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Forum on  
**NEUROSCIENCE** and  
**NERVOUS SYSTEM DISORDERS**

## **Advancing Therapeutic Development for Pain and Opioid Use Disorders through Public-Private Partnerships: A Workshop**

*October 11–12, 2017*  
*Keck Center | Room 100*  
*500 Fifth Street, NW | Washington, DC*

**Background:** Pain is a leading cause of disability in the United States, affecting more people than cancer, diabetes, and heart disease combined. Many physicians have come to prescribe opioids to their pain patients and pain patients have come to expect such prescriptions. The resulting dramatic increase in opioid prescriptions within the last decade has been a major factor contributing to the opioid epidemic that the country currently faces, with alarming rates of misuse, abuse, and overdose deaths. The dramatic increase in the cost of Naloxone—the only FDA-approved opioid overdose reversal medication—has made it more challenging to gain access to the life-saving medication. In the 2011 Institute of Medicine report on *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research*, the committee advocated a multidisciplinary approach for pain research and public-private partnerships to improve the process for developing new pain medications. While several initiatives are underway to enhance pain research and improve care in the country, including the National Institutes of Health (NIH) Pain Consortium and Interagency Pain Research Coordinating Committee’s *National Pain Strategy*, additional efforts are needed to foster collaborations between the public and private sectors in order to reduce the adverse risks of prescribed opioids and to accelerate the development of non-opioid medications.

In June and July 2017 NIH hosted three small meetings focused on creating public-private partnerships to address the urgent public health need associated with opioids. NIH is joining with private partners in the pharmaceutical industry and the research community to launch an opioid research initiative with the goal of cutting in half the amount of time required to develop new therapies for 1) safe, more effective strategies for pain management; 2) new and innovative opioid addiction treatments; and 3) overdose reversal interventions. The Forum on Neuroscience and Nervous System Disorders proposes to host a public workshop bringing together key stakeholders to 1) advance the discussions that emerged from the three National Institutes of Health meetings held in June and July 2017 to address the opioid epidemic, and 2) examine potential implementation barriers and opportunities related to the proposed approaches discussed.

### **Workshop Objectives:**

- Review the state of the science for opioid and non-addictive pain treatments.
  - Provide an overview of emerging pain models, including those in the peripheral nervous system (e.g., induced pluripotent stem cells and human experimental biology).
  - Discuss the progress on the identification and validation of targets and biomarkers (neuroinflammation, genetic, proteomics, etc.). Explore whether there is a systematic methodology to validating biomarkers to determine their usefulness.

- Examine approaches to testing new formulations and drugs, and discuss the patient populations needed for those clinical trials.
- Consider the formulation of promising pain medications—beyond opioid analgesics—that may have been shelved by companies.
- Explore opportunities and challenges to changing the formulation of marketed prescription opioids to decrease misuse, addiction, and potential overdoses (e.g., different delivery systems and anti-tampering mechanisms).
- Consider regulatory issues related to the approval of pain medications and discuss potential opportunities to address those challenges.
- Discuss public-private partnerships that might facilitate and de-risk the development of drugs to treat opioid overdoses and non-addictive therapeutics for pain (e.g., an Accelerating Medicines Partnership [AMP] for pain). Highlight lessons learned from industry and opportunities to advance the development of these drugs (e.g., a designated clinical trial network for pain).

## Day One: October 11, 2017

- 1:30 p.m. Welcome and Overview of the Workshop  
 STORY LANDIS, Vice Chair, Forum on Neuroscience and Nervous System Disorders,  
 National Academies of Sciences, Engineering, and Medicine (*Co-chair*)  
 WALTER KOROSHETZ, National Institute of Neurological Disorders and Stroke (*Co-chair*)
- 1:45 p.m. The Opioid Epidemic and State-of-the-Science on Therapeutic Development for Pain  
 NORA VOLKOW, National Institute on Drug Abuse (*Co-chair*)
- 2:05 p.m. Living with Pain: A Patient's Perspective  
 CHRISTIN VEASLEY, Chronic Pain Research Alliance
- 2:20 p.m. The Federal Pain Research Strategy: An Overview  
 LINDA PORTER, National Institute of Neurological Disorders and Stroke
- 2:40 p.m. Discussion among Speakers and Workshop Participants
- 3:10 p.m. BREAK

### SESSION I: THERAPEUTIC DEVELOPMENT FOR OPIOID USE DISORDERS AND OVERDOSE PREVENTION AND REVERSAL

Objectives: Discuss potential methods for developing extended release formulations of marketed medicines for opioid use disorders and overdose prevention and reversal. Consider lessons learned for drug development for opioid use disorders, and explore the utility of shelved compounds as potential therapeutics.

- 3:25 p.m. Session Overview  
 NORA VOLKOW, National Institute on Drug Abuse (*Moderator*)
- 3:35 p.m. Patient Advocate  
 JESSICA HULSEY NICKEL, Addiction Policy Forum
- Case Studies**
- 3:45 p.m. Extended Release Formulations for Opioid Use Disorders  
 CHRISTIAN HEIDBREder, Indivior Inc.
- 4:05 p.m. Overdose Reversal  
 ROGER CRYSTAL, Opiant Pharmaceuticals, Inc.

