

**Partnership to Address the Opioid Crisis**  
**Face-to-Face Meeting**  
December 12–13, 2017  
Rockville, Maryland

## Executive Summary

The National Institutes of Health (NIH), the Pharmaceutical Research and Manufacturers of America (PhRMA), over 30 biopharmaceutical companies, and the Food and Drug Administration (FDA) have joined together with the Foundation for the NIH (FNIH) to initiate planning for the development of a potential public private partnership (PPP) to address the opioid crisis. This collaborative initiative—abbreviated herein for convenience as the partnership—convenes leaders from industry, academia, and government to build and execute a research plan that will facilitate the development of safe and effective treatments for opioid use disorders (OUD)/addiction and pain.

On December 12–13, 2017, more than 100 experts in the fields of substance abuse, addiction, pain, behavioral health, imaging, and neurobiology assembled in Rockville, Maryland, to discuss the mission, goals, activities, and governance of the new partnership. Two primary focus areas were represented during the meeting:

- Development of OUD treatment and overdose prevention/reversal medications (“OUD/addiction” workstream).
- Development of new, non-addictive pain medications (“pain” workstream).

Within each focus area, four major initiatives were explored: asset repurposing, data sharing, biomarkers, and clinical trials. Addressing each of these topics will require a combination of short-term, intermediate, and long-term strategies, which have been and will continue to be discussed by Working Groups focused in individual areas. Representatives from the OUD/addiction and pain focus areas described the landscape, challenges and opportunities, and progress to date for each Working Group. Ensuing discussions then explored key questions to further focus the goals and activities of each group. Discussion topics included:

- How will each working group help to address the opioid crisis?
- What are the opportunities for collaboration between the focus areas of OUD/addiction and pain?
- What is needed from other working groups to enable success?
- What would a sample project look like?
- What will be the governance structure?
- What are the anticipated costs and timelines for the working group activities?

The meeting participants arrived at consensus on key themes, research priorities, and action items during the conference.

### *Key Themes and Research Priorities*

#### **Overview**

- The activities sponsored by the partnership should focus primarily and specifically on actions designed to address the current crisis, and should be clear about which actions address the crisis in the near term, and which represent necessary but longer-term solutions.

- It is critical to involve stakeholders from across industry, third-party payers, NIH, the U.S. Food and Drug Administration (FDA), Centers for Medicare and Medicaid Services (CMS), academia, and advocacy groups. The voice of the patient and family is essential for success.
- The myriad challenges contributing to the opioid crisis can be addressed in part by partnership efforts to encourage data sharing, facilitate asset repurposing, develop relevant biomarkers, and establish new clinical trials.
  - The asset and data sharing effort will focus on bringing companies together to share information and materials from programs that have been deprioritized or abandoned.
  - The biomarkers effort will explore the development of mechanistic and target-driven markers to improve patient stratification and identify drugs that will demonstrate benefit and receive FDA approval.
  - The clinical trials network (CTN) effort will focus on establishing a network to study pain treatments, focusing on accelerating Phase II research and incorporating biomarker studies.
- Where possible, established research resources, networks, and initiatives will be leveraged to expedite progress toward partnership objectives.

### **OUD and Addiction Overview**

Multiple effective treatments for opioid use disorder, withdrawal, and overdose prevention/reversal are approved by the FDA and more are in the pipeline; increasing the utilization of multiple delivery options for already approved medications could create early success. Priority areas include developing a 6-month antagonist to treat patients when the risk of relapse is highest, an auto-injectable antagonist to address overdoses, stronger or longer duration medications to reverse overdose, better opioid receptor antagonists as well as medications to stimulate respiration, and a rapid test for fentanyl or other synthetic opioids. The existing NIDA CTN for addiction should be enhanced to test new OUD compounds. For the precompetitive space, NIDA and FDA should expand a Patient-Focused Drug Development initiative that has recently been launched to develop new clinical outcome assessments in addiction, particularly those related to cravings and withdrawal symptoms, including collaboration with industry partners and potential coordination with FDA's ACTION Network. Other initiatives may leverage existing NIH research mechanisms. For the competitive space, new requests for proposals (RFPs) will be released and will use an accelerated review process (time to award reduced by 6 months).

