

NephroGenex, Inc.
Form 424B3
December 16, 2015
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Filed pursuant to Rule 424(b)(3)
under the Securities Act of 1933
in connection with
Registration No. 333-208263

PROSPECTUS

NEPHROGENEX, INC.

10,245,099 Shares of Common Stock

This prospectus relates to the proposed resale or other disposition of up to 10,245,099 shares of NephroGenex, Inc. common stock, \$0.001 par value per share, by the selling shareholders identified in this prospectus. Of these shares, 2,156,863 shares are outstanding shares of common stock held by the selling shareholders and 8,088,236 shares are shares of common stock issuable upon the exercise of warrants held by the selling shareholders. We are not selling any shares of common stock under this prospectus and will not receive any of the proceeds from the sale or other disposition of common stock by the selling shareholders. We will, however, receive the net proceeds of any warrants exercised for cash.

The selling shareholders or their pledgees, assignees or successors-in-interest may offer and sell or otherwise dispose of the shares of common stock described in this prospectus from time to time through public or private transactions at prevailing market prices, at prices related to prevailing market prices or at privately negotiated prices. The selling shareholders will bear all commissions and discounts, if any, attributable to the sales of shares. We will bear all other costs, expenses and fees in connection with the registration of the shares. See Plan of Distribution beginning on page 13 for more information about how the selling shareholders may sell or dispose of their shares of common stock.

Our common stock is listed on the NASDAQ Capital Market, under the symbol NRX. On December 15, 2015, the last reported sale price of our common stock on the NASDAQ Capital Market was \$1.76 per share.

Investing in our common stock involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks that we have described on page 7 of this prospectus under the caption Risk Factors and in the documents incorporated by reference into this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is December 15, 2015.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we have filed with the Securities and Exchange Commission (the "SEC") pursuant to which the selling shareholders named herein may, from time to time, offer and sell or otherwise dispose of the securities covered by this prospectus. You should not assume that the information contained in this prospectus is accurate on any date subsequent to the date set forth on the front cover of this prospectus or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus is delivered or securities are sold or otherwise disposed of on a later date. It is important for you to read and consider all information contained in this prospectus, including the Information Incorporated by Reference herein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you under the captions "Where You Can Find More Information" and "Incorporation of Information by Reference" in this prospectus.

Neither we nor the selling shareholders have authorized any dealer, salesman or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus. This prospectus does not constitute an offer to sell or the solicitation of an offer to buy any of our securities other than the securities covered hereby, nor does this prospectus constitute an offer to sell or the solicitation of an offer to buy any securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. Persons who come into possession of this prospectus in jurisdictions outside the United States are required to inform themselves about, and to observe, any restrictions as to the offering and the distribution of this prospectus applicable to those jurisdictions.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Unless the context otherwise requires, references in this prospectus to "NephroGenex," "the Company," "we," "us," and "our" refer to NephroGenex, Inc.

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PROSPECTUS SUMMARY

The following is a summary of what we believe to be the most important aspects of our business and the offering of our securities under this prospectus. We urge you to read this entire prospectus, including the more detailed financial statements, notes to the financial statements and other information incorporated by reference from our other filings with the SEC. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities.

Overview

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

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

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

Pyridorin has demonstrated preliminary evidence of efficacy in slowing the progression of diabetic nephropathy in relevant patient populations in three Phase 2 clinical studies. Based on these results, Pyridorin entered into a Phase 3 program in 2014 termed the PIONEER trial which was agreed to by the U.S. Food and Drug Administration (FDA), with fast track designation, under a Special Protocol Assessment (SPA). This Phase 3 program is using a novel, events-based endpoint based on end stage renal disease (ESRD) or a 50% increase in serum creatinine (SCr). We believe this change will significantly reduce the cost and time for

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completion of our Phase 3 program compared to the traditional endpoint used in previous pivotal trials for diabetic nephropathy which is a 100% increase in SCr from baseline or end stage renal disease (ESRD). Based on an analysis of the Irbesartan Type II Diabetic Nephropathy Trial (IDNT) used for the approval of the drug irbesartan, the follow-up time required to reach the new endpoint of a 50% SCr increase would be approximately 50% less than the follow-up time required to reach the traditional endpoint in a similar patient population. We believe that we are the first company to use this novel endpoint in a Phase 3 trial.

