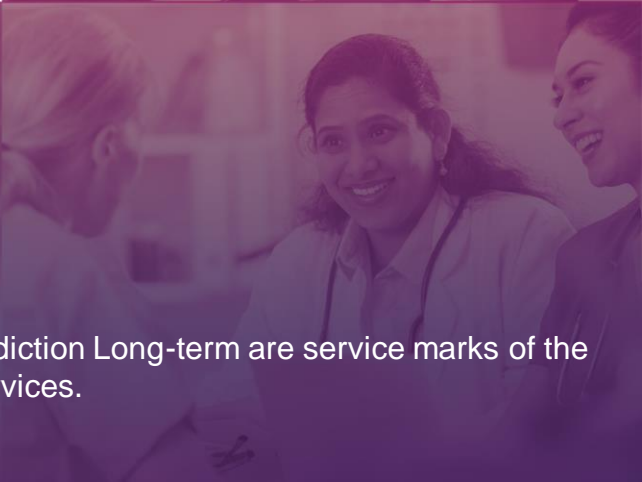
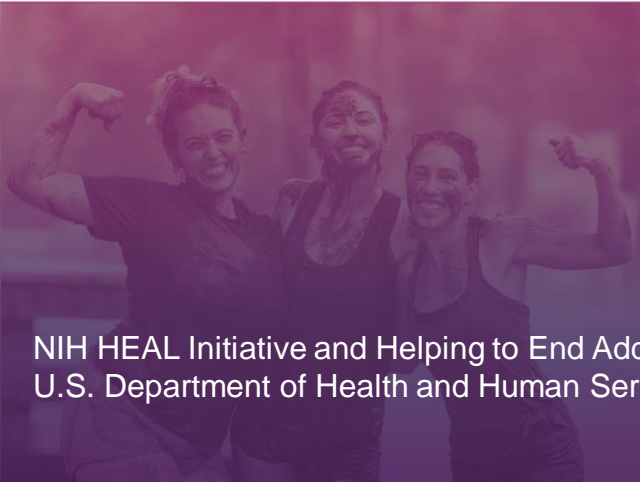




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# NIH HEAL Multi-Disciplinary Working Group

August 31, 2020



**NIH** National Institutes of Health  
*HEAL Initiative*

NIH HEAL Initiative and Helping to End Addiction Long-term are service marks of the U.S. Department of Health and Human Services.

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# Welcome and Introductions

NIH HEAL Initiative and Helping to End Addiction Long-term are service marks of the U.S. Department of Health and Human Services.

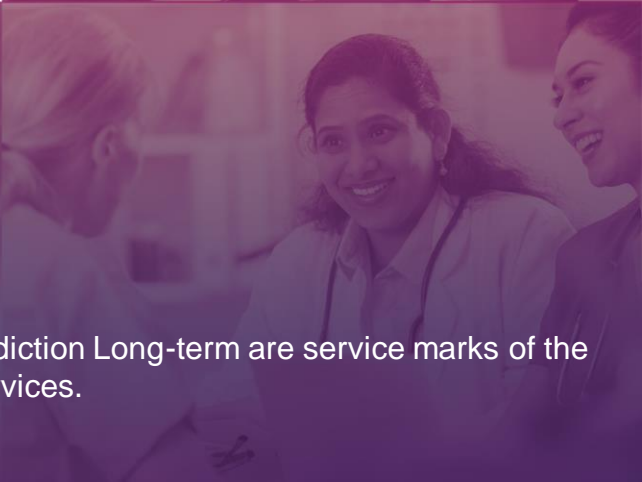
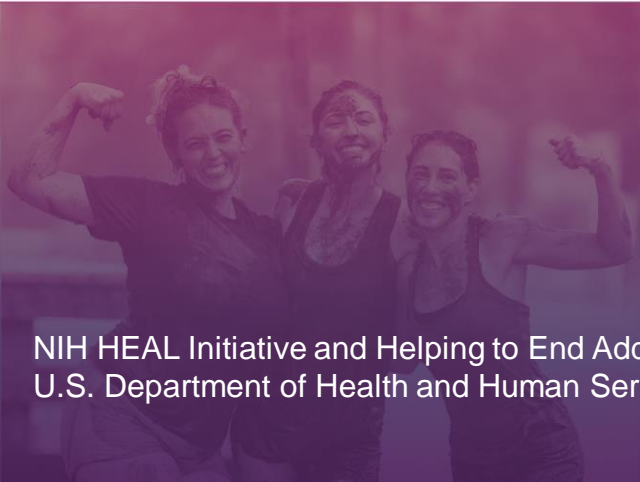


