other drugs in clinical development.

We are initiating coverage on NRX with a Buy rating and an 18-month price target of $25.00 per share, implying a total firm value of ~$320mm, assuming ~13mm shares outstanding as of mid-2015. An investment in NRX may involve above-average risk and volatility, since the firm is still a development-stage entity.

Investment Positives

Solid Safety Profile. In our view, Pyridorin™ represents a small molecule drug with a relatively benign and innocuous safety profile. The drug has been tested in over 300 patients with nephropathy and was well-tolerated at doses up to 300mg twice-daily. We would anticipate that positive interim data from the upcoming PIONEER Phase 3 pivotal study should enable the firm to ink a transformative partnership with an established firm or attract acquisition interest from larger pharmaceutical companies. If the interim data analysis proves positive, we believe that NephroGenex could start the mandated second confirmatory Phase 3 trial early in 2016 and complete enrollment in early 2017. Positive final data from PIONEER and interim data from the second Phase 3 trial should permit the firm, either independently or with a future partner, to file for approval of Pyridorin™ in late 2018. In our view, Pyridorin™ could be launched in the U.S. in late 2019.

Significant Market Opportunity / Lucrative Benchmarks. NephroGenex benefits from a singular focus on a substantial unmet medical need. We project that there are roughly three million individuals who would be likely candidates for Pyridorin therapy in the U.S. alone, corresponding to a $3 billion peak annual sales opportunity. Further, we would point investors to the partnership that Abbott Laboratories (prior to the spin-out of the AbbVie pharmaceutical division) inked with Reata Pharmaceuticals in September 2010, which involved upfront and near-term milestone payments totaling $450 million, additional development- and sales-related milestones, and royalties on net sales of Reata's lead drug candidate in solely ex-U.S. markets for chronic kidney disease (CKD).

Capital-Efficient Development Pathway. As of March 31st, 2014, NephroGenex had recorded an accumulated deficit of roughly $43 million since inception in May 2004. In our view, the fact that the firm has burned so little money since inception is extremely encouraging. We would point investors to the fact that management has guided towards the cost of Pyridorin clinical development and filing as being under $80 million. Each Phase 3 trial is projected to cost $30 million.

Investment Risks

Financial Outlook and History of Unprofitable Operations. NephroGenex has incurred operating losses since inception and, in our view, may not achieve sustainable profitability for several years. Although the firm has been able to obtain capital in order to fund its operations, it is not known whether the company will be able to continue this practice, or be able to obtain other types of financing to meet operating needs. While the firm recently managed to raise $37.2 million in gross proceeds through an initial public offering (IPO) to support the advancement of its lead pipeline drug candidate in the U.S., which in our view removes any financing overhang for at least 12 – 15 months, we believe that any additional broadening of the clinical-stage pipeline could require additional capital. Furthermore, the company is expected to expend significant resources on the pivotal trial program for its lead candidate, Pyridorin™. NephroGenex would likely have to raise additional capital in order to support the completion of a second confirmatory pivotal trial with Pyridorin™, along with a regulatory filing and commercialization if it elected to launch the product independently. Given these factors, shares of NephroGenex may constitute above-average risk and volatility, in our opinion.

FDA Unpredictability. Drug development is a multi-year process that requires human clinical trials prior to market entry. The agency may require more clinical data from NephroGenex prior to granting approval for any of its regulatory applications, necessitating further trials. Review times at the FDA may prove longer than expected. Also, the agency could elect not to accept NephroGenex's regulatory filings petitioning for approval of Pyridorin™. If clinical data and/or other supporting evidence are not accepted or considered insufficient grounds for approval, marketing authorization for NephroGenex's only drug candidate could be delayed or might not occur at all, preventing the firm from realizing the commercial potential of its lead program.

Partnership Risk. NephroGenex is focusing on clinical advancement of its lead drug candidate in diabetic nephropathy, while eschewing any initiative to become a fully-integrated biopharmaceutical company. The firm aims to either partner the drug with an established company or become acquired. This introduces several elements of risk from a partnering perspective – the possibility that the company's partnership deals may not involve terms that are lucrative enough to justify the investment that NephroGenex has made in the development of its lead agent; the possibility that NephroGenex's partners do not invest sufficiently in the commercialization of NephroGenex's products; and the risk that the firm's partners may not be the best-positioned competitively to ensure maximal penetration of NephroGenex's most advanced drug into their target markets. Furthermore, should NephroGenex fail to attract a partner at all, the company would have to raise substantial additional capital to fund the establishment of a proprietary sales force or the hiring of a contract sales force. Such infrastructure may not be capable of supporting a successful launch.

Insufficient Diversification Risk. While we view NephroGenex as at least a partially risk-mitigated investment opportunity because of the fact that Pyridorin™ has been extensively tested in diabetic nephropathy patients with a solid safety and tolerability profile, we note that the firm does not have a pipeline beyond Pyridorin™ for diabetic nephropathy. Accordingly, if Pyridorin™ fails to show statistically significant efficacy in the planned PIONEER study, NephroGenex may find itself without strategic options.

Competitive Landscape. NephroGenex is aiming to compete with other, more established firms within the pharmaceutical sector. Some of these competitors include Eli Lilly & Co., Novartis, and Pfizer, all of which have drugs already on the market for the treatment of diabetes and many of their franchises are well-entrenched, although these firms do not currently have marketed products focusing specifically on diabetic nephropathy. In addition, these competitors may develop new or enhanced products or processes that may be more effective, less expensive, safer or more readily available than any products or processes that NephroGenex may be capable of developing.

Intellectual Property Risk. The company relies on patents and trade secrets to protect its products from competition. A court might not uphold NephroGenex's intellectual property rights, or it could find that NephroGenex infringed upon another party's property rights. The current patent estate on Pyridorin™ begins to expire in 2016, although additional synthesis and method of use patents extend coverage to the 2024 / 2025 time frame without Hatch-Waxman extensions. However, we note that Pyridorin™ is unlikely to secure regulatory approval until the 2019 time frame. Potential licensees might regard the current patent estate as too short-lived to permit them to readily realize sufficiently significant profits from sales of Pyridorin™ prior to patent expiration that would justify licensing the drug or acquiring NephroGenex.

Reimbursement Risk. Following the institution of broad healthcare reform policy, reimbursement agencies have grown more wary of systematically reimbursing for drugs that are either unnecessary or provide marginal benefit at excessive cost. If Medicare spending growth continues to outpace GDP growth, and the government's ability to fund healthcare becomes impaired, changes could be made to reimbursement policy that would negatively affect NephroGenex, despite what we feel to be compelling value inherent in the firm's lead drug candidate for treatment of diabetic nephropathy.

Additional Risks. Following its recent IPO in February 2014, NephroGenex had about $33.5 million in cash and equivalents. While the firm is not projected to burn a significant amount of cash near-term, these estimates could change if the firm began developing additional candidates beyond the current pipeline or if the firm were to be required to perform further studies beyond the envisaged pivotal trials. Other sources of cash could include: licensing fees from partnerships, warrant and option exercises, or the issuance of more shares. If Pyridorin™ fails to demonstrate efficacy and safety in pivotal clinical development, NephroGenex may not be able to raise cash at all.

Industry Risks. Emerging biotechnology and pharmaceuticals stocks are inherently volatile and increasingly subject to development and regulatory risk. Meeting or missing commercialization milestones may result in a significant change in the perception of the company and the stock price. We do not anticipate volatility subsiding in the near term.

For additional risk considerations, please refer to the company's SEC filings.

Valuation

Comparables Analysis: Since NephroGenex is unprofitable and given our belief that sustainable profitability is some distance off, we use a discounted cash flow-based approach to value the shares. Based on a comparables analysis, it appears the stock is worth $25.00 per share, utilizing our estimate of a ~$250 million risk-adjusted net present value (rNPV) for Pyridorin™ in the treatment of diabetic nephropathy and additional value of $20 million for the firm's pipeline. This assumes that the shares trade in-line with the comps' present average enterprise value of ~$270 million and that the firm has ~13 million shares outstanding (fully-diluted) and ~$53 million in cash at end-2015.

Table 1: Comparable Company Analysis
(Millions, Except Per-Share Data)

Development stage	Therapeutic focus	Company Name	Ticker	Rating	Closing Price (06/16/14)	Shares (MM)	Market cap ($MM)	Cash ($MM)	Debt ($MM)	Enterprise value ($MM)
Phase 2b	Infectious Diseases	Achillion Pharmaceuticals	ACHN	Not Rated	$7.82	97	757	141	0	617
Phase 2 / 3	Various	Auspex Pharmaceuticals	ASPX	Not Rated	$21.42	23	488	120	14	382
Phase 3	Infectious Diseases	Cempra	CEMP	Not Rated	$9.97	33	331	80	15	266
Phase 2b	Hepatology	Conatus Pharmaceuticals	CNAT	Not Rated	$8.43	15	130	51	1	80
Phase 2b / 3	Oncology	CytRx Corporation	CYTR	Buy	$5.11	56	285	113	0	172
Marketed	Infectious Diseases	Durata Therapeutics	DRTX	Not Rated	$16.16	27	431	42	25	414
Phase 3	Gastroenterology	Evoke Pharma	EVOK	Buy	$8.00	6	49	22	3	30
Marketed	CNS / Pain / Gastroenterology	Progenics Pharmaceuticals	PGNX	Not Rated	$4.43	70	308	94	0	214
Phase 3	Cardiovascular Disease	Regado Biosciences	RGDO	Not Rated	$6.44	34	216	35	5	186
Phase 3	Gastroenterology	Synergy Pharmaceuticals	SGYP	Buy	$4.14	94	388	71	0	317
		Average					**339**			**270**
								Discrepancy		
Current valuation	**Pain**	**NephroGenex, Inc.**	**NRX**	**Buy**	**$5.77**	**9**	**49**	**34**	**0**	**16**
					Derived 18-month target price					
										Projected
Target valuation (18-month)	**Pain**	**NephroGenex, Inc.**	**NRX**	**Buy**	**$25.00**	**13**	**323**	**53**	**0**	**270**

Source: First Call and Aegis Capital Corp. estimates

Free Cash Flow: We estimate that NephroGenex is likely to be free cash flow negative for the foreseeable future. We define free cash flow as operating cash flow minus capital expenditures and dividend payments. We utilize a discounted cash flow analysis supporting a risk-adjusted Net Present Value (rNPV) framework to derive our $25.00 price target. This approach is described further in the next section of the report.

Our detailed analysis is split into three principal components – our discounted cash flow model including the rNPV assessment of Pyridorin™ (presented overleaf); our assessment of the market for this agent and the associated sales model for the drug; and the near-term financial outlook for the company. Our historical income statement and financial projections are presented at the back of this report.

Risk-Adjusted Net Present Value Analysis

We have computed a risk-adjusted Net Present Value (rNPV) assessment of NephroGenex's pipeline – consisting principally of Pyridorin™ and related analog compounds – in order to derive our fundamental valuation of the company. As shown below, our rNPV analysis yields a total firm value of ~$320 million, or approximately $25.00 per share. The firm's preclinical pipeline and Pyridorin™ for acute kidney injury contribute an additional $20 million, which we consider conservative. We project that Pyridorin™ could be launched in the 2019 – 2020 time frame. We have only modeled sales in the U.S. and Europe, which may prove conservative. We assume that the U.S. market represents the lion's share of the global opportunity for NephroGenex.

Table 2: Composite Risk-Adjusted Net Present Value Analysis

Pyridorin Formulations - Global	
Total Type 2 diabetes patients[1]	52.4MM
Patients seeking treatment[2]	8.8MM
Peak market share[3]	21%
Treatment revenue/prescription/course of therapy[4]	$970
Peak sales[5]	$1.9B
Launch[6]	2019 / 2020
Peak sales year	2024
Protection expires[7]	2024 / 2025
Discount rate	20%
Probability of success[8]	60%
Risk-adjusted NPV[9]	$250MM
NPV per share	$20.00
Estimated Net Cash Position ($MM; end-2015)	$53MM
Additional Value Drivers (pyridoxamine analogs)	$20MM
Total enterprise value	$323MM
Shares Outstanding (MM; end-2015)	13MM
Present value-derived price target	$25.00

Notes on assumptions:

[1] Adult post-operative pain patients - primarily U.S. and European markets
(Source: National Institute of Health, Centers for Disease Control and Prevention; American Diabetes Association)

[2] Patients with intermediate-stage kidney disease
(Source: Aegis Capital Corp. estimates)

[3] Peak market share - blended; factoring in competition from existing drugs and future therapeutic approaches

[4] Revenue/year/prescription - projected ~$1,000 per year for Pyridorin™; 3% annual price increases

[5] Peak sales - treatment revenue/year x treated patients x peak market share

[6] Launch in late 2019 in the U.S. / mid- to late 2020 in Europe

[7] Patent expiry starting in 2024; Hatch-Waxman extensions may provide up to an additional five years of protection

[8] Probability of success - proof-of-concept activity in Phase 2 studies; starting Phase 3 trial

[9] Cash flow fully taxed at 40% following launch; no significant net operating loss carry-forwards assumed

Source: Company reports; Aegis Capital Corp. estimates

Since NephroGenex has built up an extremely modest accumulated deficit of only $43 million since inception in 2004, we believe that it is unlikely for the company to be able to offset taxes to any significant extent. While NephroGenex is likely to remain cash flow-negative for the foreseeable future and therefore could accumulate additional net losses in the coming years, we have chosen to utilize a 40% corporate tax rate and apply this to all future cash flows obtained from Pyridorin™. Furthermore, we have modeled out the discounted cash flows required to derive our risk-adjusted Net Present Value (rNPV) using the assumption that NephroGenex would out-license Pyridorin for the purposes of commercialization, and that the company would thus receive royalties on net sales of the drug from its putative future partner.