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

Our Lead Product Candidate

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

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

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

To date, our Pyridorin development program has:

- verified the mechanism of action in in-vitro, animal and human studies;
- verified inhibition of diabetic nephropathy in animal models;

- demonstrated preliminary evidence of efficacy in slowing the progression of diabetic nephropathy in relevant patient populations in three Phase 2 clinical studies; and

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- identified the patient population currently being studied in Phase 3 with the highest potential to demonstrate a significant treatment effect.

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

Additional Pipeline Opportunity

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

Our Strategy

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

- advancing Pyridorin through Phase 3 development for the treatment of diabetic nephropathy in patients with type 2 diabetes;
- submission and approval of a new drug application (NDA) in the United States and a Market Authorization Application (MAA) in Europe;
- commercializing Pyridorin using a highly-targeted sales force in the United States and the rest of the world;
- continued development of an intravenous formulation of Pyridorin for AKI, with an investigational new drug

application (IND) filing and launch of the initial clinical study during the second half of 2015; and

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- deploying capital strategically to develop our portfolio of product candidates and create shareholder value.

Description of the Private Placement

On November 3, 2015, we entered into a securities purchase agreement (the "Purchase Agreement") with certain institutional investors (the "Investors") pursuant to which we agreed to sell to the Investors an aggregate of 2,156,863 shares of our common stock, par value \$0.001 per share (the "Common Stock") at a purchase price of \$2.55 per share for total gross proceeds of approximately \$5.5 million. Pursuant to the Purchase Agreement, we also agreed to issue and sell (i) warrants to purchase up to an aggregate of 1,617,647 shares of Common Stock, at an exercise price of \$3.56 per share, subject to adjustment, for a period of five years from the date of issuance (the "Series A Warrants"), (ii) warrants to purchase up to an aggregate 2,156,863 shares of Common Stock, at an exercise price of \$3.56 per share, subject to adjustment, for a period of twelve months and one day from the date of issuance (the "Series B Warrants"), (iii) warrants to purchase up to an aggregate 2,156,863 shares of Common Stock, at an exercise price of \$3.56 per share, subject to adjustment, for a period of eighteen months from the date of issuance (the "Series C Warrants"), and (iv) warrants to purchase up to an aggregate 2,156,863 shares of Common Stock, at an exercise price of \$3.56 per share, subject to adjustment, for a period of eight months from the date of issuance (the "Series D Warrants" and together with the Series A Warrants, the Series B Warrants and the Series C Warrants, the "Warrants"). The Warrants are not exercisable for the first six months after issuance. In addition, we issued warrants to purchase up to an aggregate of 107,843 shares of Common Stock with the same terms as the Series A Warrants to H.C. Wainwright & Co., LLC and its representatives, as placement agent for the transaction.

The Warrants contain limitations that prevent the holder thereof from acquiring shares upon exercise of a Warrant that would result in the number of shares beneficially owned by it and its affiliates exceeding 4.99%, or 9.99% upon notice to us, of the total number of shares of our Common Stock then issued and outstanding (which limit may be adjusted upon the request of the holder).

In connection with the Purchase Agreement we also entered into a registration rights agreement with the Investors (the "Registration Rights Agreement"), pursuant to which we agreed to register the shares of Common Stock acquired from us (including upon any exercise of Warrants). We are required to file a registration statement for the resale of such securities within 30 days following the closing date and to use our commercially reasonable efforts to cause each such registration statement to be declared effective no later than 90 days following the closing date (or 120 days following closing date, if the SEC determines to review the registration statement). We may incur liquidated damages if we do not meet certain deadlines with respect to our registration obligations under the Registration Rights Agreement or if certain other events occur. We also agreed to other customary obligations regarding registration, including indemnification and maintenance of the effectiveness of the registration statement.

The net proceeds of the private placement will be used for working capital purposes.