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# Overview of Current Portfolio

August 31, 2020

Rebecca Baker, Director, NIH HEAL Initiative



**NIH** National Institutes of Health  
*HEAL Initiative*

NIH HEAL Initiative and Helping to End Addiction Long-term are service marks of the U.S. Department of Health and Human Services.

# By the Numbers: \$500 million/year Sustained Research Investment

## 25+ HEAL Research Programs



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20 NIH ICs collaborating on studies

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Trans-NIH governance structure

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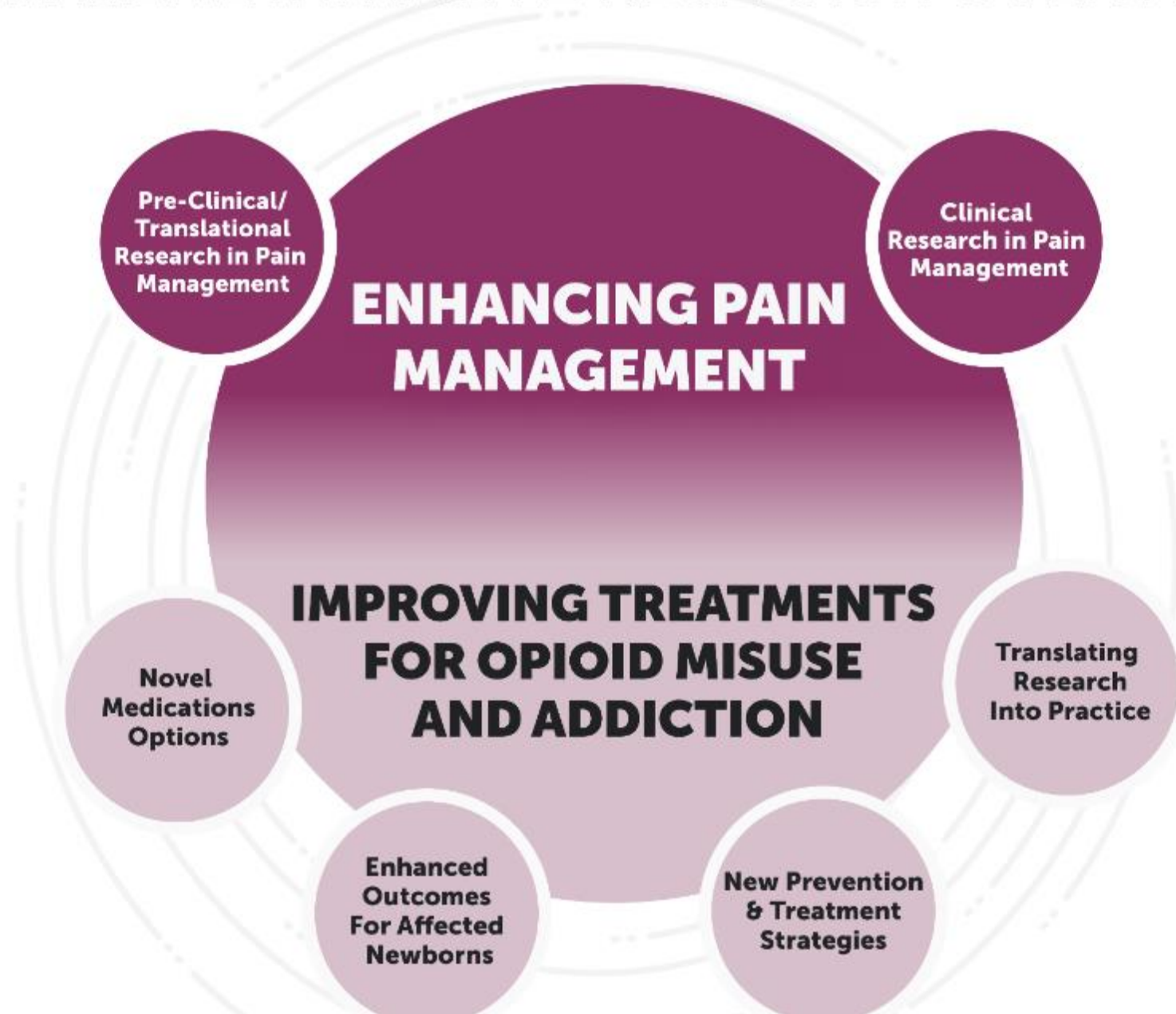
Partnerships across government,  
communities, and the private sector

