DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

IND 129194

**SPECIAL PROTOCOL - AGREEMENT**

NeuroRx, Inc.
Attention: Jonathon C. Javitt, MD, MPH
CEO
913 North Market Street
Suite 200
Wilmington, DE 19801

Dear Dr. Javitt:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act (FDCA or the Act) for NRX-101 (fixed dose combination of D-cycloserine and lurasidone) sequential therapy.

We acknowledge your request dated March 8, 2018, received on March 8, 2018, for a special protocol assessment (SPA) of a clinical protocol. We also refer to your email responses dated April 17, 2018 and April 20, 2018, to our information requests dated April 13, 2018, April 19, 2018, and April 20, 2018. The protocol is titled, NRX-101 for Treatment of Severe Bipolar Depression in Patients with Acute Suicidal Ideation and Behavior: The SBD-ASIB Study (Study NRX101-002).

We have completed our review and, based on the information submitted, agree that the design and planned analyses of your study adequately address the objectives necessary to support a regulatory submission, given that you will adequately address the remaining concerns as listed below. You would need to submit the revised protocol and statistical analysis plan accordingly. We advise you that, if you make any other changes to this protocol, this agreement may be invalidated. If you choose to revise this protocol, submit your modifications as "**Special Protocol Assessment - Amendment**". This agreement is subject to modification only as outlined in section 505(b)(4)(C) of the Act.

As stated in the "Guidance for Industry: Special Protocol Assessment," a special protocol assessment documents our agreement that the design and planned analysis of a study can adequately address objectives in support of a regulatory submission. However, final determinations for marketing application approval are made after a complete review of a marketing application and are based on the entire data in the application.

The following are statistical comments in response to your emails received April 17, 2018, and April 20, 2018 (proprietary methodology comments redacted).

You are responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) [42 USC §§ 282 (i) and (j)], which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No, 110-85, 121 Stat. 904). Title VIII of FDAAA amended the PHS Act by adding new section 402(j) [42 USC § 282(j)], which expanded the current database known as ClinicalTrials.gov to include mandatory registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices.

In addition to the registration and reporting requirements described above, FDAAA requires that, at the time of submission of an application under section 505 of the FDCA, the application must be accompanied by a certification that all applicable requirements of 42 USC § 282(j) have been met. Where available, the certification must include the appropriate National Clinical Trial (NCT) numbers [42 USC § 282(j)(5)(B)].

You did not include such certification when you submitted this new clinical protocol. You may use Form FDA 3674, "Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank," [42 U.S.C. § 282(j)] to comply with the certification requirement. The form may be found at http://www.fda.gov/opacom/morechoices/fdaforms/default.html.

Please note the following FDA guidance: "Certifications To Accompany Drug, Biological Product, and Device Applications/Submissions: Compliance with Section 402(j) of The Public Health Service Act, Added By Title VIII of the Food and Drug Administration Amendments Act of 2007," that describes the Agency's current thinking regarding the types of applications and submissions that sponsors, industry, researchers, and investigators submit to the Agency and accompanying certifications. Additional information regarding the certification form is available at: https://www.fda.gov/scienceresearch/specialtopics/runningclinicaltrials/fdasroleclinicaltrials.govinformation/default.htm . Additional information regarding Title VIII of FDAAA is available at: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-014.html. Additional information for registering your clinical trials is available at the Protocol Registration System website http://prsinfo.clinicaltrials.gov/.

When submitting the certification for this application, **do not** include the certification with other submissions to the application. Submit the certification within 30 days of the date of this letter.

In the cover letter of the certification submission clearly identify that it pertains to **IND 129194**, clinical protocol submitted on March 8, 2018, your clinical protocol number, if available, and that it contains the FDA Form 3674 that was to accompany that submission.

If you have already submitted the certification for this submission, please disregard the above.

Sincerely,

*{See appended electronic signature page}*

Mitchell V. Mathis, MD
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation I

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**

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/s/

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MITCHELL V Mathis
04/20/2018