The description of the Purchase Agreement and the Registration Rights Agreement are not complete and are qualified in their entirety by reference to the forms of Purchase Agreement and the Registration Rights Agreement, each of which has been filed as an exhibit to the registration statement of which this prospectus is a part. See "Where You Can Find More Information" and "Incorporation of Information by Reference." The representations, warranties and covenants made by us in such agreements were made solely for the benefit of

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the parties to such agreements, including, in some cases, for the purpose of allocating risk among the parties thereto, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were made as of an earlier date. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Corporate Information

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

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

THE OFFERING

This prospectus relates to the resale of to 10,245,099 shares of our common stock, of which 2,156,863 shares are outstanding shares of common stock held by the selling shareholders and 8,088,236 shares are shares of common stock issuable upon the exercise of warrants held by the selling shareholders identified in this prospectus, including their transferees, pledgees, donees or successors. See **Selling Shareholders**.

The selling shareholders may offer to sell the shares being offered in this prospectus at fixed prices, at prevailing market prices at the time of sale, at varying prices or at negotiated prices. Our common stock is listed on the NASDAQ Capital Market under the symbol **NRX**.

We have agreed to register the offer and sale of the common stock to satisfy registration rights we have granted to the selling shareholders. We will not receive any proceeds from the sale of the securities by the selling shareholders.

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RISK FACTORS

Please carefully consider the risk factors described in our periodic reports filed with the SEC, which are incorporated by reference in this prospectus. Before making an investment decision, you should carefully consider these risks as well as other information we include or incorporate by reference in this prospectus. Additional risks and uncertainties not presently known to us or that we deem currently immaterial may also impair our business operations or adversely affect our results of operations or financial condition.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

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

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

- our ability to obtain additional financing;
- our ability to borrow under our credit facility;
- our limited operating history and our recurring losses from operations;
- the success and timing of our preclinical studies and clinical trials;
- our ability to obtain and maintain regulatory approval of Pyridorin and any other product candidates we may develop, and the labeling under any approval we may obtain;
- regulatory developments in the United States and other countries;
- the performance of third-party manufacturers;
- our plans to develop and commercialize our product candidates;

- our ability to obtain and maintain intellectual property protection for our product candidates;
- the successful development of our sales and marketing capabilities;

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- the potential markets for our product candidates and our ability to serve those markets;
- competition from other biotechnology and pharmaceutical companies;
- the rate and degree of market acceptance of any future products;
- the success of competing drugs that are or become available; and
- the loss of key scientific or management personnel.

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

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

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

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USE OF PROCEEDS

We will not receive any of the proceeds from the sale of shares of our common stock in this offering. The selling shareholders will receive all of the proceeds from this offering.

A portion of the shares covered by this prospectus are issuable upon the exercise of warrants to purchase shares of our common stock. Pursuant to conditions set forth in the warrants, the warrants are exercisable under certain circumstances on a cashless basis, and should a selling shareholder elect to exercise on a cashless basis we will not receive any proceeds from the sale of common stock issued upon the cashless exercise of the warrant. Upon any exercise for cash of the warrants, the selling shareholders will pay us the exercise price of the warrants of \$3.56 per share. If the selling shareholders exercise, on a cash basis, all of the warrants underlying the shares being registered, we would receive gross proceeds of approximately \$28.8 million. We intend to use such proceeds, if any, for general corporate purposes, including working capital. The exercise price and number of shares of common stock issuable upon exercise of the warrants may be adjusted in certain circumstances, including subdivisions and stock splits, stock dividends, combinations, reorganizations, reclassifications, consolidations, mergers or sales of properties and assets and upon the issuance of certain assets or securities to holders of our common stock, as applicable.

The selling shareholders will pay any underwriting discounts and commissions and expenses incurred by the selling shareholders for brokerage, accounting, tax or legal services or any other expenses incurred by the selling shareholders in disposing of the shares. We will bear all other costs, fees and expenses incurred in effecting the registration of the shares covered by this prospectus, including, without limitation, all registration and filing fees, fees and expenses of our counsel, certain expenses of counsel to the selling shareholders and our independent registered public accountants.