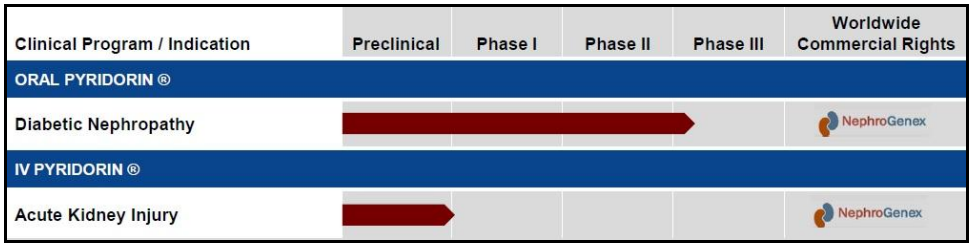
Company Overview

NephroGenex, Inc. is an emerging biopharmaceutical firm developing a novel small molecule drug called Pyridorin for the treatment of nephropathy (kidney disease) in diabetic patient populations. The firm was founded in May 2004. NephroGenex received initial funding from Care Capital and Rho Ventures, a division of Rho Capital Partners. Care Capital, based in Princeton, NJ, was founded in 2001 and currently oversees the deployment of roughly $500 million across a range of life sciences companies. The firm is currently investing its third fund, Care Capital Investments III, L.P. Care Capital has had 16 exits over the course of its existence, including the public listings of Anacor Pharmaceuticals, Dynavax, and Vanda Pharmaceuticals, and the acquisitions of Anadys Pharmaceuticals in 2011 by Roche for roughly $230 million and Tercica by Ipsen in 2008 for $404 million.

Rho Capital Partners has offices in New York, Palo Alto, CA, and Montreal, Canada. Rho Ventures, which has a track record spanning over 30 years, has also achieved various notable exits involving its portfolio companies, including the acquisition of Human Genome Sciences by GlaxoSmithKline for roughly $3 billion (net of cash and debt) in 2012 and the takeover of Gloucester Pharmaceuticals by Celgene in 2009 for $340 million upfront and up to $300 million in potential milestone payments. Rho Ventures and Care Capital have overlapped with investments in certain firms, including Tercica and Vanda Pharmaceuticals.

The figure below showcases NephroGenex's development pipeline:

Figure 1: Development Pipeline



Source: NephroGenex, Inc.

NephroGenex initially licensed patents covering methods of use and synthesis of Pyridorin™ from BioStratum, Inc. in May 2006. The firm subsequently acquired Pyridorin™-related patents from BioStratum through a Series A financing completed in May 2007. At the time of acquisition, BioStratum – through its contracted investigators, contract research organizations, and collaborators – had completed five preclinical efficacy studies, 36 preclinical safety studies, four Phase 1 studies and five Phase 2 studies with Pyridorin™. NephroGenex subsequently conducted a multi-center, randomized, placebo-controlled Phase 2b study, PYR-210. In addition, the firm has worked closely with the FDA to establish a new regulatory pathway to approval.

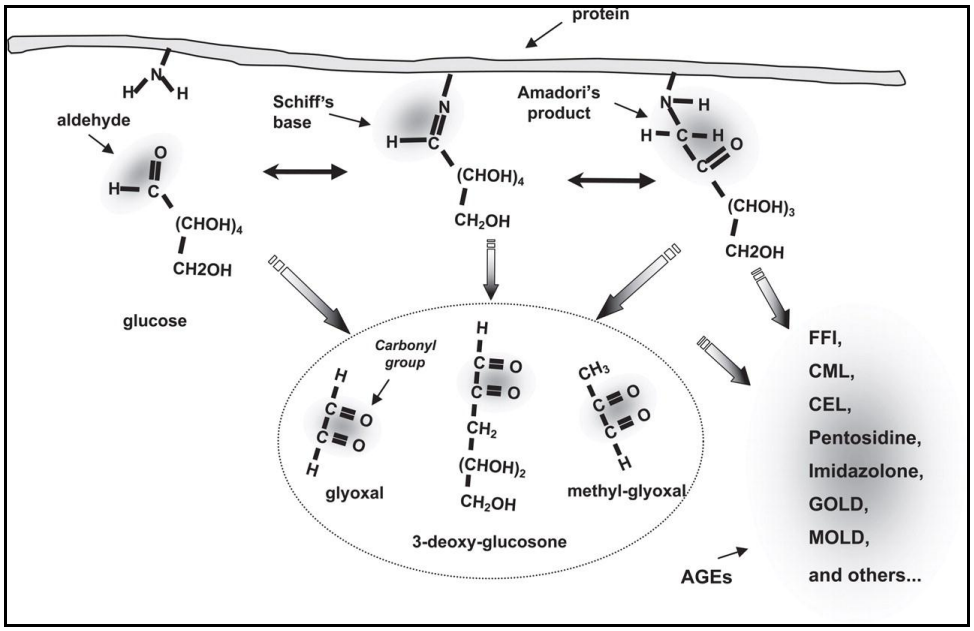
Pyridorin™ has demonstrated preliminary evidence of efficacy in slowing the progression of diabetic nephropathy in relevant patient populations in three Phase 2 clinical studies. Based on these results, Pyridorin™ is slated to be further developed in a Phase 3 program that is under a Special Protocol Assessment (SPA) from the FDA. This Phase 3 program will use a novel primary outcome measure involving an events-based endpoint based on either progression to 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 either a 100% increase in SCr from baseline or progression to ESRD. Based on an analysis of the Irbesartan Type 2 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 NephroGenex could be the first company to use this novel endpoint in a Phase 3 trial.

In addition to the use of oral Pyridorin™ for diabetic nephropathy, NephroGenex is 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. The basis for the company's work on the various formulations of Pyridorin™ and its related analogs in kidney disease and other disorders with similar underlying pathologies stems from the theory behind the involvement of oxidative chemistries in tissue damage.

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 broad-based disturbance or interruption 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 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). The figure below shows some of the molecular cascades that lead to the formation of these AGE species.

Figure 2: Advanced Glycation End-Product Production Pathways

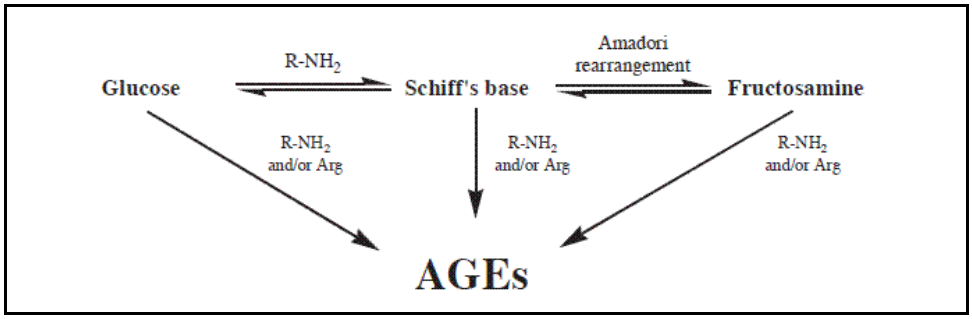


Source: Nature Medicine (2008)

One pathway of particular interest is the post-Amadori cascade leading to AGE formation. The study of this pathway led to the discovery of Pyridorin™ as a promising drug candidate for diabetic nephropathy. NephroGenex's founding scientists first isolated protein-Amadori intermediates and then deployed these molecules in order to identify 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, did not exhibit an ability to inhibit the formation of the well-characterized AGE species carboxymethlylysine (CML) under these conditions. However, Pyridorin™ uniquely exhibited potent post-Amadori inhibitory activity. 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 was demonstrated in various preclinical studies. The figure below shows the involvement of the Amadori rearrangement in the formation of AGE species.

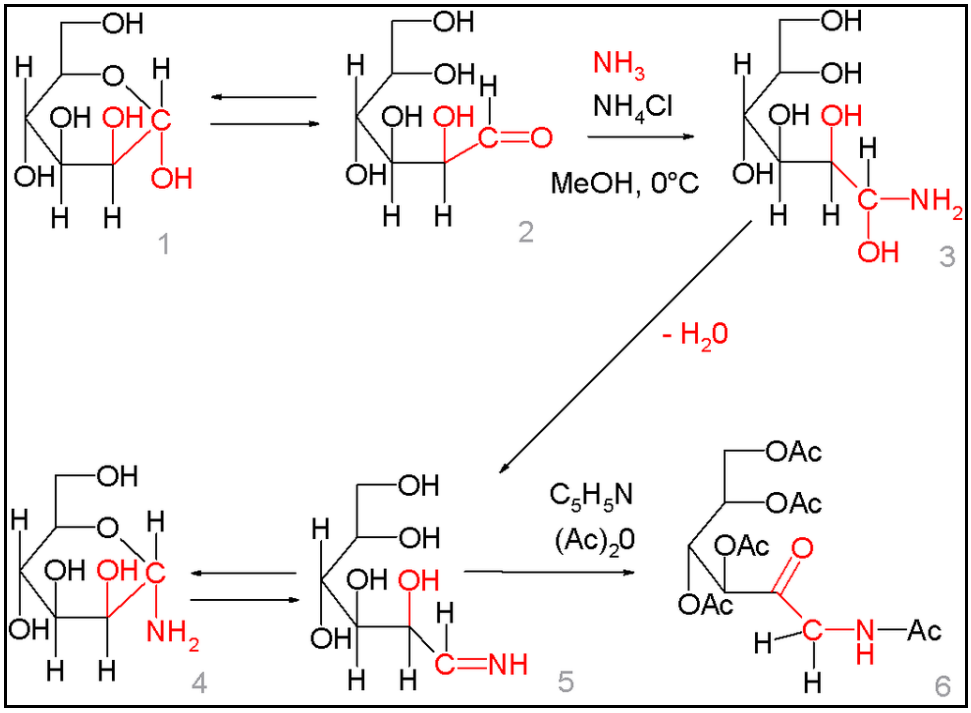
Figure 3: AGE Formation Via Amadori Rearrangement



Source: Nature Medicine (2008)

The Amadori rearrangement is an organic reaction describing the acid or base catalyzed isomerization or rearrangement reaction of the N-glycoside of an aldose or the glycosylamine to the corresponding 1-amino-1-deoxy-ketose, and is important in carbohydrate chemistry. The mechanism is shown below, starting from the reaction of D-mannose in its closed (1) and open-form (2) with ammonia to produce the 1,1-amino-alcohol (3), which is unstable and loses water to the glycosylamine – again the open imine (5) and the closed form hemiaminal (4) – the starting point for the rearrangement.

