



DIVISION OF  
CORPORATION FINANCE

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

December 6, 2013

Via E-mail

Pierre Legault  
Chief Executive Officer  
NephroGenex, Inc.  
79 T.W. Alexander Drive  
4401 Research Commons Building  
Suite 290  
P.O. Box 14188  
Research Triangle Park, NC 27709

**Re: NephroGenex, Inc.  
Confidential Draft Registration Statement on Form S-1  
Submitted November 8, 2013  
CIK No. 0001338095**

Dear Mr. Legault:

We have reviewed your confidential draft registration statement and have the following comments. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure.

Please respond to this letter by providing the requested information and either submitting an amended confidential draft registration statement or publicly filing your registration statement on EDGAR. If you do not believe our comments apply to your facts and circumstances or do not believe an amendment is appropriate, please tell us why in your response.

After reviewing the information you provide in response to these comments and your amended confidential draft registration statement or filed registration statement, we may have additional comments.

General

1. Please submit all outstanding exhibits as soon as practicable. We may have further comments upon examination of these exhibits.
2. Please provide us proofs of all graphic, visual or photographic information you will provide in the printed prospectus prior to its use, for example in a preliminary prospectus. Please note that we may have comments regarding this material.

3. Please supplementally provide us with copies of all written communications, as defined in Rule 405 under the Securities Act, that you, or anyone authorized to do so on your behalf, present to potential investors in reliance on Section 5(d) of the Securities Act, whether or not they retain copies of the communications. Similarly, please supplementally provide us with any research reports about you that are published or distributed in reliance upon Section 2(a)(3) of the Securities Act of 1933 added by Section 105(a) of the Jumpstart Our Business Startups Act by any broker or dealer that is participating or will participate in your offering.

Prospectus Summary, page 1

4. Please briefly expand the description of Pyridorin to explain what type of compound it is, with specific attention to its status as a molecular component of Vitamin B6.

Risk Factors

“Our insurance policies are expensive...,” page 27

5. Please quantify the amount of coverage provided under your general liability insurance and products liability insurance policies in this risk factor.

“The patent positions of biotechnology and pharmaceuticals companies...,” page 28

6. We note your statement in this section that others have filed patent applications covering products and technologies that are similar, identical or competitive to yours. Please disclose any specific instances known to you of patent applications that have been filed which are similar, identical or competitive to yours, as well as instances in which another person or entity has a competing claim to your intellectual property, including the nature of any such claim, the intellectual property covered, and the current status of the dispute.
7. We note your disclosure in this risk factor that you do not possess composition-of-matter protection for your product candidates. Please revise to create a separate risk factor stating this specific risk and describing the effects that lack of composition-of-matter protection may have on your ability to protect your intellectual property and successfully market any approved product candidate. Please additionally include the disclosure that you lack composition-of-matter protection in your intellectual property section on pages 77-78.

“If the FDA, EMA or other regulatory agencies fail to monitor and enforce...,” pages 31-32

8. Please expand this risk factor to discuss, to the extent known to you, whether pyridoxamine is still available for sale from websites and other vendors as a dietary supplement. Please additionally clarify the extent to which regulatory authorities, including but not limited to the FDA, are able to restrict the international sale and

shipment of pyridoxamine to U.S. customers and the related risks involved to your business.

Cautionary Note Regarding Forward-Looking Statements and Industry Data, page 40

9. Please note that it is not appropriate to state or imply that you do not have liability for the statements in your registration statement. Your statements in the last paragraph of this section that you have not independently verified market and industry data obtained from third-party sources or your own internal company research could imply that you are not taking liability for the statistical and other industry and market data included in your registration statement. In order to eliminate any inference that you are not liable for all of the information in your registration statement, please delete these statements or include a statement specifically accepting liability for these statements.

Business  
General

10. Please define and explain the significance of the following terms the first time they are used in this section:
- reactive oxygen species (ROS);
  - reactive carbonyl intermediates (carbonyl stress);
  - glomerular filtration rate (GFR);
  - lipoxidation and lipoxidation intermediates;
  - hydroxyl radicals; and
  - redox transition metal ions.
11. We note your statement on pages 1 that Pyridorin has “demonstrated evidence of efficacy in slowing the progression of diabetic nephropathy in preclinical models and in three Phase 2 clinical studies” and similar statements on pages 1, 2 and 61. Please revise this disclosure to make clear that your statements regarding “evidence of efficacy” are your own, are not based on the FDA’s or any other comparable governmental agency’s assessment of Pyridorin and do not indicate that Pyridorin will achieve favorable efficacy results in any later stage trials or that the FDA or comparable agency will ultimately determine that Pyridorin is effective for purposes of granting marketing approval.
12. In addition, when you refer to evidence of efficacy in connection with your preclinical testing, please limit your statements to any observed efficacy in animal, rather than human, test subjects.
13. We also note your characterization of Pyridorin as “safe” several times on pages 65 and 71 in reference to clinical trial results. Because FDA approval is dependent on the agency making a determination (according to criteria specified in law and agency regulations) that a drug or biologic is both safe and effective, it is premature for you to describe

Pyridorin, or any of the dosages administered, as safe. Accordingly, please delete this wording throughout your prospectus, as applicable.

