Request for Information (RFI) on Phase 2 Ready Compounds for use in Accelerating Medicines® Schizophrenia (SCZ) Program Proof of Principle Trials in Clinical High Risk for Psychosis (CHR)

AMP SCZ is seeking Phase 2 ready compounds with relevance to Clinical High Risk for Psychosis

Opportunity to:

- Contribute to the design of the study with the shared expertise of a multi-stakeholder consortium
- Be one of the first to test a compound in an area of major unmet medical need in psychiatry
- Receive early insights on how your compound performs in a CHR population trial including biomarkers and clinical outcome measures
- Potentially join as a partner pending AMP SCZ Steering Committee approval
- Access a rich dataset for future analysis

Background and Purpose

The Foundation for the National Institutes of Health, a non-profit, 501(c) (3) charitable organization that supports the NIH in its mission to improve health by forming and facilitating public-private partnerships for biomedical research, is issuing a Request for Information (RFI) to identify Phase 2 ready compounds that are available for use in a proof of principle (PoP) trial(s) in support of the Accelerating Medicines Partnership® Schizophrenia (AMP® SCZ) program.

Schizophrenia ranks among the top 15 leading causes of disability worldwide. Signs of risk for developing this illness can occur months to years before diagnosis in a period called the clinical high for psychosis (CHR) state.

Schizophrenia is a severe mental illness that presents with positive, negative and cognitive symptoms and ranks among the top 15 leading causes of disability worldwide. Signs of risk for developing this illness can occur months to years before diagnosis. This early period, referred to as the clinical high risk (CHR) for psychosis state, reflects a time during which attenuated positive symptoms, marked declines in social and role functioning, and non-psychotic comorbidity are noted. Intervention in the CHR state has the potential to prevent future illness-related disability (Fusar-Poli P, Salazar de Pablo G, Correll CU et al. *JAMA Psychiatry* 2020;77:755-65).

The AMP SCZ program is a large, international collaboration designed to develop and implement a set of drug development tools—biomarkers combined with clinical and cognitive assessments—to create algorithms that reliably distinguish clinical course types in CHR. The primary outcome of interest is conversion to psychosis. The secondary outcomes of interest include remission and non-conversion/non-remission. The goal is to develop algorithms that accurately predict individuals that are likely to undergo conversion to psychosis, remission, or non-conversion/non-remission and their trajectory of disease progression.

AMP SCZ is looking for Phase 2 ready compounds with a compelling biological hypothesis and which might produce a detectable signal on a biological and/or clinical outcome measure(s) within 16 weeks.

The validated biomarker algorithms and biological and clinical outcome measures (attenuated positive symptoms, patient rated severity of CHR as a patient reported outcome, negative symptoms, cognitive symptoms, depression, general psychiatric symptoms, substance abuse, psychosocial functioning, anxiety, mood, psychosocial functioning, and sleep) will be used to design a PoP trial that will test a compelling biological hypothesis in CHR. The algorithm has the potential to guide selection and stratification of participants with CHR for future clinical trials based on the primary outcome of interest. In addition, the developed tools may have clinical utility in decision making about stepping interventions up/down as risk is assessed over time (e.g., clinical trajectory, treatment response) and in response to incoming biomarker information. The algorithms will have the potential to serve as early indicators of treatment efficacy in individuals with CHR.

To prepare for the PoP trial, the overall goal of the RFI is to identify readily available Phase 2 compounds that are active on a mechanism hypothesized to be pathophysiologically relevant and which is likely to produce a signal that can be detected on a biological and/or clinical outcome measure(s) within a 16 week period of time.

The AMP SCZ program brings together a breadth of scientific and regulatory expertise and lived experience from the partners: the US National Institute of Mental Health (NIMH), the US Food and Drug Administration (FDA), and the European Medicines Agency (EMA); private industry (Boehringer Ingelheim; Janssen Research & Development; Otsuka Pharmaceutical Development & Commercialization); non-profit and patient advocacy organizations (American Psychiatric Association Foundation; National Alliance on Mental Illness; One Mind; Schizophrenia & Psychosis Action Alliance); and a charitable foundation (Wellcome).

Clinical Outcome Measures in CHR

- **Attenuated positive symptoms**
- **Patient reported severity of CHR**
- **Negative symptoms**
- **Cognitive symptoms**
- **Depression symptoms**
- **Anxiety symptoms**
- **General psychiatric symptoms**
- **Substance abuse**
- **Functioning**
- **Sleep**
- **Suicidality**
- **Physical Health**
- **Treatment & health utilization**

More information about the AMP SCZ program is available here: https://www.ampscz.org/

Requested Compound Profiles

The RFI is requesting responses from pharmaceutical companies and other organizations for candidate Phase 2 ready compounds (new chemical entities and/or repurposed compounds, mechanisms other than dopamine D2) to be considered for use in a PoP trial(s) in individuals with CHR. Safety and tolerability data for the compound are paramount (trial duration anticipated to be 16 weeks). Equally important in compound consideration is a compelling hypothesis linked to the pathophysiology in CHR or the potential to reduce core symptoms in CHR. The following information is being requested for each Phase 2 ready compound:

- *Brief rationale for testing the compound in CHR*
- *Describe the potential to impact to a specific core symptom(s) in CHR*
- *Summary of existing safety and toxicity data*
- *Summary of known pharmacokinetic and pharmacodynamic (PK/PD) data*

- *Summary of measures available to assess CNS target engagement or pharmacodynamic action of the compound related to the mechanism of action*
- *Summary of existing tolerability data*

Additional Information

This RFI is for planning purposes only and should not be construed as a solicitation for applications or any obligation on the part of FNIH. FNIH will not pay for the preparation of any information submitted. Responses are voluntary and the provided data will be treated as confidential. The information provided will be shared with the members of the AMP SCZ Steering Committee under non-disclosure agreements. There will be an expectation that data generated by use of the compound(s) will be shared within the AMP SCZ consortium.

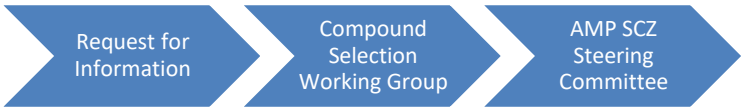
Application and Submission Instructions

I. Submission Deliverables
Application write-up which describes the Phase 2 compound profile (summary of information as noted above)

II. Page Limit
Please keep your responses under 5 pages in length (single spaced, no smaller than Calibri 11 pt font).

III. Submission Instructions
Send responses via e-mail to Beth Marden emarden@fnih.org with a copy to Dr. Alessio Travaglia, Director, Neuroscience (atravaglia@fnih.org).

Response Date



RFI Response Date: on or before February 3, 2023, 5:00 PM Eastern Time

A. FNIH RFI NUMBER: 2022-1330-01	**B. DATE ISSUED:** December 02, 2022	
C. ISSUED BY:	**D. ADDRESS OFFERS TO:**	
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