Figure 4: Amadori Rearrangement Process



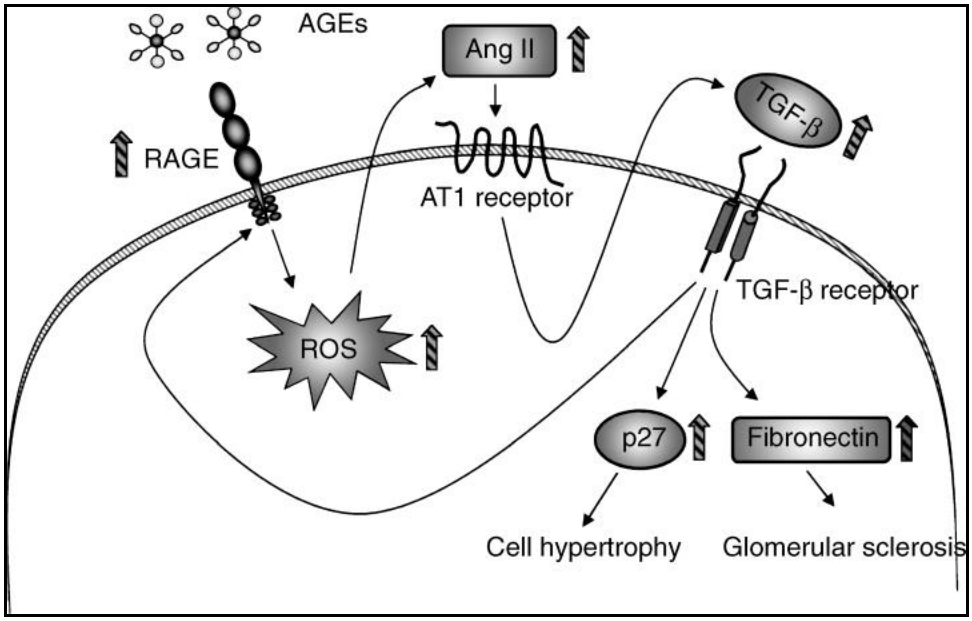
Source: Laszlo Kurti, Strategic Applications of Named Reactions in Organic Synthesis

Through treatment of the glycosylamine with pyridine and acetic anhydride, the imine group rearranges and the intermediate enol, in turn, rearranges to the ketone. In this particular reaction, all the alcohol and amino groups are acylated as well. The reaction is associated with the Maillard reaction, in which the reagents are naturally occurring sugars and amino acids. As mentioned previously, an Amadori product is an intermediate in the production of AGE species as a result of glycation. The formation of an AGE molecule via the Amadori rearrangement involves the following:

1. Formation of a Schiff base: For example, the aldehyde group of a glucose molecule will combine with the amino group of a lysine molecule (in a protein) to form an imine or Schiff base, which is a double bond between the carbon atom of the glucose and the nitrogen atom of the lysine.
2. Formation of an Amadori product: The Amadori product is a re-arrangement from the Schiff base, wherein the hydrogen atom from the hydroxyl group adjacent to the carbon-nitrogen double bond moves to bond to the nitrogen, leaving a ketone.
3. Formation of an advanced glycation end-product (AGE): The Amadori product is oxidized, most often by transition metal catalysis.

The first two steps in this reaction are both reversible, but the last step is irreversible. The figure below shows how the formation of AGE species is tied to the initiation of cellular hypertrophy (abnormal growth) and glomerular sclerosis, which refers to scarring of the glomeruli – the filtering units within the kidney.

Figure 5: AGE Involvement in Nephropathy



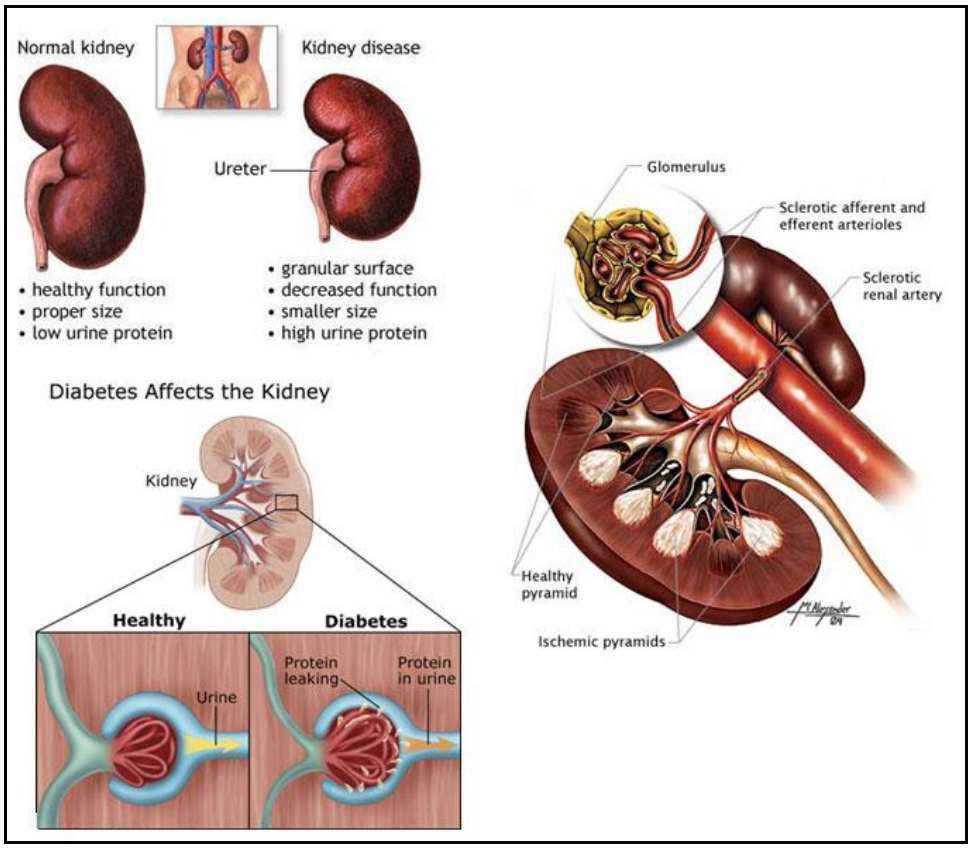
Source: Nature Medicine (2008)

Chronic hyperglycemia is directly associated with end-organ damage in patients with diabetes. The major target organs affected – the kidney, peripheral nerves, retina, and the vasculature – are all exposed to the deleterious impact of glucose fluctuations, since they are not under insulin regulation. This hyperglycemia-related 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 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. Blood enters the kidneys

through arteries that branch inside the kidneys into tiny clusters of looping blood vessels. Each cluster is called a glomerulus, which comes from the Greek word meaning filter. The plural form of the word is glomeruli. There are approximately 1 million glomeruli, or filters, in each kidney. The glomerulus is attached to the opening of a small fluid-collecting tube called a tubule. Blood is filtered in the glomerulus, and extra fluid and wastes pass into the tubule and become urine. Eventually, the urine drains from the kidneys into the bladder through larger tubes called ureters. Each glomerulus-and-tubule unit is called a nephron. Each kidney is composed of about 1 million nephrons. In healthy nephrons, the glomerular membrane that separates the blood vessel from the tubule allows waste products and extra water to pass into the tubule while keeping blood cells and protein in the bloodstream.

As shown in the figure below, the kidneys can be harmed under diabetic conditions, which lead to scarring of the glomeruli and thus cause proteins to leak out of the bloodstream into the urine. One protein in particular, albumin, acts as a "sponge" to draw extra fluid from the body into the bloodstream, where it is circulated until removed through the kidneys. If albumin is allowed to leak into the urine, the blood loses its ability to efficiently remove excess fluid from the body's tissues. The excess fluid then accumulates, causing swelling of the face, hands, feet and ankles (edema) that can be painful and restrict movement.

Figure 6: Diabetic Nephropathy

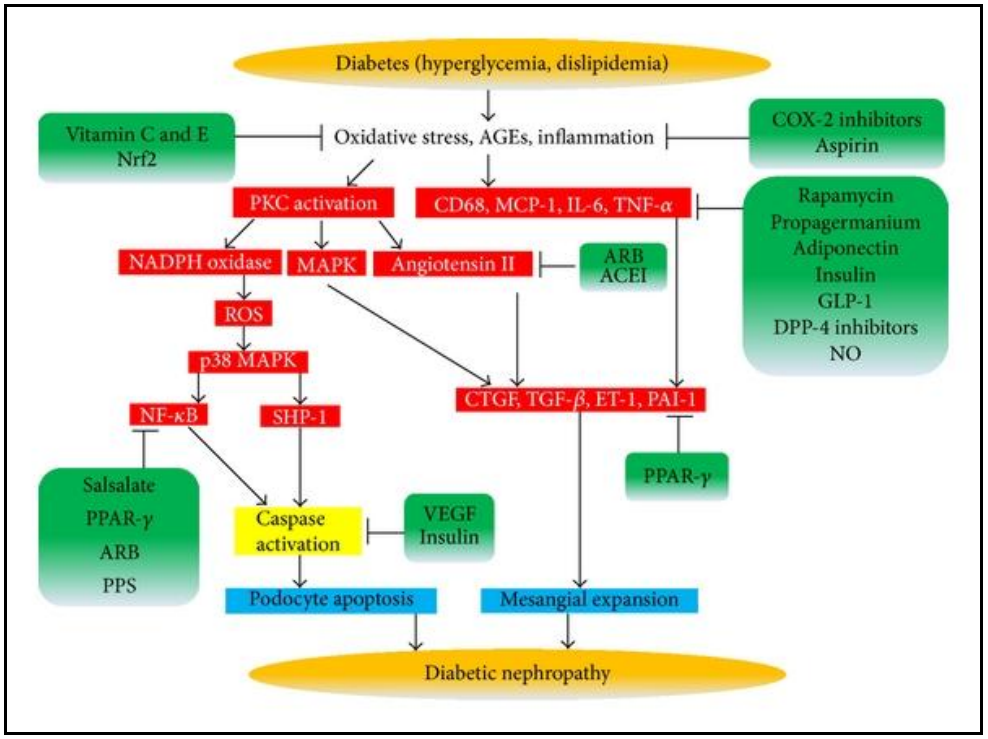


Source: American Diabetes Association

Thus, the various symptoms of glomerular disease include albuminuria (large amounts of protein in the urine); hematuria (blood in the urine); reduced GFR (inefficient filtering of waste products from the blood); hypoproteinuria (low blood protein content); and edema (swelling in various body tissues due to excess fluid accumulation). The molecular

pathways underlying diabetic nephropathy are depicted in the figure below. As shown in this schematic, various drugs can have a beneficial impact on such pathways, but none of these directly act upon the formation of AGEs. Vitamins primarily suppress oxidative stress by soaking up ROS molecules, while cyclooxygenase-2 (COX-2) inhibitors and aspirin primarily suppress inflammation. Drugs such as rapamycin and dipeptidyl peptidase IV (DPP-4) inhibitors work by directly suppressing the upregulation of cellular hypertrophy-inducing growth factors, such as interleukin-6 (IL-6) and transforming growth factor beta (TGF-β). However, since these growth factors play important roles under normal conditions, interfering with their functions means that these drugs often cause unwanted off-target effects that can make them difficult for patients to tolerate.

Figure 7: Diabetic Nephropathy Signaling Pathways



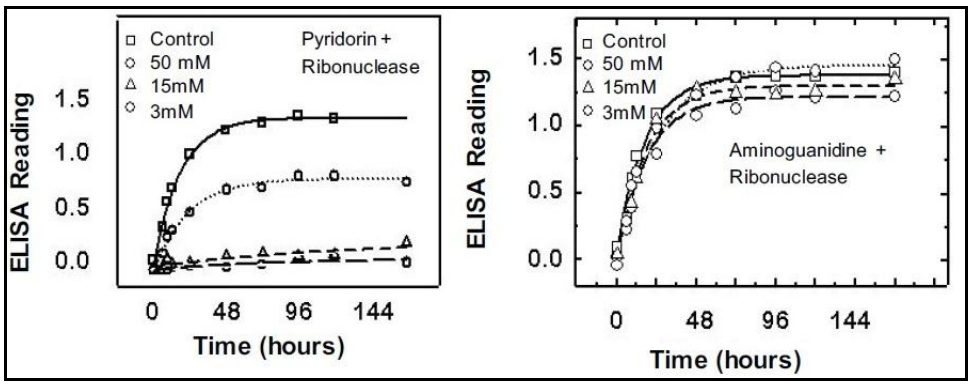
Source: Nature Medicine (2008)

Diabetic nephropathy is the leading cause of glomerular disease and of total kidney failure in the United States. Kidney disease is one of several problems caused by elevated levels of blood glucose, the central feature of diabetes. In addition to scarring the kidney, elevated glucose levels appear to increase the speed of blood flow into the kidney, putting a strain on the filtering glomeruli and raising blood pressure.

Typically, the processes causing diabetic nephropathy can take many years to cause damage. People with diabetes can slow down damage to their kidneys by controlling their blood glucose through healthy eating with moderate protein intake, physical activity, and medications. Diabetics should also be careful to keep their blood pressure at a level below 140/90 mm Hg, if possible. Blood pressure medications, such as angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) are particularly effective at minimizing kidney damage and are now frequently prescribed to control blood pressure in patients with diabetes and in patients with many forms of kidney disease. However, these drugs do not address the underlying pathology of AGE formation and oxidative damage to glomeruli in diabetic nephropathy. Accordingly, therefore, additional therapeutic approaches are needed. In our view, direct suppression of AGE formation could be effective without inducing unwanted side effects.

The graphs below depict the inhibitory capacity of Pyridorin™ on formation of AGE species. Figure 8 (left) shows that Pyridorin™ dose-dependently inhibits post-Amadori AGE formation. The right-hand graph shows that aminoguanidine (Pimagedine) has surprisingly little ability to block AGE formation from Amadori intermediates.