14. You state on page 61 that your anticipated Phase 3 program will use a novel endpoint based on a 50% increase in serum creatinine and that “the use of this endpoint has the potential to reduce the cost of and time for completion of the Phase 3 program by approximately 50% over the cost and time for the traditional endpoint used in previous pivotal trials for diabetic nephropathy.” Please revise to clarify the basis for your estimate.
15. Please clarify in your discussion of the preclinical trials, Phase 1 trials and Phase 2 trials whether you or a third party conducted and/or sponsored each of the trials. If a third party was responsible for conducting and/or sponsoring any trial, please identify the third party and explain your relationship, if any, to the party, its role in the trial, and why the party served in such role rather than the company. In addition, please indicate the dates during which each trial was conducted.
16. Please expand the introduction to your business section to briefly discuss the development of Pyridorin by BioStratum, your acquisition of any rights related to this product candidate, the extent of NephroGenex’s development efforts following the acquisition from BioStratum, and any other material information regarding the developmental history of the drug. Please also include this disclosure in your prospectus summary.

Rationale for Development of Pyridorin, page 62

17. Please replace the graphic on this page with a higher resolution and enlarged graphic and text to improve legibility.

Preclinical Efficacy Results, page 63

18. Please define rat serum albumin (RSA).
19. Please replace the graphic on page 64 with a higher resolution and enlarged graphic and text to improve legibility.
20. In your discussion of the STZ-treated rat model of type 1 diabetic nephropathy, please define and explain the significance of the following terms the first time they are used:
  - plasma creatinine;
  - albuminuria;
  - aminoguanidine; and
  - pepsin digestibility, AGE fluorescence, and carboxymethyllysine AGE content.

21. Please discuss how improvement was measured, the specific results observed, and the level or absence of statistical significance for the following preclinical studies:

- the AGE-albumin nephropathy study in rats;
- the first and second STZ studies in rat models;
- the second db/db 16-week mouse study;
- the non-diabetic study in rats; and
- the study in Type 2 diabetic KK-Ay/Ta mice.

Preclinical Safety Summary, page 65

22. Please define “P450 enzyme system” and explain the significance of the lack of evidence of it interacting with Pyridorin.

Clinical Safety Summary, page 65

23. Please disclose whether there is an effective investigational new drug (IND) application for Pyridorin, and if so, please disclose the identity of the filer, the indication for which the IND was filed and the date of filing. If no IND was filed, please explain why.

24. Please define the term “QT/QTc interval,” the limitations of the retrospective ECG analysis and explain the significance of Pyridorin’s lack of effect using “Fridericia’s and Bazett’s formula.”

25. Please expand your disclosure regarding the various Phase 1 trials of Pyridorin to briefly discuss the following:

- the location and design of the clinical trials, including the number of patients in each trial;
- the specific results of the Phase 1 testing that led to the conclusion that advancement to Phase 2 testing was warranted; and
- serious adverse events, if any, and the frequency with which they occurred.

26. Because PYR-206 was designed as a safety and tolerability study, rather than a study of efficacy, please discuss any limitations inherent in the post-hoc analyses performed on various efficacy parameters.

27. Please explain the distinction between the Intent to Treat patient population and patients with type 2 diabetes and baseline SCr  $\geq 1.3$  mg/dL.

28. For each Phase 2 trial you discuss in this section, please include a discussion of serious adverse events observed, if any, and the frequency with which they occurred.

PYR-205/207, page 67

29. Please clarify the meaning of “trending toward significance” and explain how this differs from statistical significance.

PYR-210, page 68

30. Please revise to clarify what you mean by the statement that patients who were not on a stable regimen of SOC at screening “confounded” the results in the ITT population.
31. Please clarify why the prior long term endpoint (time to SCr doubling or ESRD) required by the FDA “made it nearly impossible to evaluate the drug against a similar endpoint in a Phase 2 trial.”
32. Please make clear the criteria you used to identify Phase 2 patients most appropriate for your contemplated Phase 3 study.
33. Please disclose the new, lower SCr increase-based endpoint and confirm that the FDA has agreed to this.

Acute Kidney Injury (AKI)

34. Please replace the graphic on page 63 with a higher resolution and enlarged graphic and text to improve legibility.

Patents and Proprietary Rights Covering Our Drug Candidates, page 76

35. Please clarify what you mean by your reference in this section to “the accelerated regulatory approval pathway” for your product candidate. To the extent you refer to the SPA negotiated with the FDA, please delete this statement. Although the clinical endpoint you are using may lead to faster approval for your product candidate than it otherwise would receive, this is not a certainty, and expedited approval by the FDA is not the purpose behind an SPA.
36. We note that you have method-of-use patents covering Pyridorin that will expire in 2016. Please expand disclosure to indicate what effects, if any, you expect these expirations to have on your ability to protect your intellectual property and what steps, if any, you plan to take to mitigate such effects. Please additionally include such expanded disclosure in the risk factor regarding intellectual property on page 29.