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**Prevention – Basic & Translational Research  
– Clinical Trials – Implementation Science**



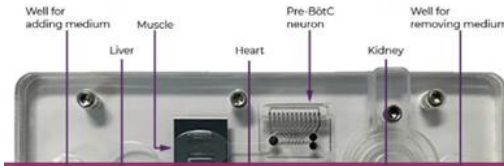
# NIH HEAL INITIATIVE RESEARCH OVERVIEW





## Help for Babies Born Dependent on Opioids

Infant/Child Outcomes



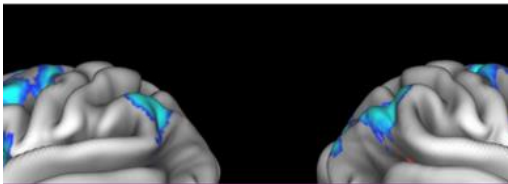
## "Human-on-a-Chip" Models Effects of Opioid Overdose

Pain – Preclinical/Translational Research



## The Search for New, More Targeted Pain Treatments

From surgery and drugs to cell-based therapies, researchers will test innovative, non-addictive approaches for treating pain.



## Can Exposures Before Birth Predict Health Later in Life?

Infant/Child Outcomes



## Is Lack of Sleep a Risk Factor for Relapse?

Preventing/Treating OUD

# Research Spotlights

- 1 Sensors on the **prosthesis** convey information about contact, force, and angle to the sensor processor.
- 2 The **sensor processor** interprets the signals from the prosthesis and conveys a command to the implantable stimulator.
- 3

**Next-gen Device Could Relieve Phantom Limb Pain**

Pain – Preclinical/Translational Research

How do I manage my asthma, my acid reflux and my opioid use disorder.

*Buprenorphine is a prescription medication that is used along with counseling and/or behavioral therapies to treat opioid use disorder.*



*Buprenorphine can be part of a treatment plan for opioid use disorder.*

**Staying on the Road to Recovery**

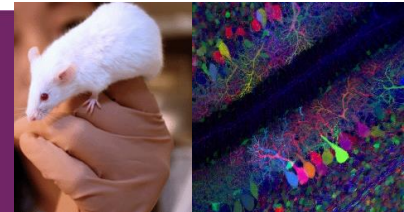
Preventing/Treating OUD

# HEAL

NIH • Helping to End Addiction Long-term

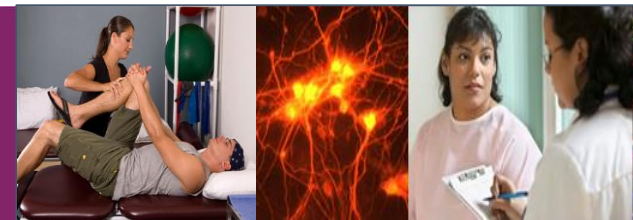
# Pre-Clinical and Translational Research in Pain Management

