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To: Colleagues in the Neuroscience Community

This letter is to inform you about a new program with the goal of stimulating the discovery of new approaches to the treatment of schizophrenia and bipolar illness. For several decades, treatments for psychotic illnesses have focused on refinements of mechanisms known for the past 40-50 years. The genomic era and emerging new genomics of both illnesses are revealing discoveries of genes that confer risk for schizophrenia and bipolar illness. We are writing you because we believe you share both our excitement about such discoveries and interest in translating such discoveries to greater understanding of the molecular pathogenesis of both illnesses, and potentially to new treatments as pathways involved in pathogenesis are elucidated. However, in today's economic climate, large pharmaceutical companies and venture capital firms are risk-averse to unproven creative attempts aimed at discovering medicines with new mechanisms of action.

Thus, to stimulate a flow of new ideas to treat psychotic illnesses and potentially discover drugs with novel mechanisms of action, we are initiating a new program enabled by funding from the Stanley Medical Research Institute. This program is distinct and independent from the Stanley Center for Psychiatric Research. It will fit within the existing Broad Institute Chemical Biology and Novel Therapeutics ('CBNT') Programs' process for proposing and executing high-throughput screening (HTS) projects. For this 'PsychHTS' Initiative we will work with investigators who have novel innovative ideas relevant to psychiatric disease to (1) help formulate new screens; (2) develop such screens into a format suitable for HTS; and (3) do some follow-up work including medicinal chemistry. Detailed documents and descriptions of the guidelines that govern the Broad's general program, with specific modifications relevant to this special 'PsychHTS' initiative, are available as a downloadable 'PsychHTS application package' at this website: (<http://www.broad.mit.edu/science/programs/psychiatric-disease/psychhts> )

The specific documents in this package are:

1. "PsychHTS Letter": *This letter.*
2. "Broad Institute Chemical Biology Platform and Novel Therapeutics Platform: Overview of Principles and Processes (Focus: PsychHTS)": *General principles for working effectively with the Chemical Biology Platform, and an overview of the process for investigators to propose and execute projects.*
3. **"Broad Institute Chemical Biology Platform High-Throughput Screening Application (Focus: PsychHTS)": To be completed for each new PsychHTS project proposal.**
4. "Broad Institute High-Throughput Assay Readiness Assessment": *To be completed for projects favorably evaluated by the Application Review Committee.*
5. "Broad Institute Chemical Biology Platform Screening Services and Data Sharing Agreement": *DSA to be completed for projects that are assessed as HTS-ready and accepted for execution.*
6. "Broad Institute Chemical Biology Platform Incoming Materials Transfer Agreement": *MTA to be completed for projects that are assessed as HTS-ready and accepted for execution.*

Our first application deadline will be **March 30, 2009**; then June 4, September 1, December 3, following the same schedule as the CBNT Program. The specific number of applications that will be accepted will depend on the quality, readiness, and relevance of the set of applications received.

Investigators will have the opportunity to gain advice from Dr. Edward Scolnick and a professional team at the Broad Institute in implementing their ideas while retaining their principal investigator status in the new effort. Types of screens can include (1) whole-organism screens focused amenable to medium- or high-throughput screening; (2) cell-based screens aimed at correcting an abnormal state of a cell, or (3) cell-free molecular targets believed to be relevant to the pathogenesis of psychotic illness. The principal investigator should consider follow up *in vivo* behavioral assays which could be used to carry out proof of principle behavioral experiments. If desired and if needed, this initiative could offer help with *in vivo* behavioral assays also. Multiple mechanisms to advance a project are possible. We envision discussing potential paths with the principal investigator once screening results are obtained.

In closing, the ultimate purpose of this program is to stimulate industry to pursue new targets for the treatment of psychiatric illnesses. Thus, agreeing to the CBNT rules governing public dissemination of the data [see documents #2 and #5, overview of guidelines and the DSA, respectively] and publication of results by the principle investigator are a requirement in return for the funding of the screen.

We anticipate that questions will arise as investigators receive and study this letter and associated information. Thus we have arranged a **conference call for Thursday, Feb. 12 at 3 pm ET when Dr. Scolnick and others will be available for discussion and questions**. If you would like to participate in this call, please contact [stanleyadmin@broad.mit.edu](mailto:stanleyadmin@broad.mit.edu) for the dial-in information. (We apologize for the short notice--scheduling conflicts preclude having this from Feb. 13-March 1.) Additionally, if at any time you would like to discuss this opportunity or ask further questions, investigators may contact Dr. Scolnick through his assistant at [stanleyadmin@broad.mit.edu](mailto:stanleyadmin@broad.mit.edu).

This is a unique opportunity for creative investigators to receive technical and financial support to implement their ideas while retaining their principal investigator status. **We encourage you to share this letter and information with any of your colleagues**. We hope many dedicated scientists will avail themselves of this new opportunity. We look forward to hearing from you and learning together how to make this effort a success.

Sincerely,



Edward Scolnick, MD

Director, Psychiatric Disease Program  
Director, Stanley Center for Psychiatric Research  
The Broad Institute of Harvard and MIT