DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

IND 129194

GRANT –
BREAKTHROUGH THERAPY DESIGNATION

NeuroRx, Inc.
Attention: Jonathan 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) dated December 2 ,2016, submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for NRX-101 (fixed dose combination of D-cycloserine and lurasidone).

We also refer to your September 10, 2018, request for Breakthrough Therapy designation. We have reviewed your request and have determined that NRX-101 for the treatment of severe depression and acute suicidal ideation and behavior in patients with bipolar depression after initial stabilization with ketamine or other effective therapy meets the criteria for Breakthrough Therapy designation. Therefore, we are granting your request for Breakthrough Therapy designation. Please note that if the clinical development program does not continue to meet the criteria for Breakthrough Therapy designation, we may rescind the designation.

FDA will work closely with you to provide guidance on subsequent development of NRX-101 for the treatment of severe depression and acute suicidal ideation and behavior in patients with bipolar depression after initial stabilization with ketamine or other effective therapy to help you design and conduct a development program as efficiently as possible. For further information regarding Breakthrough Therapy designation and FDA actions to expedite development of a designated product, please refer to section 902 of the Food and Drug Administration Safety and Innovation Act (FDASIA) and the *Guidance for Industry: Expedited Programs for Serious Conditions – Drugs and Biologics.*[1]

In terms of next steps, please submit a Type B meeting request. This meeting will be for a multidisciplinary comprehensive discussion of your drug development program, including planned clinical trials and plans for expediting the manufacturing development strategy. Please refer to MAPP 6025.6 - *Good Review Practice: Management of Breakthrough Therapy-*

[1] http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM358301.pdf

Designated Drugs and Biologics, Attachment 1, for potential topics for discussion at this initial Breakthrough Therapy meeting[2]. Please refer to the draft *Guidance for Industry: Formal Meetings between FDA or Sponsors and Applicants*[3] for procedures on requesting a meeting. If you feel that submitting a meeting request for such a meeting at this point is pre-mature or if you have recently held a major milestone meeting, please contact the Regulatory Health Project manager noted below to discuss the timing of this meeting.

If the Breakthrough Therapy designation for NRX-101 for the treatment of severe depression and acute suicidal ideation and behavior in patients with bipolar depression after initial stabilization with ketamine or other effective therapy is rescinded, submission of portions of the NDA will not be permitted under this program. However, if you have Fast Track designation you will be able to submit portions of your application under the Fast Track program.

If you have any questions, contact Hiren Patel, Regulatory Project Manager, at hiren.patel@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

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

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[2] http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/default.htm.

[3] https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM590547.

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/s/

MITCHELL V Mathis
11/09/2018