### **Drug Development**

- 4:25 p.m. Facilitating Therapeutic Development for Opioid Use Disorders: An Academic Perspective  
SHARON WALSH, University of Kentucky
- 4:45 p.m. Discussion among Speakers and Workshop Participants
- 5:45 p.m. Day One Wrap-Up  
*Workshop Co-Chairs*
- 6:00 p.m. Adjourn Day One
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## **Day Two: October 12, 2017**

- 8:30 a.m. Day Two Opening Remarks  
*Workshop Co-Chairs*

### **SESSION II: IDENTIFYING OPPORTUNITIES FOR THERAPEUTIC DEVELOPMENT IN NON-ADDICTIVE PAIN MEDICINES**

Objectives: Innovative public private partnerships are needed for the development of safe, effective and non-addictive pain treatments. Incentives will be necessary to encourage pharmaceutical and biotechnology company investment in this space. What new targets exist and what would be required to accelerate the process of moving toward therapeutics for non-addictive pain medicines?

- 8:35 a.m. Session Overview  
JOHN DUNLOP, Amgen (*Moderator*)

### **Novel Methods for Identifying Targets for Pain**

- 8:45 a.m. Genomic/Genetic Approaches  
LUDA DIATCHENKO, McGill University
- 9:00 a.m. Identifying potent targets for pain management using human cells/organoids, tissue  
CLIFFORD WOOLF, Harvard Medical School
- 9:15 a.m. Monitoring and modulating circuit activity in pain – promise of the BRAIN Initiative  
ROBERT GEREAU, Washington University in St. Louis
- 9:30 a.m. Discussion among Speakers and Workshop Participants
- What can be done to improve target validation in developing non-addictive pain medicines?**
- 10:00 a.m. What has worked and what hasn't worked in the preclinical space to predict success.  
TONY YAKSH, University of California, San Diego
- 10:15 a.m. What new preclinical efforts are needed to improve the process of therapy development (e.g., companion animals)?  
DOROTHY CIMINO BROWN, Elanco Animal Health

- 10:30 a.m. Can a public-private partnership engineer preclinical testing platforms with better predictive validity?  
JOHN KEHNE, National Institute on Neurological Disorders and Stroke
- 10:45 a.m. Discussion among Speakers and Workshop Participants: *Launching Public-Private Partnerships to accelerate the development of therapeutics for non-addictive pain medicines*
- 11:15 a.m. BREAK

### SESSION III: ADDRESSING CLINICAL CHALLENGES AND IMMEDIATE NEEDS FOR DEVELOPING PAIN THERAPEUTICS

Objectives: Discuss challenges and opportunities to identifying and validating objective biomarkers of pain, including approaches focusing on homogenous populations. Consider mechanisms that might block the acute to chronic pain transition. Explore the role of a public-private partnership to advance therapeutic development for pain (e.g., a designated clinical trial network for pain).

- 11:30 a.m. Session Overview  
WALTER KOROSHETZ, National Institute of Neurological Disorders and Stroke (*Moderator*)
- Developing biomarkers to aid Phase II studies of target engagement and/or proof of principle.**
- 11:40 a.m. An industry perspective on biomarker-based drug discovery  
ANDREW AHN, Eli Lilly & Co.
- 11:55 a.m. Imaging  
TOR WAGER (*via WebEx*), University of Colorado at Boulder
- 12:10 p.m. miRNA Biomarkers  
SEENA AJIT, Drexel University
- 12:25 p.m. Discussion among Speakers and Workshop Participants
- 12:40 p.m. PANEL: How to implement a targeted approach to therapy development by focusing on homogenous populations; dissecting pain mechanisms and clinical research in specific pain conditions– natural history biomarkers, clinical trial readiness.  
  
KATHERINE DAWSON, Biogen  
SHARON HERTZ (*invited*), Food and Drug Administration  
SEAN MACKEY, Stanford University  
WILLIAM MAIXNER, Duke University  
KEN VERBURG (*via WebEx*), Pfizer Inc.
- 1:20 p.m. LUNCH
- Process to developing therapies to prevent the acute to chronic pain transition - What is needed?**
- 2:00 p.m. Preclinical perspective  
THEODORE PRICE, The University of Texas at Dallas

- 2:15 p.m. Clinical perspective  
ROBERT DWORKIN, University of Rochester Medical Center
- 2:30 p.m. Discussion among Speakers and Workshop Participants
- 2:45 p.m. PANEL: A US network for pain research (including pediatric research). Where's the value?  
  
ROBERT DWORKIN, University of Rochester Medical Center  
PETRA KAUFMANN, National Center for Advancing Translational Sciences  
SCOTT POWERS, Cincinnati Children's Hospital
- 3:15 p.m. Discussion among Speakers and Workshop Participants: *Launching Public-Private Partnerships to advance clinical work in understanding and treating the transition from acute to chronic pain.*
- 3:45 p.m. BREAK

#### SESSION IV: MOVING FORWARD AND NEXT STEPS

Objectives: Synthesize and discuss key highlights from the workshop presentations and discussions and, most importantly, identify next steps and promising areas for future action and research.

- 4:00 p.m. Workshop Synopsis and Potential Next Steps  
Moderator: STORY LANDIS, Vice Chair, Forum on Neuroscience and Nervous System Disorders, National Academies of Sciences, Engineering, and Medicine (*Co-chair*)  
  
Session I: NORA VOLKOW, National Institute on Drug Abuse  
Session II: JOHN DUNLOP, Amgen  
Session III: WALTER KOROSHETZ, National Institute of Neurological Disorders and Stroke  
Discussants: DAVID SHURTLEFF, National Center for Complimentary and Integrative Health  
SHARI LING, Centers for Medicare and Medicaid Services  
ANDREY OSTROVSKY, Center for Medicaid and CHIP Services
- 4:25 p.m. Discussion among Moderators and Workshop Participants
- 4:55 p.m. Final Comments
- 5:00 p.m. ADJOURN