Table of Contents**SELLING SHAREHOLDERS**

The shares of common stock being offered by the selling shareholders are those previously issued to the selling shareholders, and those issuable to the selling shareholders, upon exercise of the warrants. For additional information regarding the issuances of those shares of common stock and warrants, see Prospectus Summary Description of the Private Placement above. We are registering the shares of common stock in order to permit the selling shareholders to offer the shares for resale from time to time. Except for the ownership of the shares of common stock and the warrants, the selling shareholders have not had any material relationship with us within the past three years.

The table below lists the selling shareholders and other information regarding the beneficial ownership of the shares of common stock by each of the selling shareholders. The second column lists the number of shares of common stock beneficially owned by each selling shareholder, based on its ownership of the shares of common stock and warrants, as of November 24, 2015, assuming exercise of the warrants held by the selling shareholders on that date, without regard to any limitations on exercises. On November 24, 2015, 12,945,518 shares of our common stock were outstanding.

The third column lists the shares of common stock being offered by this prospectus by the selling shareholders.

In accordance with the terms of a registration rights agreement with the selling shareholders, this prospectus generally covers the resale of the sum of (i) the number of shares of common stock issued to the selling shareholders on November 6, 2015 pursuant to a Securities Purchase Agreement dated as of November 3, 2015 and (ii) the maximum number of shares of common stock issuable upon exercise of the related warrants, determined as if the outstanding warrants were exercised in full as of the trading day immediately preceding the date this registration statement was initially filed with the SEC, without regard to any limitations on the exercise of the warrants and all subject to adjustment as provided in the registration right agreement. The fourth column assumes the sale of all of the shares offered by the selling shareholders pursuant to this prospectus.

Under the terms of the warrants, a selling shareholder may not exercise the warrants to the extent such exercise would cause such selling shareholder, together with its affiliates and attribution parties, to beneficially own a number of shares of common stock which would exceed 4.99% of our then outstanding common stock following such exercise, excluding for purposes of such determination shares of common stock issuable upon exercise of the warrants which have not been exercised. The number of shares in the second column does not reflect this limitation. The selling shareholders may sell all, some or none of their shares in this offering. See Plan of Distribution.

Name of Selling Shareholder	Number of shares of Common Stock Owned Prior to Offering	Maximum Number of shares of Common Stock to be Sold Pursuant to this Prospectus (1)	Number of shares of Common Stock Owned After Offering (2)
Biotechnology Value Fund II, L.P. (3)	476,463	476,463	
Biotechnology Value Fund, L.P. (3)	824,927	824,927	
Biotechnology Value Trading Fund OS, L.P. (3)	169,803	169,803	
Investment 10, L.L.C. (3)	150,243	150,243	
MSI BVF SPV, L.L.C. (3)	241,305	241,305	
Brio Capital Master Fund, Ltd. (4)	931,370	931,370	

CVI Investments, Inc. (5)	1,303,923	1,303,923
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Dolphin Offshore Partners, L.P. (6)	1,117,656	1,117,656	
EcoR1 Capital Fund Qualified, L.P. (7)	1,979,073	1,979,073	
EcoR1 Capital Fund, L.P. (7)	815,043	815,043	
Empery Asset Master, LTD (8)	772,208	735,856	36,352
Empery Tax Efficient II, LP (9)	698,384	653,509	44,875
Empery Tax Efficient, LP (10)	502,149	473,376	28,773
Intracoastal Capital, LLC (11)	482,552	372,552	110,000

(1) Assumes the exercise for cash of all warrants to purchase common stock offered in this prospectus held by the selling shareholders.

(2) Assumes that all shares being registered in this prospectus are resold to third parties and that with respect to a particular selling shareholder, such selling shareholder sells all shares of common stock registered under this prospectus held by such selling shareholder.