License Agreements

Kansas University Medical Center (KUMC) Exclusive License Agreement, pages 78-79

37. Please disclose the following additional information in your discussion of this agreement:

- aggregate future potential milestone amounts you may pay;
- other provisions by which KUMC may terminate the license; and
- any other material provisions, including significant payment obligations.

The South Carolina Research Foundation (SCRF) Exclusive License Agreement, pages 79-80

38. Please disclose the following additional information in your discussion of this agreement:

- The amounts, if material, of the annual license fee you must pay for each year you market Pyridorin and the one-time sub-license fee;
- aggregate future potential milestone amounts you may pay;
- the expiration date of the patent to which the duration of the agreement is tied;
- other provisions by which SCRF may terminate the agreement; and
- any other material provisions, including significant payment obligations.

Vanderbilt University (VU) Exclusive License Agreement, page 80

39. Please disclose the following additional information in your discussion of this agreement:

- aggregate future potential milestone amounts you may pay;
- other provision by which VU may terminate the agreement; and
- any other material provisions, including significant payment obligations.

BioStratum, Inc. (BioStratum) Grant Back License Agreement

40. Please disclose the following additional information in your discussion of this agreement:

- the specific patents and patent applications licensed to BioStratum;
- any applicable royalty rates;
- any milestone payment obligations and the aggregate amounts that may be paid or payable under such provisions;
- material provisions governing duration and termination; and
- any other material provisions, including significant payment obligations.

Please additionally confirm, if true, that any rights retained by BioStratum to Pyridorin and AGE inhibitor products are limited solely to Japan, Taiwan, Korea and China, and that there are no provisions in the agreement that might allow for any other licensure rights to revert back to BioStratum.

Security Ownership of Certain Beneficial Owners and Management, page 104

41. In footnotes 7 and 8 to your beneficial owners table, please identify the natural person(s) holding sole or shared beneficial ownership of the shares held by Rho Ventures and BioStratum, respectively.

Shares Eligible for Future Sale, page 114

42. Once available, please file the form of lock-up agreement as an exhibit to your registration statement.

Audited Financial Statements

Notes to Financial Statements

Note D – Note Payable, page F-10

43. You disclose that “if the Company has a liquidation event, as defined, prior to the maturity date of the notes and the notes are not converted, the Company will be obligated to pay the holders of the notes an amount equal to twice the amount of the unpaid principal amount of the notes plus accrued interest.” Please disclose the liquidation events, as defined and provide a description of your accounting for this feature. Reference for us the authoritative literature you rely upon to support your accounting.
44. You disclose on page 109 that all of your convertible notes (other than the August 2013 notes) have been amended and the maturity date has been extended to December 31, 2013. Please disclose herein the original maturity dates and your accounting treatment for the changes in the maturity dates. Provide us your analysis for your accounting with reference to authoritative literature.

Financial Statements for the nine months ended September 30, 2013, unaudited

Notes to Financial Statements

Note E – Stockholder’s Deficiency

Warrant 1 and 2, page F-31

45. Please provide us an analysis supporting your fair value of warrant 2 of \$201,598 at September 30, 2013. In your response, explain how the apparent increase in your common stock evidenced by your proposed IPO range of \$12 - \$14 per share was considered.

Note F – Stock Option Plan, page F-33

46. Please disclose herein or in MD&A under critical accounting policies and estimates each significant factor contributing to the difference between the fair value of \$0.31 per common share used to value stock options granted during the nine months ended September 30, 2013 and the estimated IPO price of \$12.00 - \$14.00. Also, indicate if you



obtained a contemporaneous valuation by an unrelated valuation specialist to determine the valuation of your common stock.

Part II

Item 15. Recent Sales of Unregistered Securities, page II-2

47. As to each sale of convertible notes, please indicate the section of the Securities Act or the rule of the Commission under which exemption from registration was claimed and state briefly the facts relied upon to make the exemption available as required by Item 701 of Regulation S-K.

If you intend to respond to these comments with an amended draft registration statement, please submit it and any associated correspondence in accordance with the guidance we provide in the Division's October 11, 2012 announcement on the SEC website at <http://www.sec.gov/divisions/corpfin/cfannouncements/drsfilingprocedures101512.htm>.

Please keep in mind that we may publicly post filing review correspondence in accordance with our December 1, 2011 policy (<http://www.sec.gov/divisions/corpfin/cfannouncements/edgarcorrespondence.htm>). If you intend to use Rule 83 (17 CFR 200.83) to request confidential treatment of information in the correspondence you submit on EDGAR, please properly mark that information in each of your confidential submissions to us so we do not repeat or refer to that information in our comment letters to you.

You may contact Ibolya Ignat at (202) 551-3656 or Jim Rosenberg at (202) 551-3679 if you have questions regarding comments on the financial statements and related matters. Please contact Austin Stephenson at (202) 551-3192, Dan Greenspan at (202) 551-3623, or me at (202) 551-3715 with any other questions.

Sincerely,

*/s/ Daniel Greenspan for*

Jeffrey P. Riedler  
Assistant Director

cc: Via E-mail  
Joel Papernik, Esq.  
Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.