- Discovery and validation of novel targets for safe and effective pain treatment
  - 3 publications in basic and translational research area
- Translating discoveries into effective devices for pain treatment
- Optimizing non-addictive therapies to treat pain
  - Fast tracked FDA decision for new pain candidate
- Engineering preclinical screening platforms
- Biomarkers, signatures and endpoints for pain



# Clinical Research in Pain Management

- Early Phase Pain Investigation Pain Network
- Back Pain Consortium Research Program
  - Dynamic back pain model
  - Predictive models for individualized responses to multimodal interventions
- Pain Management Effectiveness Research Network
- Pragmatic and Implementation Studies for the Management of Pain (PRISM)
  - Partner with CMS on effectiveness of acupuncture for low back pain
- Integrated Approach to Pain and Opioid Use in Hemodialysis Patients





# New Prevention & Treatment Strategies for Opioid Use Disorder

- Preventing OUD among at risk adolescents
  - 9 projects focused on vulnerable populations (e.g. homeless youth and American Indian/Alaskan Natives)
- Optimizing care for people with OUD and common mental disorders
- Managing opioid misuse and low severity OUD
- Understanding the role of sleep dysfunction
- Determining the optimal length of medication treatment

# Translation of Research into Practice for Effective Treatments for OUD

- Integrating multiple evidence-based interventions: HEALing Communities Study
- Enhancing the NIDA Clinical Trials Network to address opioids
- Promoting innovation in the criminal justice system (JCOIN)
  - 13 research studies across 21 states; >40K justice-involved youth
  - COVID-19 guidelines developed and distributed
- Understanding the role of behavioral health interventions (BRIM)



# Novel Medication Options for Opioid Addiction and Overdose

- Increase effective medication options:
  - Enhanced formulations; addressing craving and withdrawal; novel targets for addiction and overdose
  - 8 HEAL-funding projects obtained IND
- Immune-based therapies for heroin and fentanyl
  - Consortium established



# Enhanced Outcomes for Affected Newborns

- Advancing Clinical Trials in Neonatal Opioid Withdrawal Syndrome: ACT NOW Study
  - Completed site selection across 20 states.
    - Clinical trials to begin early September 2020
    - Longitudinal Study launched Aug 5
- Understanding the long-term consequences of early opioid exposure: HEALthy BCD Study