Figure 8: Pyridorin Inhibition of Post-Amadori AGE Formation



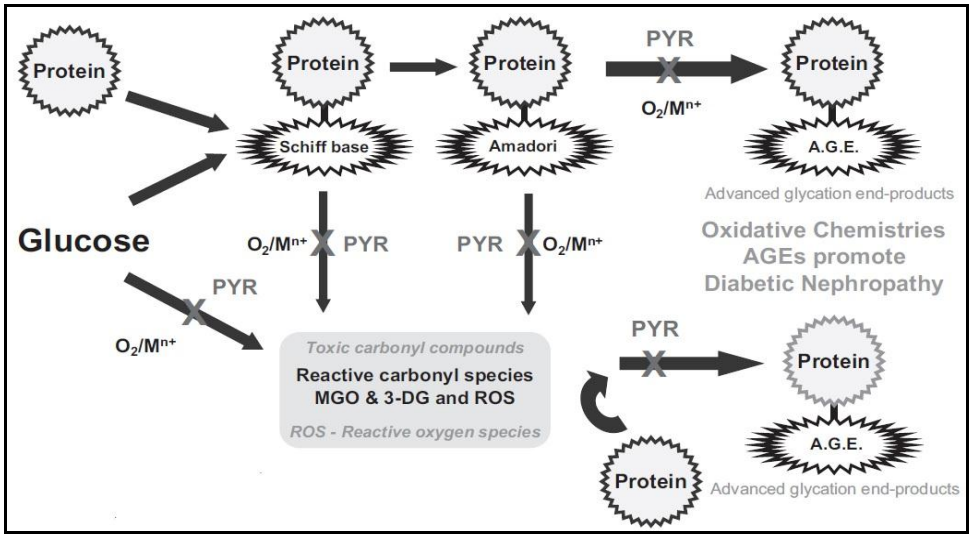
Source: Khalifah et al., Biochemical & Biophysical Research Communications (1999)

In vitro studies show that Pyridorin™ inhibits AGE formation and scavenges ROS molecules and toxic carbonyl compounds. For example, Pyridorin™ has been shown to:

- inhibit the degradation of glycated proteins to AGEs;
- block lipoxidation (lipid oxidation) by trapping lipoxidation intermediates, particularly 1,4-dicarbonyls;
- scavenge intermediates of carbonyl stress such as glyoxal and methylglyoxal;
- trap the hydroxyl radical (a highly reactive and short-lived neutral form of the hydroxide ion (HO−); and
- bind to redox transition metal ions – such as copper (Cu^{2+}), manganese (Mn^{2+}), and iron (Fe^{2+}) – which interfere with their catalytic role in oxidative reactions (redox chemical reactions are common physiological electron transfer reactions).

All of the above have been implicated in diabetic microvascular disease. The figure below depicts the various pathogenic pathways that are targeted by Pyridorin™ (PYR):

Figure 9: Specific Pathogenic Oxidative Chemistry Targeting

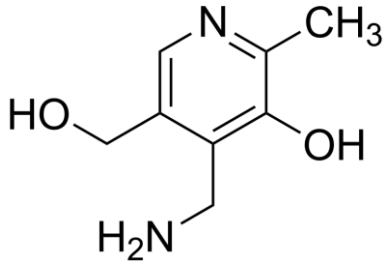


Source: NephroGenex, Inc.

Pyridorin™ (Pyridoxamine HCl) Overview

A novel small molecule with significant structural similarity to vitamin B6 (pyridoxine), Pyridorin™ is based on a pyridine ring structure, with hydroxyl, methyl, aminomethyl, and hydroxymethyl substituents. It differs from pyridoxine by the substituent at the 4-position. The phenol at position 3 and aminomethyl group at the fourth position of its ring endow pyridoxamine with a variety of chemical properties, including the scavenging of free radical species and carbonyl species formed in sugar and lipid degradation and chelation of metal ions that catalyze Amadori reactions.

Figure 10: Pyridoxamine Chemical Structure



Source: ADIS R&D Insight

Pyridorin™ is classified as a vitamer – a molecule with structural similarity to a known vitamin compound that can have vitamin-like properties in a vitamin-deficient organismal system. Pyridoxamine is typically converted in the body to the biologically active form of vitamin B6, pyridoxal-5-phosphate, via the vitamin B6 salvage pathway. It is found in food as a 5'-phosphate derivative, which is hydrolyzed by intestinal phosphatases to pyridoxamine and absorbed in the jejunum of the small intestine[1]. Absorbed pyridoxamine is converted to pyridoxamine 5'-phosphate by pyridoxal kinase, which is further converted to the active pyridoxal 5-phosphate by pyridoxamine-phosphate transaminase or pyridoxine 5'-phosphate oxidase[2].

As mentioned earlier, pyridoxamine can form fairly weak complexes with a number of transition metal ions, with a preference for Cu^{2+} and Fe^{3+}. The 3'-hydroxyl group of pyridoxamine allows for efficient hydroxyl radical scavenging. Pyridoxamine inhibits the Maillard reaction[3]. The compound is hypothesized to trap intermediates in the formation of Amadori products released from glycated proteins, possibly preventing the breakdown of glycated proteins by disrupting the catalysis of this process through disruptive interactions with the metal ions crucial to the redox reaction. One research study found that pyridoxamine specifically reacts with the carbonyl group in Amadori products, but inhibition of post-Amadori reactions (that can create advanced glycation end-products) is much more likely due to the metal-chelating capabilities of the molecule.

A variety of preclinical studies in animal models of diabetes indicated that pyridoxamine improved kidney histology in a manner comparable or superior to aminoguanidine[4]. Given this data, NephroGenex is focused on assessing the drug's clinical utility in the treatment of diabetic nephropathy[5]. We note that, while pyridoxamine was previously sold in the U.S. as a dietary supplement, the FDA ruled in 2009 that it must be regulated as a pharmaceutical product. This ruling was in response to a Citizen's Petition made in 2005 by BioStratum, NephroGenex's predecessor in the development of Pyridorin™.

[1] Merrill *et al*., Annals of the New York Academy of Sciences 585: 110-117 (1990)
[2] Ink and Henderson. Annual Reviews of Nutrition 4: 455-470 (1984)
[3] Voziyan *et al*., Annals of the New York Academy of Sciences 1043: 807-816 (2005)
[4] Giannoukakis. Current Opinion on Investigational Drugs 6: 410-418 (2005)
[5] Williams *et al*., American Journal of Nephrology 27: 605-614 (2007)

Pyridorin™ Clinical Development Program

In this section, we provide an overview of the Pyridorin clinical development program. This cannot be fully understood without a description of the natural course of diabetic nephropathy. The table below depicts the natural history of different stages of diabetic nephropathy in terms of various parameters – time, blood pressure, and kidney function.

Table 3: Natural History of Diabetic Nephropathy

	Designation	Characteristics	GFR (minimum)	Albumin Excretion	Blood Pressure	Chronology
Stage 1	Hyperfunction and hypertrophy	Glomerular hyperfiltration	Increased in type 1 and type 2	May Be Increased	Type 1 normal Type 2 normal hypertension	Present at time of diagnosis
Stage 2	Silent stage	Thickend BM Expanded mesangium	Normal	Type 1 normal Type 2 may be <30-300 mg/d	Type 1 normal Type 2 normal hypertension	First 5 years
Stage 3	Incipient stage	Microalbuminuria	GFR begins to fall	30-300 mg/d	Type 1 increased Type 2 normal hypertension	6-15 years
Stage 4	Overt diabetic nephropathy	Macroalbuminuria	GFR below N	>380 mg/d	Hypertension	15-25 years
Stage 5	Uremic	ESRD	0-10	Decreasing	Hypertension	25-30 years

Source: American Diabetes Association

Phase 2 Proof-of-Concept Clinical Data

While six Phase 2 trials were done with Pyridorin™, we are herein focusing our analysis on PYR-206, PYR-205 / PYR-207, and PYR-210, the largest of these studies.

PYR-206

PYR-206 was a multi-center, placebo-controlled, randomized, double-blind U.S. study of oral Pyridorin™ (50mg capsules) given twice-daily for 24 weeks. 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. Pyridorin™ reduced the change in SCr concentration from baseline by 27% for all patients. While Pyridorin™ did not reach significance in the intent-to-treat (ITT) population, it was statistically significant for the prospectively defined subgroup of diabetic subjects with a starting baseline SCr level ≥ 1.3 mg/dL.

Table 4: Phase 2 PYR-206 Trial Clinical Data

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

(1) Mean ± SD in mg/dL
** Statistically significant, p<0.01
(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)

Source: NephroGenex, Inc.

PYR-205 / PYR-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 pre-specified 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 twice-daily dosages of 50mg and 100mg for two weeks, and 250mg for 20 weeks. The study was conducted from July 2002 to September 2003 in the U.S., Belgium, the U.K., 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 sub-groups. The renal protection effect of Pyridorin™ vs. placebo was seen to an equal degree across all groups, with a ~70% reduction relative to placebo with respect to increase in SCr from baseline (see below).

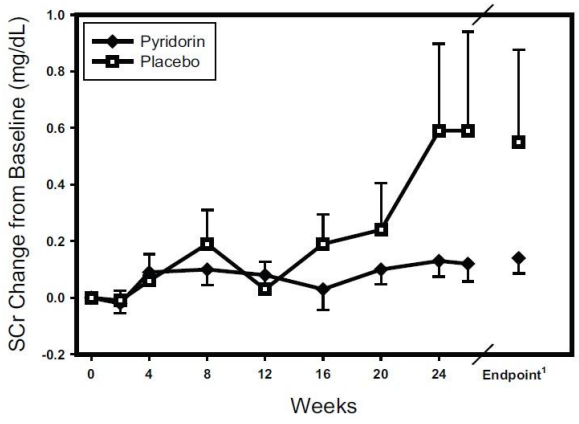
Table 5: Phase 2 PYR-205 / PYR-207 Trial Clinical Data

Patient Population	Number of Subjects	Baseline SCr		SCr Change from Baseline		Pyridorin Treatment Effect	P value
	PYR, Placebo	PYR	Placebo	PYR	Placebo		
All Patients	57, 27	1.75 ± 0.64	1.96 ± 0.86	0.11 ± 0.26 ⟷	0.34 ± 0.92	68%	0.0322*
Type 2 Diabetes	45, 22	1.74 ± 0.67	1.94 ± 0.92	0.12 ± 0.27 ⟷	0.38 ± 1.02	68%	0.0498*
Baseline SCr ≥ 1.3 mg/dL	42, 19	2.00 ± 0.55	2.37 ± 0.67	0.12 ± 0.30 ⟷	0.47 ± 1.09	74%	0.0454*
Type 2 Diabetes, Baseline SCr ≥ 1.3 mg/dL	33, 15	2.00 ± 0.58	2.40 ± 0.73	0.14 ± 0.31 ⟷	0.55 ± 1.22	75%	0.058

Source: NephroGenex, Inc.

The figure below illustrates the impact over time of Pyridorin™ therapy on SCr levels vs. placebo. As can be seen from this graph, the treatment effect appeared to increase as patients progressed through the study, which indicates that Pyridorin™ may have a cumulative impact on the course of the disease, reducing the likelihood of renal damage.

Figure 11: Phase 2 PYR-205 / PYR-207 SCr Increase Reduction



Source: NephroGenex, Inc.

PYR-210

PYR-210 was a randomized, double-blind, placebo-controlled study of Pyridorin™ at twice-daily doses of 150mg and 300mg or placebo for 12 months. PYR-210 was designed to further study Pyridorin™ efficacy and safety, and to identify the appropriate dose and patient population for Phase 3 pivotal trials. This was the only Pyridorin™ clinical study actually conducted by NephroGenex, which used Medpace, a well-known CRO. The study was conducted from August 2008 to August 2010 in the U.S., Australia and Israel. The population selected had macroalbuminuria and impaired renal function. Although previous pivotal trials for diabetic nephropathy (notably, the IDNT study of irbesartan and the RENAAL study of 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 herein to evaluate Pyridorin™ safety in more advanced renal disease patients.

Patients were required to be on an established diabetic nephropathy standard of care (SOC) at screening. Specifically, patients needed to have received a renin-aldosterone-angiotensin-system (RAAS) inhibitor (ACE-I) or an ARB for at least three months prior to screening. Patients also had to be on stable blood pressure medications (other than an ACE-I or ARB) for two months prior to screening, or had to undergo a blood pressure medication introduction and run-in period prior to screening. Since changes in ACE-I/ARB or blood pressure medications are known to affect baseline SCr values, a pre-specified analysis of patients on SOC at screening was included in the statistical analysis plan. Eligible patients also had a history of overt diabetic nephropathy, as 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 a 24-hour urine collection Protein to Creatinine Ratio (PCR) > 1200mg/g.

The trial did not reach its primary endpoint on the intent to treat (ITT) population, with Pyridorin™ failing to show a significant impact on change in SCr vs. baseline after 12 months. However, results from a pre-specified analysis of patients on established SOC at screening showed a treatment effect of 45% for the 300mg twice-daily dose and 21% for the 150mg twice-daily dose vs. placebo. When patients with a baseline SCr < 3.0 mg/dL that were on established SOC at screening were analyzed, a statistically significant treatment effect of 57% for the Pyridorin™ 300mg dose (p=0.0094) and 45% for the Pyridorin™ 150mg dose (p=0.0414) was observed. The more robust effect observed in the Pyridorin™ 300mg twice-daily group over the Pyridorin™ 150mg twice-daily group suggests a potential dose response in this population. This subgroup represents the target population to be studied in the Phase 3 trial. We note that the subgroup analysis carries the inherent risk that the results may not be repeatable in subsequent studies, and therefore the effect seen in PYR-210 may not be reproducible in pivotal development.