(3) Biotechnology Value Fund, L.P., Biotechnology Value Fund II, L.P., Biotechnology Value Trading Fund OS, L.P., Investment 10, L.L.C. and MSI BVF SPV, LLC are affiliated entities. BVF Partners L.P. as the general partner of Biotechnology Value Fund, L.P. and Biotechnology Value Fund II, L.P., the managing member of BVF Partners OS, Ltd., itself general partner of Biotechnology Value Trading Fund OS, L.P., and the investment adviser of each of Investment 10, LLC and MSI BVF SPV, LLC, may be deemed to beneficially own the shares listed above that are beneficially owned in the aggregate by Biotechnology Value Fund, L.P., Biotechnology Value Fund II, L.P., Biotechnology Value Trading Fund OS, L.P., Investment 10, L.L.C. and MSI BVF SPV, LLC. BVF Inc., as the general partner of BVF Partners L.P., may be deemed to beneficially own the shares that are beneficially owned by BVF Partners L.P. Mark Lampert, as a director and officer of BVF Inc., may be deemed to beneficially own the shares that are beneficially owned by BVF Inc. BVF Partners L.P. is located at One Sansome Street, 30th Floor, San Francisco, California 94104.

(4) Shaye Hirsch has authority to vote and dispose of the shares held by Brio Capital Master Fund, Ltd. (Brio) and may be deemed the beneficial owner of such shares. The principal business address of Brio is c/o Brio Capital Management LLC, 100 Merrick Road, Suite 401W, Rockville Centre, NY 11570. Brio is not a registered broker-dealer or an affiliate of a registered broker-dealer.

(5) Heights Capital Management, Inc., the authorized agent of CVI Investments, Inc. (CVI), has discretionary authority to vote and dispose of the shares held by CVI and may be deemed to be the beneficial owner of these shares. Martin Kobinger, in his capacity as Investment Manager of Heights Capital Management, Inc., may also be deemed have investment discretion and voting power over the shares held by CVI. The address for CVI; c/o Heights Capital Management, Inc., its authorized agent is 101 California Street, Suite 3250, San Francisco, CA 94111.

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- (6) Dolphin Mgmt. Services, Inc., is the Managing General Partner of Dolphin Offshore Partners, L.P. Peter E. Salas is the President and controlling person of Dolphin Mgmt. Services, Inc. Therefore, Mr. Salas has voting and dispositive power over the shares beneficially owned by Dolphin Offshore Partners, L.P. The principal business address of Dolphin Offshore Partners, L.P. is PO Box 16867, Fernandina Beach, FL 32035.
- (7) Oleg Nodelman, with an address of 409 Illinois Street, San Francisco, California, 94158, owns and controls EcoR1 Capital LLC, the general partner of EcoR1 Capital Fund Qualified, L.P., and EcoR1 Capital Fund, L.P., and has voting and disposition power over these securities.
- (8) Empery Asset Management LP, the authorized agent of Empery Asset Master Ltd (EAM), has discretionary authority to vote and dispose of the shares held by EAM and may be deemed to be the beneficial owner of these shares. Martin Hoe and Ryan Lane, in their capacity as investment managers of Empery Asset Management LP, may also be deemed to have investment discretion and voting power over the shares held by EAM. EAM, Mr. Hoe and Mr. Lane each disclaim any beneficial ownership of these shares. The principal business address of EAM is c/o Empery Asset Management LP, 1 Rockefeller Plaza, Suite 1205, New York, New York 10020. EAM is not a registered broker-dealer or an affiliate of a registered broker-dealer.
- (9) Empery Asset Management LP, the authorized agent of Empery Tax Efficient, LP (ETE), has discretionary authority to vote and dispose of the shares held by ETE and may be deemed to be the beneficial owner of these shares. Martin Hoe and Ryan Lane, in their capacity as investment managers of Empery Asset Management LP, may also be deemed to have investment discretion and voting power over the shares held by ETE. ETE, Mr. Hoe and Mr. Lane each disclaim any beneficial ownership of these shares.
- (10) Empery Asset Management LP, the authorized agent of Empery Tax Efficient II, LP (ETE II), has discretionary authority to vote and dispose of the shares held by ETE II and may be deemed to be the beneficial owner of these shares. Martin Hoe and Ryan Lane, in their capacity as investment managers of Empery Asset Management LP, may also be deemed to have investment discretion and voting power over the shares held by ETE II. ETE II, Mr. Hoe and Mr. Lane each disclaim any beneficial ownership of these shares.
- (11) Mitchell P. Kopin (Mr. Kopin) and Daniel B. Asher (Mr. Asher), each of whom are managers of Intracoastal Capital LLC (Intracoastal), have shared voting control and investment discretion over the securities reported herein that are held by Intracoastal. As a result, each of Mr. Kopin and Mr. Asher may be deemed to have beneficial ownership (as determined under Section 13(d) of the Securities Exchange Act of 1934, as amended (the Exchange Act)) of the securities reported herein that are held by Intracoastal.