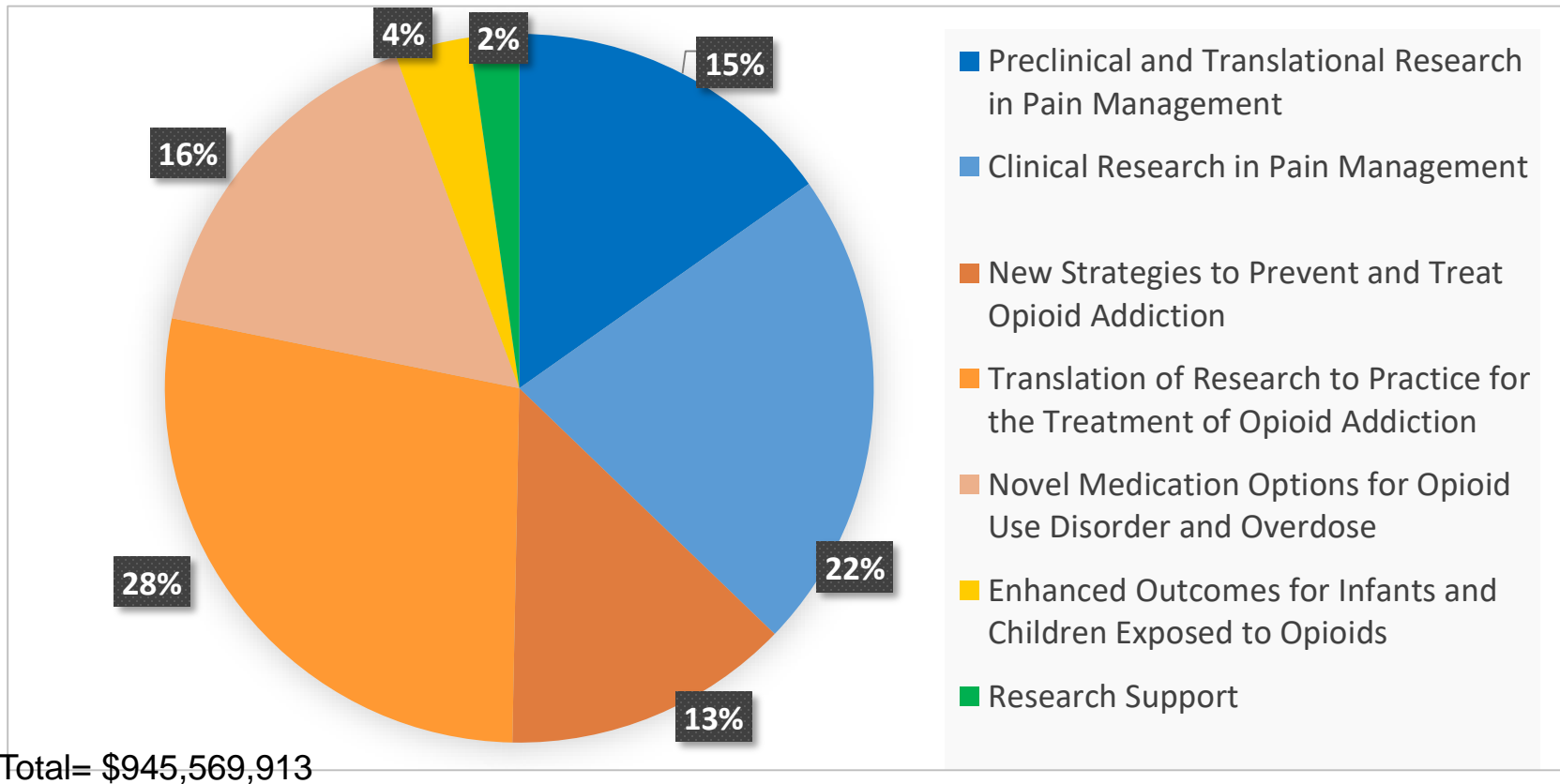


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**Investment in Pain and Addiction  
Research  
5-year Budget Summary**

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# Existing HEAL Investment by Research Focus Area (FY2019 Obligations)



# Addressing Gaps in Research: Selected Examples of FY20 Investments



Understanding the Relationship Between Pain and Opioid Use Disorder

- Pain Management in the Setting of Opioid Use
- Strategies to Reduce Stigma in Pain Management and Addiction Treatment
- Workshop:** Interventions for Managing Comorbid Chronic Pain & OUD



Addressing OUD and Co-occurring Mental Health Conditions

- Social Network Analyses to Reduce AI/AN OUD and Related Risk for Suicide
- Research to Manage Common Co-occurring Conditions
- Research Networks for the Study of Recovery Support Services for Persons Treated with Medications for OUD