Table 6: Phase 2 PYR-210 Trial Efficacy Data

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 on SOC @ screening in the RENAAL population (bSCr < 3.0)[1]	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	

*; p<0.05; **; p<0.01

Source: NephroGenex, Inc.

The safety profile of Pyridorin™ was encouraging in all Phase 2 trials, with no serious adverse events, no meaningful differences between the treatment and placebo groups with respect to adverse event incidence, and no effect of Pyridorin™ on QT_c interval.

Phase 3 Pivotal Trial Program

In our view, one of the main advantages that NephroGenex possesses is the novel pivotal clinical trial design for Pyridorin™. The previous approvable endpoint required in pivotal trials by the FDA (time to SCr doubling or ESRD) made it nearly impossible to evaluate the drug candidate against a similar endpoint in Phase 2 testing. Consequently, many companies instead chose to study surrogate endpoints that could be evaluated in shorter trials. They also chose patient populations where a treatment effect on the surrogate endpoint would be the most pronounced. Since the FDA would not accept these surrogate endpoints and narrow patient populations for the Phase 3 pivotal trial, this made their transition to Phase 3 risky. All of the companies that previously attempted Phase 3 development in diabetic nephropathy ended up evaluating a significant number of patients in Phase 3 testing that they had never studied before using an endpoint for which they had no previous results.

NephroGenex took a different approach with Pyridorin™ and instead chose to work more closely with the FDA on its Phase 2 study design. The company examined broader, FDA approvable patient populations, under different conditions of standard of care, and also used a SCr increase-based endpoint that would correlate as closely as possible with the FDA approvable endpoint. Simultaneously, the company provided the FDA with analyses from previously-completed Phase 3 clinical studies that supported a new, fully approvable, lower SCr increase-based endpoint. Use of such an endpoint would not only significantly reduce the time and cost of the Phase 3 trials necessary to secure approval, but also brought the Phase 2b endpoint even closer to the fully-approvable endpoint. In April 2012, NephroGenex reached agreement with the FDA on an SPA for the Pyridorin™ Phase 3 program. The Pyridorin™ Phase 3 pivotal trials are slated to be conducted on a patient population in which Pyridorin™ has previously shown a >50% treatment effect on a one-year SCr endpoint in three completed Phase 2 studies. This patient population excludes patients not on long-term standard of care at screening who were found to have blood pressure control problems during the treatment period in the Phase 2b study. Changes in blood pressure affect SCr baseline levels in patients with limited renal function. We believe that this removes a potential confounding factor that could have made it much more difficult to predict the outcome of the pivotal study.

The Phase 3 program will use a new 50% SCr increase event endpoint that the Pyridorin™ Phase 2b year-1 SCr change endpoint directly predicts. Thus, Pyridorin™ is actually entering Phase 3 development studying the same patient population using a very similar endpoint that was used in the Phase 2 studies. Therefore, in our view, the drug's transition to Phase 3 is being done at a substantially lower risk level than previously conducted pivotal trials in diabetic nephropathy. Although NephroGenex acknowledges that its trial design parameters are informed by efficacy data generated in a subgroup of patients who exhibited responses to Pyridorin™ during the previously-conducted Phase 2 PYR-210 study, we believe that this subgroup analysis has validity because of the statistically significant magnitude of the efficacy signal and the fact that the subgroup in question was prospectively defined. Unlike PYR-206, in which a *post hoc* subgroup assessment was performed, the PYR-210 study included prospectively defined subgroups. We note that both the PYR-206 and PYR-210 studies demonstrated the positive impact of Pyridorin™ among Type 2 diabetics with intermediate-stage disease.

NephroGenex has partnered with the Collaborative Study Group (CSG), a leading nephrology-focused academic research organization with 300 affiliated clinics worldwide, and Medpace, a contract research organization with demonstrated expertise and experience in nephrology. These firms will collaborate with NephroGenex to conduct the Pyridorin™ Phase 3 PIONEER study. NephroGenex expects to launch this, the first of two Phase 3 trials, in the first half of 2014. Both trials are slated to enroll roughly 600 patients each, with a 42-month duration (30-month follow-up).

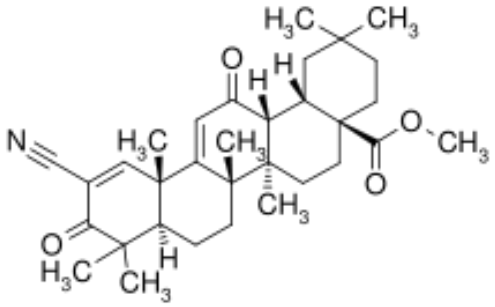
Competitive Landscape

While the diabetic nephropathy product opportunity is a substantial one, various firms have attempted to pursue the clinical development of therapeutic compounds in this indication with mixed degrees of success. Although several drugs are currently deployed in the treatment of this disease, none of them have a label specifically for diabetic nephropathy, and indeed their primary mode of action is targeted elsewhere. Examples of such drugs include the ACE inhibitors and ARBs, which are aimed mainly at control of hypertension and cardiac disease; the DPP-4 inhibitors, which were designed to manage Type 2 diabetes by reducing glucagon and blood glucose levels; and products such as rapamycin, which were aimed at suppression of growth factor expression known to be involved in the induction of cellular hypertrophy and glomerular sclerosis.

Clinical Trial Failures

There have been several failed mid- and late-stage trials in diabetic nephropathy (Pimagedine, Sulonex, Avosentan, bardoxolone methyl and CTP-499). One of the most notorious failures was that of the Reata Pharmaceuticals compound known as bardoxolone methyl. Reata managed to out-license the ex-U.S. rights to Abbott Laboratories (now AbbVie) in September 2010, in a transaction that involved $450 million in upfront and proximal milestone payments along with significant royalties on future net sales. Abbott appeared to have been enthused about the prospects of bardoxolone methyl, a novel synthetic triterpenoid agent that was characterized as an inducer of the Nrf2 pathway implicated in suppression of oxidative stress, based on positive data generated in Phase 2 development. A multi-center, double-blind, placebo-controlled Phase 2b clinical trial (BEAM) conducted in the U.S. studied 227 patients with moderate to severe CKD (eGFR 20 – 45 ml/min/1.73m²) and type 2 diabetes. The primary endpoint was change in estimated GFR following 24 weeks of treatment.

Figure 12: Bardoxolone Methyl Chemical Structure



Source: Reata Pharmaceuticals, Inc.

After 24 weeks, patients treated with bardoxolone methyl experienced a mean increase in estimated GFR of over 10 ml/min/1.73m², vs. no change in the placebo group. Roughly three-quarters of bardoxolone methyl-treated patients experienced an improvement in eGFR of 10% or more, including one-quarter who saw a significant improvement of 50% or more compared to less than 2% of patients on placebo. Adverse events were generally manageable and mild to moderate in severity. The most frequently reported adverse event in the bardoxolone methyl group was muscle spasm. Final data was published in the *New England Journal of Medicine*[6]. While the top-line data appeared impressive, concerns were raised as to whether there was a real improvement in kidney function because of the significant weight loss experienced by the patients in the active treatment group, which ranged from 7.7 kg – 10.1 kg (7% – 10% of the total initial body weight)

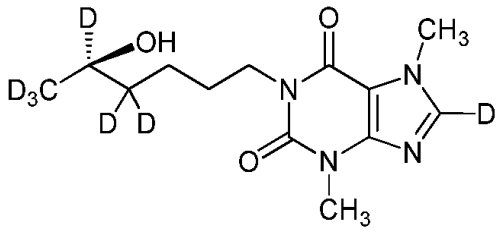
[6] Pergola *et al*., New England Journal of Medicine 365: 327-336 (2011)

and whether this weight loss in patients receiving bardoxolone included muscle wasting, with a commensurate decrease in the serum creatinine level. If this had been the case, the decrease in creatinine would not necessarily be a true improvement in kidney function.

Subsequently, after the deal was struck with Abbott, Reata embarked upon a multinational, double-blind, placebo-controlled Phase 3 outcomes study (BEACON), which was started in June 2011, testing bardoxolone methyl's impact on progression to ESRD or cardiovascular death in 1600 patients with Stage 4 chronic kidney disease (CKD), defined as eGFR 15 – 30 ml/min/1.73m², and Type 2 diabetes. This Phase 3 trial was halted in October 2012 because of adverse effects; namely, a higher cardiovascular mortality rate in the treatment arm[7]. Abbott subsequently dropped bardoxolone methyl and returned all rights to the compound back to Reata.

Recently, Concert Pharmaceuticals announced that its drug candidate, CTP-499, which was previously observed to protect against large increases in serum creatinine, had failed to reach its primary endpoint in a large, long-term Phase 2 study. CTP-499 is a multi-subtype inhibitor of phosphodiesterase enzymes, developed using Concert Pharmaceuticals' patented deuteration chemistry platform. The chemical structure of the drug is shown below, with the deuterium atoms clearly demarcated by the letter "D".

Figure 13: CTP-499 Chemical Structure



Source: Concert Pharmaceuticals, Inc.

In April 2014, Concert announced 48-week results of its trial of CTP-499 in patients with diabetic kidney disease. CTP-499, used in addition to the standard of care, is being developed to delay the progression of these patients to end-stage renal failure, which requires dialysis or kidney transplantation. The firm indicated that the results suggested that CTP-499 has protective effects on kidney function in patients with type 2 diabetic kidney disease, a condition in which kidney function is progressively lost. In addition, an observed, statistically significant reduction of certain fibrotic biomarkers suggests that CTP-499 may act as an anti-fibrotic agent.

The results were presented during a Late-Breaking session at the National Kidney Foundation 2014 Spring Clinical Meeting by Dr. Bhupinder Singh, a clinical investigator and Medical Director of Apex Research of Riverside. At 48 weeks, a measurable impact on serum creatinine, a key secondary endpoint, was observed. Increased serum creatinine is a marker of impaired kidney function. These data may indicate a slower decline of kidney function in patients treated with CTP-499 vs. those who received placebo.

The primary endpoint of the trial was the change after 24 weeks in urine-albumin creatinine ratio (UACR), a marker of kidney tissue damage. While the trial did not meet this endpoint, at 48 weeks the longer-term treatment duration suggests a favorable trend in UACR for patients receiving CTP-499 as compared to placebo. At 48 weeks, UACR in patients receiving CTP-499 increased 24mg/g from baseline vs. 223mg/g increase in patients receiving placebo ($p = 0.097$). These data may indicate a stabilization of UACR in patients administered CTP-499 vs. those subjects who were given a placebo.

[7] De Zeeuw *et al*., New England Journal of Medicine 369: 2492-2503 (2013)

Pyridorin™ Market Model

We have modeled sales for Pyridorin™ only in patients with Type 2 diabetes who have intermediate-stage kidney disease, as defined by the parameters of the patient enrollment criteria in the PIONEER (formerly known as PYR-311) trial. Our market model does not include projected sales for intravenous Pyridorin™ to treat acute kidney injury. The epidemiology of diabetes in both the U.S. and Europe reveals the pandemic nature of this disease condition. In the U.S., it is estimated that as many as 26 million people have diabetes, among which roughly 90% – 95% are projected to have the Type 2 form of the disease. There are about 60 million people with diabetes in the European region, or about 10.3% of men and 9.6% of women over the age of 25. Prevalence of diabetes is increasing among all ages in both the U.S. and Europe, primarily due to increases in overweight and obesity, unhealthy diet and physical inactivity.

Our projections have utilized a number of roughly 19 million individuals in the U.S. and 24 million individuals in Europe, which appear to be conservative based on existing epidemiological data. Among all patients with Type 2 diabetes, we have assumed that approximately one-third suffer from nephropathy. Furthermore, we have projected that roughly half of this patient population is likely to meet the strict criteria for treatment with Pyridorin – i.e., intermediate-stage disease similar to that of the patients who represent the target enrollment population in the PIONEER trial. NephroGenex management have indicated potential for a target patient population size of ~10 million individuals in the U.S. alone, assuming that over six million individuals with Type 2 diabetes have nephropathy, and that these subjects can be sub-stratified as follows:

- 2.8 million patients suffering from macroalbuminuria (overt nephropathy)
- 3.5 million individuals with microalbuminuria (early-stage diabetic nephropathy)
- 3.6 million patients at high risk of progressing to nephropathy

Accordingly, we believe that our patient population assumptions are relatively conservative. We have utilized peak market penetration rates of approximately 28% in the U.S. and roughly 15% in Europe. Our pricing projections involve starting wholesale acquisition costs (WAC) of $1,000 per patient annually in the U.S., and roughly $750 annually per patient in Europe, reflecting the typical trend towards lower pricing in Europe due to differences in reimbursement environments. We note that this pricing level is comparable to the cost of various cardiovascular drugs and represents an average price of about $3 per day for a chronic therapy. Accordingly, we believe that formulary access and broad-based acceptance of this drug pricing level should be easily achievable.