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In the aggregate, Mr. Kopin and Mr. Asher may be deemed to have beneficial ownership (as determined under Section 13(d) of the Exchange Act) of 482,552 of our ordinary shares, which consists of (i) 78,432 of our ordinary shares and (ii) 404,120 of our ordinary shares issuable upon exercise of warrants.

Mr. Asher, who is a manager of Intracoastal, is also a control person of a broker-dealer. As a result of such common control, Intracoastal may be deemed to be an affiliate of a broker-dealer. Intracoastal acquired the ordinary shares being registered hereunder in the ordinary course of business, and at the time of the acquisition of the ordinary shares and warrants described herein, Intracoastal did not have any arrangements or understandings with any person to distribute such securities.

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PLAN OF DISTRIBUTION

Each selling shareholder of the securities and any of their pledgees, assignees and successors-in-interest may, from time to time, sell any or all of their securities covered hereby on the Nasdaq Stock Market or any other stock exchange, market or trading facility on which the securities are traded or in private transactions. These sales may be at fixed or negotiated prices. A selling shareholder may use any one or more of the following methods when selling securities:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the securities as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- settlement of short sales;
- in transactions through broker-dealers that agree with the selling shareholders to sell a specified number of such securities at a stipulated price per security;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- a combination of any such methods of sale; or

- any other method permitted pursuant to applicable law.

The selling shareholders may also sell securities under Rule 144 under the Securities Act of 1933, as amended (the Securities Act), if available, rather than under this prospectus.

Broker-dealers engaged by the selling shareholders may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling shareholders (or, if any broker-dealer acts as agent for the purchaser of securities, from the purchaser) in amounts to be negotiated, but, except as set forth in a supplement to this prospectus, in the case of an agency transaction not in excess of a customary brokerage commission in compliance with FINRA Rule 2440; and in the case of a principal transaction a markup or markdown in compliance with FINRA IM-2440.

In connection with the sale of the securities or interests therein, the selling shareholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the securities in the course of hedging the positions they assume. The selling shareholders may also sell securities short and deliver these securities to close out their short positions, or loan or pledge the securities to broker-dealers that in turn may sell these securities. The selling shareholders may also enter into option or other transactions with broker-dealers or other financial institutions or create one or more derivative securities which require the delivery to such broker-dealer or other financial institution of securities offered by this prospectus, which securities such

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broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The selling shareholders and any broker-dealers or agents that are involved in selling the securities may be deemed to be underwriters within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the securities purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Each selling shareholder has informed the Company that it does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the securities.

The Company is required to pay certain fees and expenses incurred by the Company incident to the registration of the securities. The Company has agreed to indemnify the selling shareholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

We agreed to keep this prospectus effective until the earlier of (i) the date on which the securities may be resold by the selling shareholders without registration and without regard to any volume or manner-of-sale limitations by reason of Rule 144, without the requirement for the Company to be in compliance with the current public information under Rule 144 under the Securities Act or any other rule of similar effect or (ii) all of the securities have been sold pursuant to this prospectus or Rule 144 under the Securities Act or any other rule of similar effect. The resale securities will be sold only through registered or licensed brokers or dealers if required under applicable state securities laws. In addition, in certain states, the resale securities covered hereby may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

Under applicable rules and regulations under the Exchange Act, any person engaged in the distribution of the resale securities may not simultaneously engage in market making activities with respect to the common stock for the applicable restricted period, as defined in Regulation M, prior to the commencement of the distribution. In addition, the selling shareholders will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including Regulation M, which may limit the timing of purchases and sales of the common stock by the selling shareholders or any other person. We will make copies of this prospectus available to the selling shareholders and have informed them of the need to deliver a copy of this prospectus to each purchaser at or prior to the time of the sale (including by compliance with Rule 172 under the Securities Act).