### **Data and Asset Sharing**

Along with assets, contribution of relevant clinical, preclinical, and pharmacokinetic data could be valuable in informing understanding of the reasons for success or failure of past pain therapy programs. The data sharing effort will launch with a high-level survey designed to capture information about deprioritized assets to better understand opportunities for asset development and data sharing, ultimately promoting more effective use of resources for future drug development. Data sharing by companies will be incentivized through the definition of specific questions and a clear value proposition; buy-in from company leadership is critical. Following the initial data survey—which could result in a pilot data sharing program for NAV1.7 or TRPV1—deeper analyses will be conducted and results may be stored in a password-protected web portal with search and reporting capabilities. Existing data sharing infrastructures could be leveraged to store and manage data sharing initiatives that result from this process. Asset repurposing activities will be conducted in collaboration with data sharing efforts and will explore abandoned and deprioritized assets (regardless of the reason) and assets approved for

other indications that could be made available for repurposing. Prioritized compounds will include assets with known mechanisms of action, preclinical, Phase I, and pharmacokinetic data; “invest to learn” compounds that could inform scientific understanding; and assets that could be paired with existing analgesics. Existing resources, such as the National Center for Advancing Translational Sciences (NCATS) New Therapeutic Use program and The National Institute on Drug Abuse (NIDA) clinical trial network for OUD, could be adapted for supporting trials of previously abandoned assets. Additional third parties such as commercial repurposing ventures could also be considered. The first priority of the asset repurposing effort is to validate and analyze the above-mentioned survey of companies comprising abandoned and deprioritized industry programs in collaboration with the data sharing effort.

### **Biomarkers**

The biomarker initiative will aim to develop objective measures for mechanisms associated with chronic pain, identification of homogeneous pain conditions, and for treatment response to accelerate the development and approval of new medications. The development of mechanistic, target-driven biomarkers to stratify patients and pharmacodynamic biomarkers to demonstrate patient response will be prioritized. Resources, processes, or governance structures from existing consortia (i.e. The FNIH Biomarkers Consortium) could be leveraged in order to expedite timelines. When possible, biomarkers will be tested in retrospective data analyses or small proof of concept studies prior to testing in large clinical trials (some of which may be conducted through the clinical trials networks that exist for addiction or that are proposed for pain. Specific project ideas include: identification of biomarkers predictive of placebo response; development of biomarkers for OUD, addiction risk, and length of time to treat; use of wearable digital devices; patient reported outcomes, such as craving; inflammation, and genetic factors. Data, analysis, and recommendations generated through this effort will be broadly disseminated.

### **Clinical Trials Network**

As noted above, NIDA already has a well-established clinical trials network for addiction, but no such network exists for pain medications. The partnership proposes to develop a new network to address pain with aspects of both a clinical trials and clinical research network. Clinical trial activities in pain will focus initially on low prevalence conditions with a high unmet medical need but be able to grow to accommodate well-characterized populations for more common pain conditions. The CTN design should be enabled to test biomarkers and accommodate platform trial designs; identify and enrich pain populations; have both pain and addiction capabilities; and comprise high-quality and well-trained trial sites. A hub-and-spoke design will contain a clinical coordinating center, data coordinating center, and modular hubs with expertise in specific pain areas. Existing networks, such as NeuroNEXT, PCORnet, and SIREN, may be leveraged for efficiency in building the network. Although all pain CTN sites will be prepared to address misuse of pain medications and addiction, the network will primarily focus on pain. NIDA will consider ways to integrate its CTN to test new OUD compounds, and consider collaborations with the SIREN network for emergency medicine trials.

### **Governance**

- The partnership will be managed by an Executive Committee (EC) that provides overall governance for the partnership and distributes contributed funds in service to research priorities. The EC will oversee the efforts of Steering Committees responsible for the selection and oversight of execution of specific projects in three areas:

1. A combined Asset & Data Sharing Steering Committee will manage subgroups for OUD/addiction and pain.
2. A CTN Oversight Steering Committee will interface with the existing CTN governance in OUD/addiction as well as the operational governance of a new CTN in pain to be developed under the partnership.
3. A Biomarkers Steering Committee will oversee subteams that manage specific projects for development and validation of biomarkers in both OUD/addiction and pain.
  - Representatives from industry, government, and academia will be present on each Executive and Steering Committee.

*Action Items*

- Partnership Working Groups will integrate efforts across OUD/addiction and pain focus areas.
- Each Working Group will further refine the governance process, budget, and timelines to accomplish their activities, and document them in the white paper.
- NIH, FDA, industry, and key academic representatives will develop a white paper describing the partnership, thereby providing sufficient detail to guide private partner investment decisions.
- A cross-cutting survey of companies will be finalized and disseminated to collect information on programs that will inform multiple partnership workstreams.