For all future cash flows, we have applied a blanket discount rate of 20%. Furthermore, we have assumed a relatively modest inflation rate of 3% per year, which we apply to all pricing assumptions. We have applied a 60% probability of success to Pyridorin™, based on the proof-of-concept efficacy data observed in the previously-conducted Phase 2 studies and the benign safety profile of the drug. This derives a risk-adjusted Net Present Value (rNPV) of roughly $250 million, which includes a standard corporate tax rate of 40% and a royalty rate ranging from 12% to 22% on net sales of the drug.

We have not factored in the value of potential licensing agreement-related milestone payments to NephroGenex, which may be conservative. Furthermore, we note that the royalty rate assumptions may themselves be conservative given the fact that NephroGenex is only likely to license out the rights to Pyridorin once the interim analysis data from the first Phase 3 trial become available. Generally, assets with positive Phase 3 data can command higher royalty rates from potential partners because of the paucity of such late-stage, de-risked drug candidates targeting such significant market opportunities.

Table 7: Pyridorin™ Estimated Global Sales – Diabetic Nephropathy Market Size Model

	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
United States																	
Type 2 diabetes patients	19,000,000	19,380,000	19,767,600	20,162,952	20,566,211	20,977,535	21,397,086	21,825,028	22,261,528	22,706,759	23,160,894	23,624,112	24,096,594	24,578,526	25,070,096	25,571,498	26,082,928
Diabetes patients with nephropathy	6,270,000	6,395,400	6,523,308	6,653,774	6,786,850	6,922,587	7,061,038	7,202,259	7,568,920	7,720,298	7,874,704	8,032,198	8,192,842	8,356,699	8,774,534	8,950,024	9,129,025
Patients with intermediate-stage disease	3,135,000	3,197,700	3,261,654	3,326,887	3,393,425	3,461,293	3,530,519	3,601,130	3,784,460	3,860,149	3,937,352	4,016,099	4,096,421	4,178,349	4,387,267	4,475,012	4,564,512
Population Growth rate	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*
Pyridorin™ penetration	0%	0%	0%	0%	0%	1.5%	4.5%	11.1%	13.8%	21.2%	27.8%	23.2%	17.1%	16.3%	12.8%	4.2%	1.5%
Number of patients receiving Pyridorin™						51,919	158,873	399,725	522,255	818,352	1,094,584	931,735	700,488	681,071	561,570	187,951	68,468
Annual cost of therapy						$1,000	$1,030	$1,061	$1,093	$1,126	$1,159	$1,194	$1,230	$1,267	$1,305	$1,344	$1,384
Pyridorin™ U.S. sales ($ MM)	$0	$0	$0	$0	$0	$52	$164	$424	$571	$921	$1,269	$1,113	$862	$863	$733	$253	$95
Ex-U.S. markets (mainly Europe)																	
Type 2 diabetes patients	24,000,000	24,480,000	24,969,600	25,468,992	25,978,372	26,497,939	27,027,898	27,568,456	28,119,825	28,682,222	29,255,866	29,840,983	30,437,803	31,046,559	31,667,490	32,300,840	32,946,857
Diabetes patients with nephropathy	7,920,000	8,078,400	8,239,968	8,404,767	8,572,863	8,744,320	8,919,206	9,097,590	9,279,542	9,465,133	9,654,436	9,847,525	10,044,475	10,245,365	10,450,272	10,659,277	10,872,463
Patients with intermediate-stage disease	3,960,000	4,039,200	4,119,984	4,202,384	4,286,431	4,372,160	4,459,603	4,548,795	4,639,771	4,732,567	4,827,218	4,923,762	5,022,238	5,122,682	5,225,136	5,329,639	5,436,231
Population Growth rate	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*	*2.00%*
Pyridorin™ penetration	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	1.2%	3.5%	6.7%	9.2%	14.5%	13.2%	12.6%	11.5%	10.6%	9.7%	8.7%
Number of patients receiving Pyridorin™							53,515	159,208	310,865	435,396	699,947	649,937	632,802	589,108	553,864	516,975	472,952
Annual cost of therapy							$750	$773	$796	$820	$844	$869	$896	$922	$950	$979	$1,008
Pyridorin™ ex-U.S. sales ($ MM)	$0	$0	$0	$0	$0	$0	$40	$123	$247	$357	$591	$565	$567	$543	$526	$506	$477
Global Pyridorin™ sales	**$0**	**$0**	**$0**	**$0**	**$0**	**$52**	**$204**	**$547**	**$818**	**$1,278**	**$1,860**	**$1,678**	**$1,428**	**$1,406**	**$1,259**	**$758**	**$571**
Royalty rate on Pyridorin™ sales	**0%**	**0%**	**0%**	**0%**	**0%**	**12%**	**14%**	**16%**	**18%**	**20%**	**22%**	**22%**	**22%**	**22%**	**22%**	**22%**	**22%**
Total worldwide revenue to NephroGenex						**$6**	**$29**	**$88**	**$147**	**$256**	**$409**	**$369**	**$314**	**$309**	**$277**	**$167**	**$126**

Source: Company Reports and Aegis Capital Corp. estimates

Intellectual Property

The NephroGenex intellectual property (IP) portfolio is shown below. The firm is the owner or licensee of 28 issued or granted U.S. and non-U.S. patents relating to Pyridorin™ with claims on synthesis pathways for Pyridorin™, and methods of using Pyridorin™ in various indications. The firm is also the owner or licensee of four pending U.S. and non-U.S. patent applications relating to Pyridorin™ in these areas. NephroGenex owns two pending U.S. and non-U.S. applications relating to other product candidates beyond Pyridorin™, with claims directed to pharmaceutical compounds, pharmaceutical compositions and methods of using these agents in various indications. The firm anticipates that expiration in 2016 of some of its method-of-use patents covering Pyridorin™ for the treatment of diabetic nephropathy will have a limited impact on its ability to protect the drug in the U.S., Europe and Canada, where the firm has issued patents covering this use that extend until 2024. In other countries, NephroGenex's patent protection covering use of Pyridorin™ for treating diabetic nephropathy will expire in 2016. The company has various patent applications pending to cover various analogs of Pyridorin™ that would, if issued, expire in 2027.

Table 8: NephroGenex Patent Portfolio

Patent	Title	Issue Date	Expiry Date	Country	Description
8,067,444	Pyridoxamine for the treatment of diabetic intermediaries and post-amadori inhibition	11/29/2011	June 18, 2024, absent any patent term extension	US, Europe, Canada	Methods for treating diabetic nephropathy in a human diabetic patient with pyridoxamine; based on clinical trial patient population
5,985,857	Advanced glycation end-product intermediaries and post-amadori inhibition	16-Nov-99	10-Sep-16	US, Europe, Australia, Canada, Japan	Methods for treating diabetic nephropathy with pyridoxamine (claim 19); method for inhibiting the conversion of Amadori compounds to post Amadori advanced glycation end products
7,214,799	Methods for the synthesis of [illegible]	8-May-07	9-Feb-25	US only	Methods for preparing pyridoxamine, o+B16r salt [illegible]
8,431,712	Methods for the synthesis of pyridoxamine	30-Apr-13	9-Feb-25	US only	Methods for preparing pyridoxamine, or salt thereof
6,521,645	Methods for the treatment and prevention of urinary stone disease	18-Feb-03	14-Nov-21	US only	Methods for treating or preventing urinary stone disease using pyridoxamine to reduce urinary oxalate concentrations
6,472,400	Advanced gylcation end-product intermediaries and post-Amadori inhibition	29-Oct-02	9/10/2016	US; corresponding cases in Europe, Australia, Canada, Japan	Methods for treating or preventing proteinuria or impaired glomerular clearance using pyridoxamine
6,750,209	Advanced glycation end-product intermediaries and post-amadori inhibition	15-Jun-04	9/10/2016	US; corresponding cases in Europe, Australia, Canada, Japan	Method for treating retinopathy or neurodegenerative disease using pyridoxamine
7,030,146	Methods for treating diabetic neuropathy	4/18/2006	9/10/2016	US; corresponding cases in Europe, Australia, Canada,	Methods for treating diabetic neuropathy using pyridoxamine
6,730,686	Methods for inhibiting oxidative modification of proteins	5/4/2004	9/10/2016	US only	Methods for inhibiting oxidative modification of proteins, treating atherosclerosis, or inhibiting lipid peroxidation, all in a non-hyperglycemic mammal using pyridoxamine or related compounds
6,716,858	Methods for inhibiting diabetic complications	6-Apr-04	9/10/2016	US only	Methods for treating oxidative stress disorders in a hyperglycemic mammal by administering pyridoxamine or related compounds; specific disorders include arthritis, cancer, exposure to ionizing radiation, pulmonary adult respiratory distress syndrome, strokes, pancreatitis, and intestinal ulcerations
6,740,668	Methods for inhibiting diabetic complications	25-May-04	9/10/2016 in the US; 10/21/2019 elsewhere	US; corresponding cases in Europe, Australia, Canada, Japan	Method for treating diabetes-associated hypercholesterolemia, hypertriglyceridemia, hyperlipidemia, or atherosclerosis, using pyridoxamine or related compounds.

Source: Company reports

Addressing certain concerns over the patentability of Pyridorin™, the FDA has clearly indicated that it regards Pyridorin™ as a drug and that this compound would have New Chemical Entity (NCE) status if approved in the U.S. The agency responded to a Citizen's Petition by BioStratum, the predecessor to NephroGenex, by classifying Pyridorin™ as a pharmaceutical substance. Although attempts were made to commercialize the drug as a dietary supplement, it never held "generally regarded as safe" (GRAS) status, nor was it granted approval for any formal clinical indication in the U.S. We note that it should receive the standard five-year Hatch-Waxman exclusivity and also be protected by the patents NephroGenex holds, which provide composition-of-matter protection until 2016 and use protection until 2024 without extensions.

Financing History

NephroGenex has raised ~$43.9 million since inception. In our view, the firm has a capital-efficient operating history, having accumulated a deficit of only $43 million as of end-March 2014. Many pharmaceutical firms expend hundreds of millions of dollars to advance a single candidate into clinical trials. NephroGenex benefits from having a very lean organizational infrastructure and an outsourced approach to drug development.

Capital Structure

On February 11, 2014, NephroGenex priced its IPO, in which the firm sold 3.1 million shares of common stock at a price of $12.00 per share and also granted the purchase of 465,000 shares of common stock to cover over-allotments; this was not exercised, resulting in gross proceeds totaling $37.2 million, with net proceeds estimated at $33.4 million after deducting underwriting fees and cash offering expenses. The most recent capital structure (see table below) indicates that NephroGenex has ~9.2 million shares outstanding and issued (fully-diluted) following the IPO.

We project that the firm's current cash position should be sufficient to fund Phase 3 development of Pyridorin™ for diabetic nephropathy through at least the completion of enrollment and the interim analysis of data from the PIONEER trial, although more capital would be required to fund the completion of this study and the second pivotal trial, along with filing expenses associated with seeking approval in the U.S. along with sales and marketing expenses required to support the launch of the drug.

Table 9: Capital Structure

	Number of Shares	Exercise Price	Expiration Date	Total Cash
Cash, cash equivalents and marketable securities				$33,513,394
Common Stock	8,555,114			
Options	512,186	$1.60	2018 - 2019	$819,498
Warrants issued to underwriter	62,000	$15.00	2/10/2019	$930,000
Fully Diluted Shares	**9,129,300**			**$35,262,892**

Source: NephroGenex, Inc.

On February 6, 2014, the firm 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. NephroGenex filed an amended certificate of incorporation on February 14, 2014, authorizing the issuance of 100 million shares of common stock and five million shares of undesignated preferred stock.

NephroGenex had originally entered into a stock purchase agreement in 2007 with new and existing stockholders in May 2007, which involved the initial issuance of 4.8 million shares of Series A stock in exchange for $1.5 million in cash, followed by the issuance of two series of warrants (referred to as "Warrant 1" and "Warrant 2") in exchange for a further $1.1 million in cash. Warrant 1 provided the right to purchase an additional 18 million shares of Series A stock and 45,234 shares of common stock in exchange for $20 million. This right was exercised in two stages in December 2007 and March 2008.

Warrant 2 was canceled according to an agreement reached by the firm with its significant shareholders in exchange for 593,589 shares of common stock. In connection with the IPO, 3.6 million shares of common stock were issued for the conversion of all outstanding shares of Series A preferred stock, and 1.2 million shares of common stock were issued for the convertible notes and accrued interest.

Financial Review and Outlook

Revenue: We do not forecast any revenue from either product sales or research activities in either 2014 or 2015. Management does not provide guidance.