Understanding Diversity of Care Received Across Health Settings

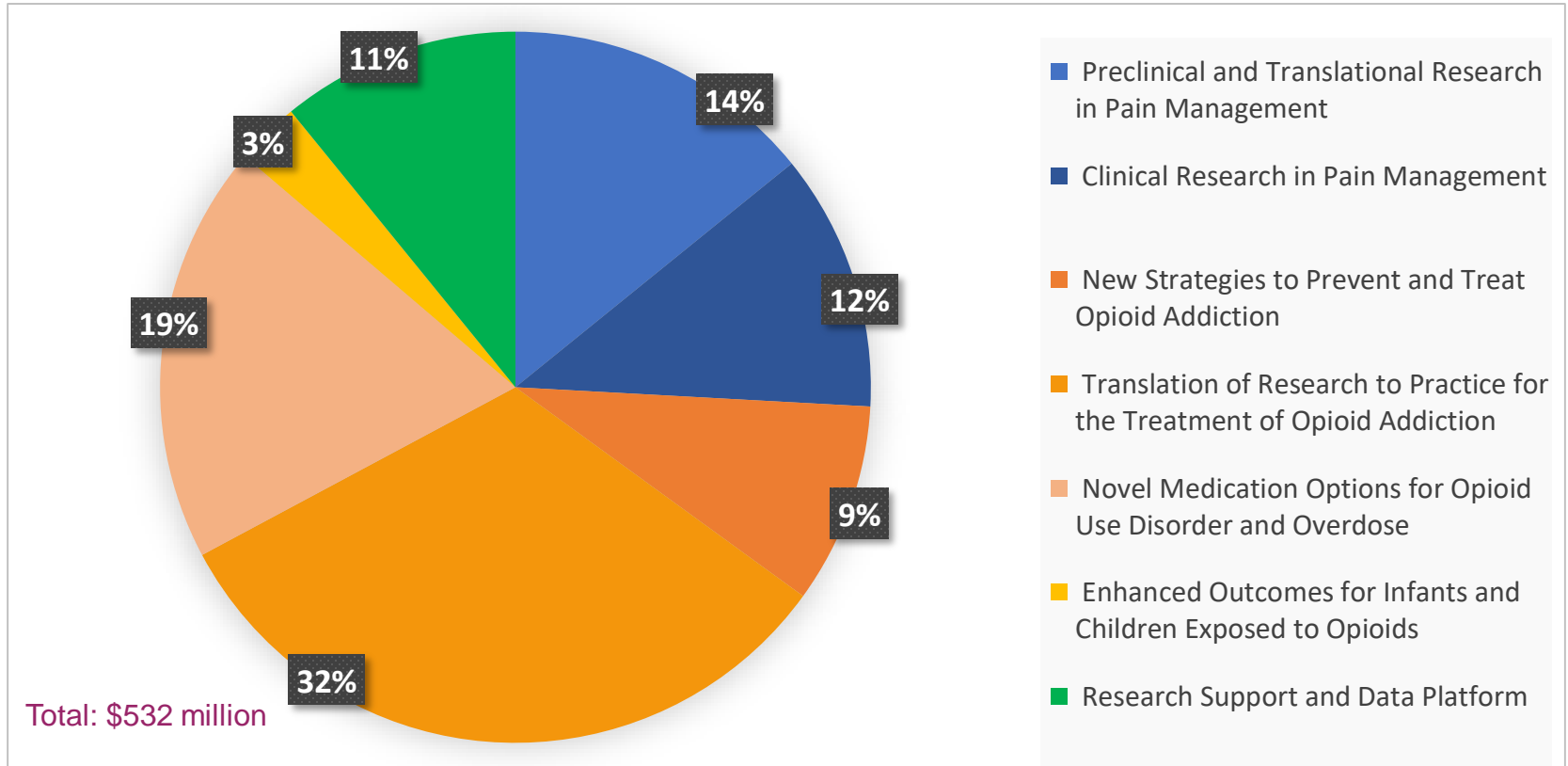
- Best Management of Specific Pain Conditions in Primary Care, Hospital, Dental, or Emergency Settings
- Workshop:** Navigating Pediatric to Adult Health Care Transition



Increasing Diversity Among HEAL Investigators

- Enhance Workforce Diversity
- Training Supplements for HEAL Network Clinical Trials
- Workshop:** Research Priorities for Addressing Social and Economic Determinants of Opioid Related Health Disparities