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LEGAL MATTERS

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., New York, New York, will pass upon the validity of the common stock being offered by this prospectus.

EXPERTS

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

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, and file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy these reports, proxy statements and other information at the SEC's public reference facilities at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference facilities. SEC filings are also available at the SEC's web site at <http://www.sec.gov>.

This prospectus is only part of a registration statement on Form S-3 that we have filed with the SEC under the Securities Act and therefore omits certain information contained in the registration statement. We have also filed exhibits and schedules with the registration statement that are excluded from this prospectus, and you should refer to the applicable exhibit or schedule for a complete description of any statement referring to any contract or other document. You may inspect a copy of the registration statement, including the exhibits and schedules, without charge, at the public reference room or obtain a copy from the SEC upon payment of the fees prescribed by the SEC.

We also maintain a website at www.nephrogenex.com, through which you can access our SEC filings. The information set forth on, or accessible from, our website is not part of this prospectus.

INCORPORATION OF INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference information that we file with them. Incorporation by reference allows us to disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. This prospectus omits certain

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information contained in the registration statement, as permitted by the SEC. You should refer to the registration statement and any prospectus supplement filed hereafter, including the exhibits, for further information about us and the securities we may offer pursuant to this prospectus. Statements in this prospectus regarding the provisions of certain documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. Copies of all or any part of the registration statement, including the documents incorporated by reference or the exhibits, may be obtained upon payment of the prescribed

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rates at the offices of the SEC listed above in [Where You Can Find More Information](#). The documents we are incorporating by reference are:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2014 filed on March 24, 2015;
- our Quarterly Reports on Form 10-Q for the fiscal quarter ended March 31, 2015 filed on May 13, 2015, for the fiscal quarter ended June 30, 2015 filed on August 12, 2015 and for the fiscal quarter ended September 30, 2015 filed on November 12, 2015;
- our Current Reports on Form 8-K filed on January 7, 2015, February 5, 2015, May 1, 2015, July 22, 2015, July 27, 2015, August 6, 2015, August 7, 2015, November 6, 2015 and November 13, 2015;
- the description of our common stock contained in our Registration Statement on Form 8-A, filed on February 6, 2014, pursuant to Section 12(b) of the Exchange Act, which incorporates by reference the description of the shares of our common stock contained in our Registration Statement on Form S-1, as amended (File No. 333-193023) filed on December 23, 2013 and declared effective by the SEC on February 11, 2014, and any amendment or report filed with the SEC for purposes of updating such description; and
- all reports and other documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act after the date of this prospectus and prior to the termination or completion of the offering of securities under this prospectus shall be deemed to be incorporated by reference in this prospectus and to be a part hereof from the date of filing such reports and other documents;

Unless otherwise noted, the SEC file number for each of the documents listed above is 001-36303.

In addition, all reports and other documents filed by us pursuant to the Exchange Act after the date of the initial registration statement and prior to effectiveness of the registration statement shall be deemed to be incorporated by reference into this prospectus.

Any statement contained in this prospectus or in a document incorporated or deemed to be incorporated by reference into this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or any other subsequently filed document that is deemed to be incorporated by reference into this prospectus modifies or supersedes the statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

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

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You should rely only on information contained in, or incorporated by reference into, this prospectus and any prospectus supplement. We have not authorized anyone to provide you with information different from that contained in this prospectus or incorporated by reference in this prospectus. We are not making offers to sell the securities in any jurisdiction in which such an offer or solicitation is not authorized or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make such offer or solicitation.

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NEPHROGENEX, INC.

10,245,099 Shares of Common Stock

December 15, 2015