Gross Margins: As a development-stage company, there are historically no costs of goods sold. We project that the gross margins on a drug like Pyridorin™ are likely to exceed 80% upon launch, which should enable healthy cash flow generation.

Operating Expenses: For 2014, we estimate approximately $9.5 million in operating expenses. We estimate R&D of $4.6 million in 2014, as the company advances its lead drug candidate into Phase 3 testing in the U.S. However, the R&D expense should rise substantially in 2015 to roughly $10.5 million as the PIONEER pivotal trial of Pyridorin™ completes enrollment and matures to yield interim data, while the firm prepares to initiate the second, confirmatory trial of the drug.

Taxes: We assume a roughly 40% corporate tax rate, since the firm does not have substantial net operating loss carry-forwards (NOLs) with which to offset taxes. Although BioStratum, NephroGenex's predecessor in developing Pyridorin™, accumulated net operating losses in excess of $100 million, none of these were passed on to NephroGenex, which as of the end of 2012 only had an accumulated NOL balance of $21.6 million, expiring between 2024 and 2032. Since we cannot be certain how much of these NOLs might be usable to offset future tax liability, we have chosen to forecast future cash flows under the assumption that NephroGenex would be taxed at a 40% rate.

Share Count: The outstanding fully-diluted share count stands at roughly 9.1 million. The fully-diluted shares account for the conversion of roughly 0.6 million shares in the form of options and warrants. Given the company's cash position, strategic goals, and capital structure, a share repurchase program is unlikely, in our view.

EPS: We forecast diluted EPS of ($1.26) and ($1.58) for 2014 and 2015, respectively. Currently, we cannot estimate when the company is likely to achieve cash flow break-even or attain sustainable profitability. However, if the firm's lead drug candidate, Pyridorin™, demonstrates statistically significant efficacy and positive safety data in the upcoming Phase 3 trial, we anticipate that NephroGenex should be able to secure a transformative licensing partnership or potentially be acquired in a lucrative transaction with an established pharmaceutical firm. In our view, the drug could achieve market entry in the 2019 / 2020 time frame.

Balance Sheet: The firm held roughly $33.5 million in cash at the end of the first quarter of 2014, following the completion of an IPO in February 2014. We anticipate that the funds raised in the IPO should cover the cost of the initial proposed Phase 3 trial for Pyridorin™, which is slated to cost roughly $30 million. Following the receipt of interim data from its Phase 3 program (PIONEER), we believe that NephroGenex may elect to raise additional capital in order to have as many strategic options available as possible (including obtaining the best possible terms from either a licensee or an acquirer).

Cash Flow: We estimate that the firm will consume roughly $9.4 million in operating cash flows during 2014 and a further $16.5 million during 2015. We think additional funding may be required within the next 15 – 18 months to support envisaged operational activities, including the completion of the pivotal development of oral Pyridorin™ and the advancement of the intravenous form of the drug into clinical testing for the treatment of acute kidney injury (AKI).

Guidance: The firm does not provide financial guidance.

Management Team

The firm's management team comprises individuals with substantial track records in the biotech and healthcare industries. The firm's CEO, Pierre Legault, has had an extensive career in the biotechnology, prescription pharmaceuticals and retail pharmacy sectors, and in our view is one of the most astute leaders we have come across.

Pierre Legault, M.B.A., C.P.A.
Chief Executive Officer
Pierre Legault was named CEO of NephroGenex on October 18, 2013 and has been a member of the firm's board of directors since November 2012. From April 2012 until October 2013, Mr. Legault was the CEO of Stone Management LLC, a consulting company. From January 2009 to April 2012, Mr. Legault was the CEO of Prosidion Ltd., a U.K.-based mid-size biotechnology firm discovering, developing and commercializing products in the therapeutic areas of diabetes and obesity. From January 2009 to September 2010, he served as Executive Vice President, CFO and Treasurer with OSI Pharmaceuticals, a mid-size biotechnology company focused on oncology that was acquired by Astellas for $4 billion in June 2010. He was also Senior Executive Vice President and Chief Administrative Officer of Rite Aid Corp., a Fortune 500 retail pharmacy-focused company, from July 2007 to December 2008. From January 2006 to July 2007, Mr. Legault served as Executive Vice President of The Jean Coutu Group (PJC) Inc. and as President of the Eckerd group, with overall management responsibilities for the Brooks Eckerd operations in the U.S. Previously, Mr. Legault held several senior positions for a period of 15 years with Sanofi-Aventis (now known as Sanofi S.A.) and its predecessor companies, last serving as Worldwide President of Sanofi-Aventis Dermatology / Dermik (2003 to 2005). Prior positions included the Senior Vice President and CFO of Aventis Pharmaceuticals Inc. (2000 to 2003), Global Senior Vice President of Finance and Treasury of Hoechst Marion Roussel, Inc. (1998 to 2000), Vice President and CFO, North America Finance, IT and Administration of Marion Merrell Dow, Inc. (1997 to 1998), and Vice President and Chief Financial Officer of Marion Merrell Dow Pharmaceutical Canada (1989 to 1996). Mr. Legault has served on several public, private and nonprofit company boards and audit committees, as well as on several advisory boards, including the following: Cyclacel Pharmaceutical Inc., a publicly-traded biotech company (2006 – 2008) and Forest Laboratories, Inc. (2012 to date). Currently, Forest Laboratories is being integrated into Actavis plc. Mr. Legault also belongs to several professional associations and has studied at McGill University, the University of Montreal (HEC) and the Harvard Business School. He has a Six Sigma Green Belt, a BAA, M.B.A., CA and C.P.A. diploma.

J. Wesley Fox, Ph.D.
President & Chief Scientific Officer
Dr. Fox is a co-founder of NephroGenex and has served as the firm's President and Chief Scientific Officer since October 2013. From 2005 until October 2013, Dr. Fox served as the company's President and CEO. He possesses over 30 years of experience in the organization, funding and management of early and developmental stage biotechnology companies. Prior to co-founding NephroGenex, Dr. Fox was co-founder and Chief Scientific Officer of BioStratum, Inc. from 1994 to 2005, where he established and directed research and development operations that identified and advanced Pyridorin™, recombinant laminins for tissue regeneration (now being sold and applied to stem cells by BioLamina AB), and licensed inhibitors of GPBP kinase with applications to autoimmune disease, fibrosis, and cancer (now being developed by FibroStatin SL). Dr. Fox is also an advisor for BioLamina AB and FibroStatin SL. Prior to these entrepreneurial activities, Dr. Fox held research and development positions with Abbott Laboratories and Idexx Laboratories, Inc. He received a B.A. in Chemistry from Washington and Jefferson College in Washington, PA. Dr. Fox received his Ph.D. in biochemistry from the University of Kansas Medical School in Kansas City, KS.

John P. Hamill, C.P.A.
Chief Financial Officer
John Hamill became NephroGenex's CFO on January 21, 2014. From June 2013 until January 2014, Mr. Hamill served as Co-President and CFO of Savient Pharmaceuticals, Inc. and as Senior Vice President and CFO of Savient since September 2012. From 2010 to 2012, Mr. Hamill served as a financial consultant for various private companies. From 2001 until 2009, Mr. Hamill worked for PharmaNet Development Group, Inc., where he served as Executive Vice President and CFO from 2006 until 2009. During the period in which Mr. Hamill served as Executive Vice President and CFO, he also maintained responsibilities as the CFO of PharmaNet Development Group, Inc.'s wholly-owned subsidiary, PharmaNet, Inc. Mr. Hamill earned his B.S. with a dual major in Accounting/Business and Computer Science from DeSales University (formerly Allentown College of St. Francis de Sales) in 1986. Mr. Hamill is a Certified Public Accountant and is affiliated with the Pennsylvania Institute of Certified Public Accountants and the American Institute of Certified Public Accountants.

Mark A. Klausner, M.D.
Chief Medical Officer
Dr. Klausner was named Chief Medical Officer of NephroGenex in December 2013, effective upon the completion of the IPO. He previously held this role at NephroGenex from November 2007 until February 2010. Since that time, he has provided consulting services to the firm and will continue to act as a consultant as Chief Medical Officer. From March 2010 until February 2012, Dr. Klausner served as Chief Medical Officer of CorMedix Inc. Additionally, from 1990 to November 2007, he held various vice presidential roles at Johnson & Johnson – a consumer health, pharmaceuticals, medical devices, and diagnostics-focused company – in the areas of medical affairs, clinical research and development, and domestic and global drug safety and surveillance. Dr. Klausner also held director positions at Wyeth Pharmaceuticals, a pharmaceutical company that is now a part of Pfizer, in the areas of cardiovascular clinical research and over-the-counter (OTC) clinical research, from 1987 to 1990. He received his B.A. in Chemistry from the University of Rochester, holds board certifications in nephrology and internal medicine and received his M.D. from Harvard Medical School.

Robert Paterson
Senior Vice President, Product Development & Regulatory Affairs
Bob Peterson has served as NephroGenex's Vice President of Product Development and Regulatory Affairs since 2009. He has over 27 years of product development experience in the pharmaceutical and cardiovascular implant industry. Prior to joining NephroGenex, Mr. Peterson served as Director of Research and Development of Cardiopolymers, Inc., which is currently named LoneStar Heart Inc., overseeing development of novel biopolymer therapy for the treatment of chronic heart failure. From 1999 to 2006, Mr. Peterson served as Director of Product Development for BioStratum, Inc. where he led the development of biopharmaceutical candidates from concept to early clinical trials. From 1986 to 1999, he worked at Baxter International, where he led the development from concept to market release of a complete line of ePTFE vascular grafts for peripheral use, and a complete line of endovascular prosthetic grafts for treatment of abdominal aortic aneurysms. Prior to entering the pharmaceutical and medical device industries, Mr. Peterson served as an officer in the United States Army. He graduated from the United States Military Academy at West Point and received his Master of Engineering Degree from the University of California at Berkeley.

Board of Directors

The firm's Board of Directors includes several senior-level individuals with substantial expertise in the biopharmaceutical industry. In particular, several of the firm's directors have extensive expertise in the funding of life sciences companies and have directed investments in life sciences-focused venture capital for many years.

Richard J. Markham
Chairman of the Board
Mr. Markham has served as a member of NephroGenex's board of directors since 2007 and as the chairman of the company's board since October 2013. Mr. Markham has been a partner in the venture capital firm Care Capital, LLC since November 2004 and continues in that role. Prior to joining Care Capital, he was the Vice Chairman of the Management Board and Chief Operating Officer (COO) of Aventis. Previously, he was the CEO of Aventis Pharma and Hoechst Marion Roussel and the President and COO of Marion Merrell Dow, Inc. and a member of its board of directors. From 1973 to 1993, Mr. Markham was associated with Merck & Co., Inc., culminating in his position as President and COO. Prior to this role Richard held a number of positions, starting as a professional representative and then becoming district manager, product manager and director, executive director and then Vice President of Marketing for the Merck Sharp & Dohme Division. He later was responsible for Merck's European pharmaceutical business before being named senior vice president of Merck & Co. and president of the Merck Human Health Division, responsible for worldwide marketing and sales of Merck's pharmaceutical products. Mr. Markham received a B.S. in Pharmacy and Pharmaceutical Sciences from Purdue University and has served as a member of the Dean's Advisory Council of the university. He has also been awarded an honorary Doctor of Science degree, the university's highest honor for achievement. Mr. Markham previously served as a member of the board of directors of Acura Pharmaceuticals, Inc. and Anacor Pharmaceuticals, Inc. In addition, Mr. Markham has been a member of the board of directors and executive committee of the Pharmaceutical Research and Manufacturers Association (PhRMA), a member of the Board of Trustees of the HealthCare Institute of New Jersey and a member of the board of directors of Aventis Pasteur and of Commerce Bank of Kansas City.

James Mitchum, M.B.A.
Non-Executive Director
Mr. Mitchum has served as a member of the board of directors at NephroGenex and as the chair of the Audit Committee of the board of directors since February 2014. From 2009 to July 2012, Mr. Mitchum served as President of the Americas for EUSA Pharma (USA), Inc., where he oversaw the streamlining of that business as well as the development, approval and successful launch of a pediatric oncology drug in 2011. From 2005 to 2008, Mr. Mitchum served as President and CEO of Enturia, Inc., a private drug-device company, based in Kansas City, MO. From 2004 to 2005, Mr. Mitchum served as the President and CEO of Sanofi-Aventis Group Japan. He has also served as a director on numerous private company and organization boards. Mr. Mitchum earned an M.B.A. in Business from the University of Tennessee in Knoxville, TN and a Bachelor of Science degree in business and mathematics from Milligan College in Johnson City, TN.

Pierre Legault, M.B.A., C.P.A.
Executive Director
See management biographies above.

