Special Notice (SN) ARPA-H-SN-26-156: Implementation of Executive Order 14401:
Accelerating Medical Treatments for Serious Mental Illness

I. INTRODUCTION

ARPA-H Innovative Solutions Opening (ISO) ARPA-H-SOL-24-106 is an open solicitation that allows the Proactive Health Office (PHO) to accept revolutionary Solutions that fall outside of the scope of a current ARPA-H program. Solutions are accepted and reviewed on an ongoing basis in accordance with the terms and conditions of the ISO.

This Special Notice (SN) notifies the proposer community of a specific PHO area of interest tied to recent Executive Order (EO) 14401: *Accelerating Medical Treatments for Serious Mental Illness*. With other stakeholders within and outside of the Department of Health and Human Services (HHS), ARPA-H will continue to play a key role in realizing the vision outlined in the EO.

Solutions related to this SN are requested by 9 August 2026. This SN is supplementary to the ISO and does not amend it in any way. Unless explicitly stated in this SN, all submissions should comply with ISO ARPA-H-SOL-24-106.

II.AREA OF INTEREST (AOI)

EO 14401 notes the Administration's policy to accelerate innovative research models and appropriate drug approvals to increase access to psychoplastogen therapeutics, such as ibogaine, that could save lives and reverse the crisis of serious mental illness in America.

ARPA-H is tasked with developing a larger program or initiative within the context of one of the serious mental illnesses identified in the EO (e.g., opioid use disorder (OUD)). The EO also directs ARPA-H to allocate funds to support and partner with State governments that have enacted or are developing programs to advance psychoplastogen therapeutics for serious mental illnesses.

Substance Use Disorders (SUD) are chronic, relapsing conditions that affect ~49 million Americans and 2.8 million Veterans [1]. OUD is a type of SUD which is estimated to affect >5 million people in the US [1]. Despite widespread efforts to address and reduce the rates of opioid overdose fatalities, the opioid epidemic remains one of the most severe public health crises in US history [2]. The current standard-of-care for treating OUD involves medications for OUD (MOUD), such as naltrexone or buprenorphine, coupled with concurrent psychotherapy to reduce overall mortality. At present, >75% of individuals with OUD go completely untreated highlighting a major gap in access to evidence-based care [1].

Although current treatments reduce risks of negative health outcomes and overdose deaths, they are far from complete solutions. In many cases, even with MOUD, treatment discontinuation and relapse rates remain high, leaving patients at increased risk of overdose and death [3-6]. The need for improved treatment strategies is further underscored by the elevated risk of death following

treatment discontinuation or a nonfatal overdose which represents a critical but frequently missed period for intervention [7, 8]. For these reasons, novel approaches for OUD care are critical for improving patient outcomes and preventable overdose deaths.

Emerging evidence suggests psychoplastogens (such as ibogaine) may have potential for treating serious mental illnesses and OUD [9-11]. In recent years, anecdotal reports from unregulated medical clinics point towards ibogaine's potential in improving OUD outcomes. To date, there are no active trials with an open IND to study ibogaine's safety and efficacy in OUD. Given the significant unmet need, ARPA-H is seeking to accelerate the next generation of highly effective treatment approaches by supporting the early clinical development of ibogaine for OUD.

III. **NEXT STEPS**

Considering the clear urgency, this SN encourages action related to a foundational element of the larger AOI to support the development and submission of an Investigational New Drug (IND) application for ibogaine to treat patients with Opioid Use Disorder (OUD) at increased risk of mortality.

Specifically, ARPA-H invites submission of Solution Summaries to the PHO ISO for the following tasks:

- Plans to develop and submit an Investigational New Drug (IND) application for ibogaine to treat individuals with treatment-resistant OUD or OUD with an elevated risk of mortality due to recent nonfatal overdose. Proposed plans should include a strategy for regulatory engagement with the FDA and a clear risk mitigation plan for potential cardiotoxicity.
- Development of a safe clinical protocol for Phase 1 clinical trials based on gold standard science; and
- Develop plan for the procurement of sufficient quantities of good manufacturing practice (GMP)-grade clinical material for human studies to include (but not limited to) activities related to Chemistry, Manufacturing, and Control (CMC) processes and compliance with Federal requirements to important, handle, and administer Schedule 1 substances.

Entities interested in submitting Solutions are advised of the following:

- In line with the need to accelerate patient access to ibogaine treatment, Solutions led by a commercial entity who is responsible for all activities related to the commercial IND with the Food and Drug Administration (FDA) may be most advantageous to ensure speedy commercialization and market entry.
- While ARPA-H actively manages all its projects, proposers are responsible for accomplishing all elements of the SOW. Thus, interested entities should account for all required team members to achieve technical success. ARPA-H *highly* encourages proposers to include a regulatory consultant with relevant expertise in psychoplastogen drug development when identifying their key personnel.
- Entities with established relationships or preexisting State-level funding for ibogaine or psychoplastogen development should detail those relationships and commitments in their Solutions; and
- Given ARPA-H's objective to increase patient access to treatments, the most advantageous

Solutions will include rough plans to maintain affordability and price transparency following advanced clinical development.

Solution Summaries will be submitted and reviewed in accordance with the ISO. Following Solution Summary review, proposers will be contacted with further guidance and next steps.

IV. DISCLAIMER

This SN is issued solely for information purposes and does not constitute a formal solicitation for proposals or solution summaries. Responses to this notice are not offers and cannot be accepted by the Government to form a binding award. Interested parties should submit solution summaries in accordance with solicitation ARPA-H-SOL-24-106, which is the formal solicitation for this AOI.

Submission of any information in response to this SN is voluntary and is not required to propose to subsequent ARPA-H ISOs or research solicitations on this or any other topic. ARPA-H will not provide reimbursement for costs incurred in responding to this SN, participation in any collaborative efforts, and/or for any formal submissions to the PHO ISO.

Respondents are advised that ARPA-H is under no obligation to acknowledge receipt of the information received or provide feedback to respondents with respect to any information received related to this SN. Finally, ARPA-H is under no obligation to pursue any further action directly or indirectly related to this SN.

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3. Glanz, J.M., et al., *The association between buprenorphine treatment duration and mortality: a multi-site cohort study of people who discontinued treatment.* Addiction, 2023. 118(1): p. 97–107.
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5. Ware, O.D., et al., *Risk of Relapse Following Discharge from Non-Hospital Residential Opioid Use Disorder Treatment: A Systematic Review of Studies Published from 2018 to 2022.* Subst Abuse Rehabil, 2025. 16: p. 105–118.
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9. Davis, A.K., et al., *Subjective effectiveness of ibogaine treatment for problematic opioid consumption: Short- and long-term outcomes and current psychological functioning.* J Psychedelic Stud, 2017. 1(2): p. 65–73.
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11. Vollenweider, F.X. and K.H. Preller, *Psychedelic drugs: neurobiology and potential for treatment of psychiatric disorders.* Nat Rev Neurosci, 2020. 21(11): p. 611–624.