J. Wesley Fox, Ph.D.
Executive Director
See management biographies above.

Robert R. Seltzer, M.B.A.
Non-Executive Director
Bob Seltzer has served as a member of the firm's board of directors since October 2013. Mr. Seltzer is a partner at Care Capital, a life sciences venture capital firm, which he joined in July 2005. He was previously a management consultant at the Boston Consulting Group (1997 – 2000 and 2004 – 2005), and he was the founder and President of Trenza Corporation (2000 – 2001). He serves on the board of directors of a number of private biopharmaceutical and drug development companies. Mr. Seltzer received his M.B.A. degree from the Wharton School, a Master's in biotechnology from the University of Pennsylvania, and a B.S. degree in molecular biophysics and biochemistry from Yale University.

Eugen Steiner, M.D., Ph.D.
Non-Executive Director
Dr. Steiner has served as a member of the NephroGenex board of directors since 2007. He is a venture partner of HealthCap, a group of multistage venture capital funds, investing globally in the life sciences. He has more than 25 years of executive management experience, and since 1997 has served as CEO of certain companies in which HealthCap has invested, leading these companies mostly in start-up and early stages of development. He has served as the CEO of Affibody AB, Biostratum Inc., Calab Medical AB, Creative Peptides AB, Eurona Medical AB, Melacure Therapeutics AB, Nordic Vision Clinics AS, PyroSequencing AB and Visual Bioinformatics AB. Dr. Steiner has served on several public, private and non-profit company boards, including Alba Therapeutics, APL, Biolipox (chairman), BioPhausia, Biostratum (chairman), Biotage, Praktikertjänst, and Stockholm School of Entrepreneurship, and also belongs to several professional medical, industry and investor associations. He studied medicine and earned his M.D. as well as Ph.D. degrees at the Karolinska Institute in Sweden. Until 1987, Dr. Steiner practiced medicine and was active in medical research at the Karolinska Hospital, Stockholm, Sweden.

Public Companies Mentioned in this Report:

Abbott Laboratories (ABT/NYSE)

AbbVie (ABBV/NYSE)

Achillion Pharmaceuticals (ACHN/NYSE)

Auspex Pharmaceuticals (ASPX/NASDAQ)

Celgene Corporation (CELG/NASDAQ)

Cempra (CEMP/NASDAQ)

Conatus Pharmaceuticals (CNAT/NASDAQ)

CytRx Corporation (CYTR/NASDAQ – Buy)

Durata Therapeutics (DRTX/NASDAQ)

Evoke Pharma (EVOK/NASDAQ – Buy)

GlaxoSmithKline (GSK/NYSE)

Novartis AG (NVS/NYSE)

Pfizer (PFE/NYSE)

Progenics Pharmaceuticals (PGNX/NASDAQ)

Regado Biosciences (RGDO/NASDAQ)

Sanofi S.A. (SNY/NYSE)

Synergy Pharmaceuticals (SGYP/NASDAQ – Buy)

Table 10: NephroGenex, Inc. (NRX) – Historical Income Statements, Financial Projections

FY end December 31
$ in thousands, except per share data

			2014E					2015E				
	2012A	2013A	1QA	2QE	3QE	4QE	2014E	1QE	2QE	3QE	4QE	2015E
Revenue												
Product revenue	-	-	-	-	-	-	-	-	-	-	-	-
Service revenue	-	-	-	-	-	-	-	-	-	-	-	-
Research and other	-	-	-	-	-	-	-	-	-	-	-	-
Total revenue	-	-	-	-	-	-	-	-	-	-	-	-
Expenses												
Cost of product and service revenue	-	-	-	-	-	-	-	-	-	-	-	-
Research & development	2,352	1,479	457	900	1,300	1,900	4,557	2,200	2,500	2,800	3,000	10,500
Selling and marketing	-	-	-	-	-	-	-	-	-	-	-	-
General and administrative	350	1,026	1,034	1,200	1,300	1,400	4,934	1,500	1,600	1,700	1,800	6,600
Total expenses	2,702	2,506	1,492	2,100	2,600	3,300	9,492	3,700	4,100	4,500	4,800	17,100
Gain (loss) from operations	(2,702)	(2,506)	(1,492)	(2,100)	(2,600)	(3,300)	(9,492)	(3,700)	(4,100)	(4,500)	(4,800)	(17,100)
Other income/expense												
Interest income/expense	(200)	(382)	(68)	30	26	22	10	18	14	38	35	105
Change in value of preferred stock warrants	(2)	(3,417)	(140)	-	-	-	(140)	-	-	-	-	-
Other income/expense	-	-	-	-	-	-	-	-	-	-	-	-
Total investment income and other	(202)	(3,799)	(209)	30	26	22	(131)	18	14	38	35	105
Loss before provision for income taxes	(2,904)	(6,305)	(1,700)	(2,070)	(2,574)	(3,278)	(9,622)	(3,682)	(4,086)	(4,462)	(4,765)	(16,995)
Deferred income tax benefit	-	-	-	-	-	-	-	-	-	-	-	-
Net loss/income	(2,904)	(6,305)	(1,700)	(2,070)	(2,574)	(3,278)	(9,622)	(3,682)	(4,086)	(4,462)	(4,765)	(16,995)
Net loss per share (basic)	(9.08)	(19.71)	(0.37)	(0.24)	(0.30)	(0.38)	(1.26)	(0.42)	(0.39)	(0.37)	(0.40)	(1.58)
Net loss per share (diluted)	(9.08)	(19.71)	(0.37)	(0.24)	(0.30)	(0.38)	(1.26)	(0.42)	(0.39)	(0.37)	(0.40)	(1.58)
Weighted average number of shares outstanding (basic)	320	320	4,587	8,580	8,630	8,680	7,619	8,755	10,355	11,955	12,055	10,780
Weighted average number of shares outstanding (diluted)	320	320	4,587	8,580	8,630	8,680	7,619	8,755	10,355	11,955	12,055	10,780

Source: Company Reports and Aegis Capital Corp. estimates

Table 11: NephroGenex, Inc. (NRX) – Historical Balance Sheet, Financial Projections

FY end December 31
$ in thousands, except per share data

			2014E					2015E				
	12/31/12A	12/31/13A	3/31	6/30	9/30	12/31	12/31/14E	3/31	6/30	9/30	12/31	12/31/15E
Assets												
Current assets:												
Cash and cash equivalents	324	2,132	33,513	31,493	28,999	25,821	25,821	22,259	63,303	58,981	54,366	54,366
Marketable securities	-	-	-	-	-	-	-	-	-	-	-	-
Restricted cash	-	-	-	-	-	-	-	-	-	-	-	-
Accounts receivable	-	-	-	-	-	-	-	-	-	-	-	-
Inventories	-	-	-	-	-	-	-	-	-	-	-	-
Other assets and prepaid expenses	24	12	668	668	668	668	668	668	668	668	668	668
Total current assets	348	2,144	34,181	32,161	29,667	26,489	26,489	22,927	63,971	59,649	55,034	55,034
Property and equipment	3	11	14	14	14	14	14	14	14	14	14	14
Intangible assets	-	-	-	-	-	-	-	-	-	-	-	-
Restricted cash	-	-	-	-	-	-	-	-	-	-	-	-
Marketable securities												
Other assets	14	465	4	4	4	4	4	4	4	4	4	4
Total Assets	364	2,620	34,199	32,179	29,685	26,507	26,507	22,945	63,989	59,667	55,052	55,052
Liabilities and shareholder equity												
Current liabilities												
Accounts payable	78	48	76	76	76	76	76	76	76	76	76	76
Accrued expenses	1,335	1,858	708	708	708	708	708	708	708	708	708	708
Preferred stock warrant liability	3,566	6,983	-	-	-	-	-	-	-	-	-	-
Current portion of long-term debt	3,355	7,917	-	-	-	-	-	-	-	-	-	-
Other current liabilities	-	-	-	-	-	-	-	-	-	-	-	-
Total current liabilities	8,334	16,805	784	784	784	784	784	784	784	784	784	784
Deferred revenue	-	-	-	-	-	-	-	-	-	-	-	-
Long-term deferred tax liability	-	-	-	-	-	-	-	-	-	-	-	-
Total Liabilities	8,334	16,805	784	784	784	784	784	784	784	784	784	784
Shareholder's equity												
Common stock	0	0	9	9	9	9	9	9	12	12	12	12
Preferred stock	24	24	-	-	-	-	-	-	-	-	-	-
Additional paid-in capital	26,701	26,789	76,106	76,106	76,106	76,106	76,106	76,106	121,103	121,103	121,103	121,103
Accumulated other comprehensive income	-	-	-	-	-	-	-	-	-	-	-	-
Deficit accumulated	(34,695)	(40,999)	(42,700)	(44,720)	(47,214)	(50,392)	(50,392)	(53,954)	(57,910)	(62,232)	(66,847)	(66,847)
Total shareholder's equity	(7,969)	(14,186)	33,416	31,396	28,902	25,724	25,724	22,162	63,206	58,884	54,269	54,269
Total liability and shareholder's equity	364	2,620	34,199	32,179	29,685	26,507	26,507	22,945	63,989	59,667	55,052	55,052

Source: Company Reports and Aegis Capital Corp. estimates

Required Disclosures

Price Target

Our 18-month price target is $25.00 per share.

Valuation Methodology

Given the fact that NephroGenex is currently unprofitable, we use a discounted cash flow-based approach to value the shares. Based on a comparables analysis, we believe that the stock is worth $25.00 per share, given our estimate of a $270 million risk-adjusted net present value (rNPV) for the firm's pipeline. This assumes that the shares trade in line with the comp group average enterprise value of $270 million and that the firm has roughly 13 million shares outstanding and $53 million in cash at the end of 2015.

Risk Factors

Issues that could prevent the achievement of our price objective include, but are not limited to, clinical, regulatory, competitive, reimbursement and financial risks. Drugs in clinical development may not advance due to inadequate safety, efficacy, or tolerability. Regulatory agencies may decline to approve regulatory submissions in a timely manner, or may not approve a drug candidate at all. The firm may require substantial funding to complete the clinical development of its candidates and establish commercial infrastructure, which could be dilutive to current shareholders. We expect competition for the company's drugs from several public and private companies developing pharmaceuticals. Future sales of the firm's drugs could depend upon reimbursement from private, as well as public, reimbursement agencies.

For important disclosures go to www.aegiscap.com.

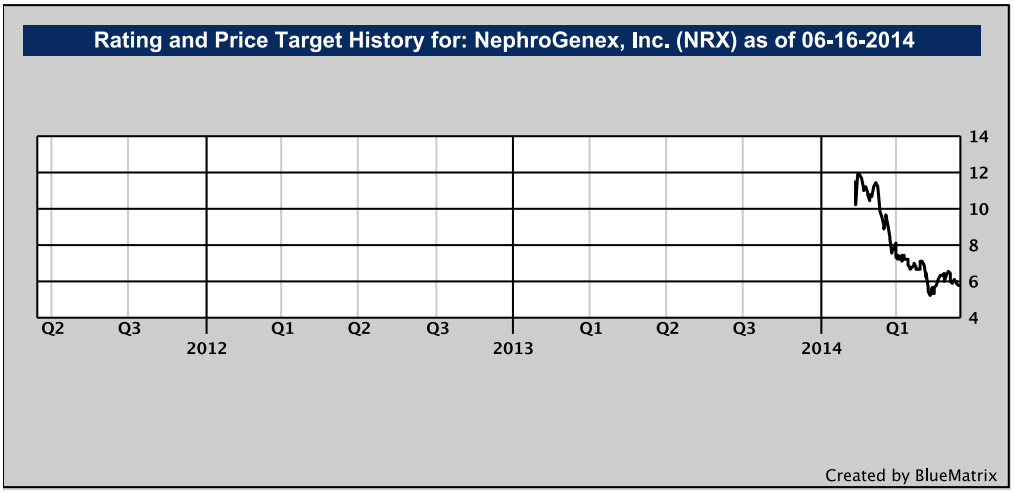
Research analyst compensation is dependent, in part, upon investment banking revenues received by Aegis Capital Corp.

Aegis Capital Corp. intends to seek or expects to receive compensation for investment banking services from the subject company within the next three months.

Aegis Capital Corp. has performed investment banking services for and received fees from Synergy Pharmaceuticals, Inc. within the past 24 months.

Aegis Capital Corp. has performed investment banking services for and received fees from NephroGenex, Inc., Ampio Pharmaceuticals, Inc., CytRx Corp. and Evoke Pharma, Inc. within the past 12 months.

Aegis Capital Corp. makes a market in NephroGenex, Inc., CytRx Corp. and Evoke Pharma, Inc..



Rating	Percent	Investment Banking Services/Past 12 Mos. Percent
BUY [BUY]	82.69	48.84
HOLD [HOLD]	17.31	22.22
SELL [SELL]	0.00	0.00

Meaning of Ratings

A) A Buy rating is assigned when we do not believe the stock price adequately reflects a company's prospects over 12-18 months.
B) A Hold rating is assigned when we believe the stock price adequately reflects a company's prospects over 12-18 months.
C) A Sell rating is assigned when we believe the stock price more than adequately reflects a company's prospects over 12-18 months.

Other Disclosures

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