# Planned FY20 Obligation by HEAL Research Focus Area

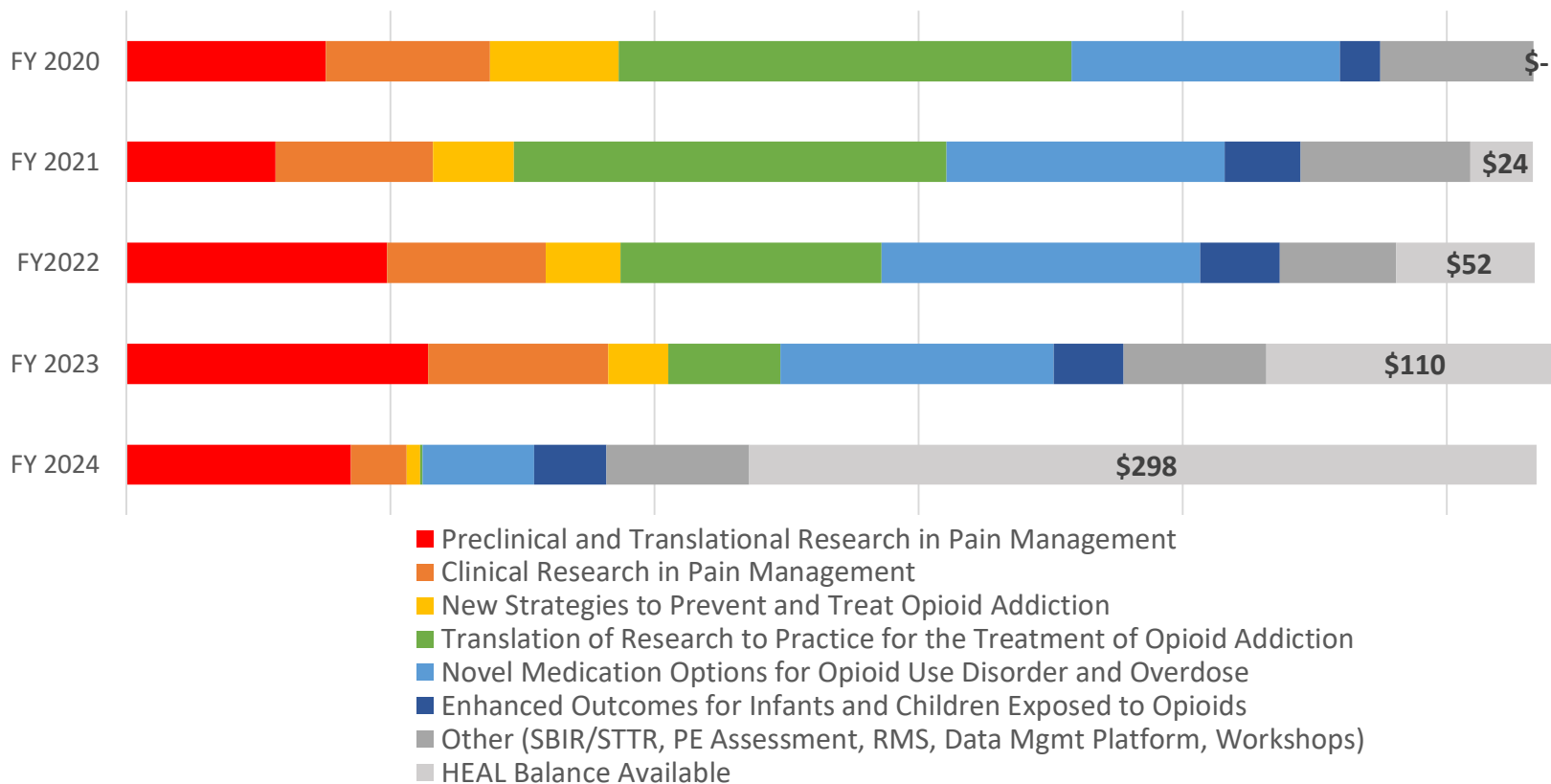




# HEAL Concepts Moving Forward in FY2021

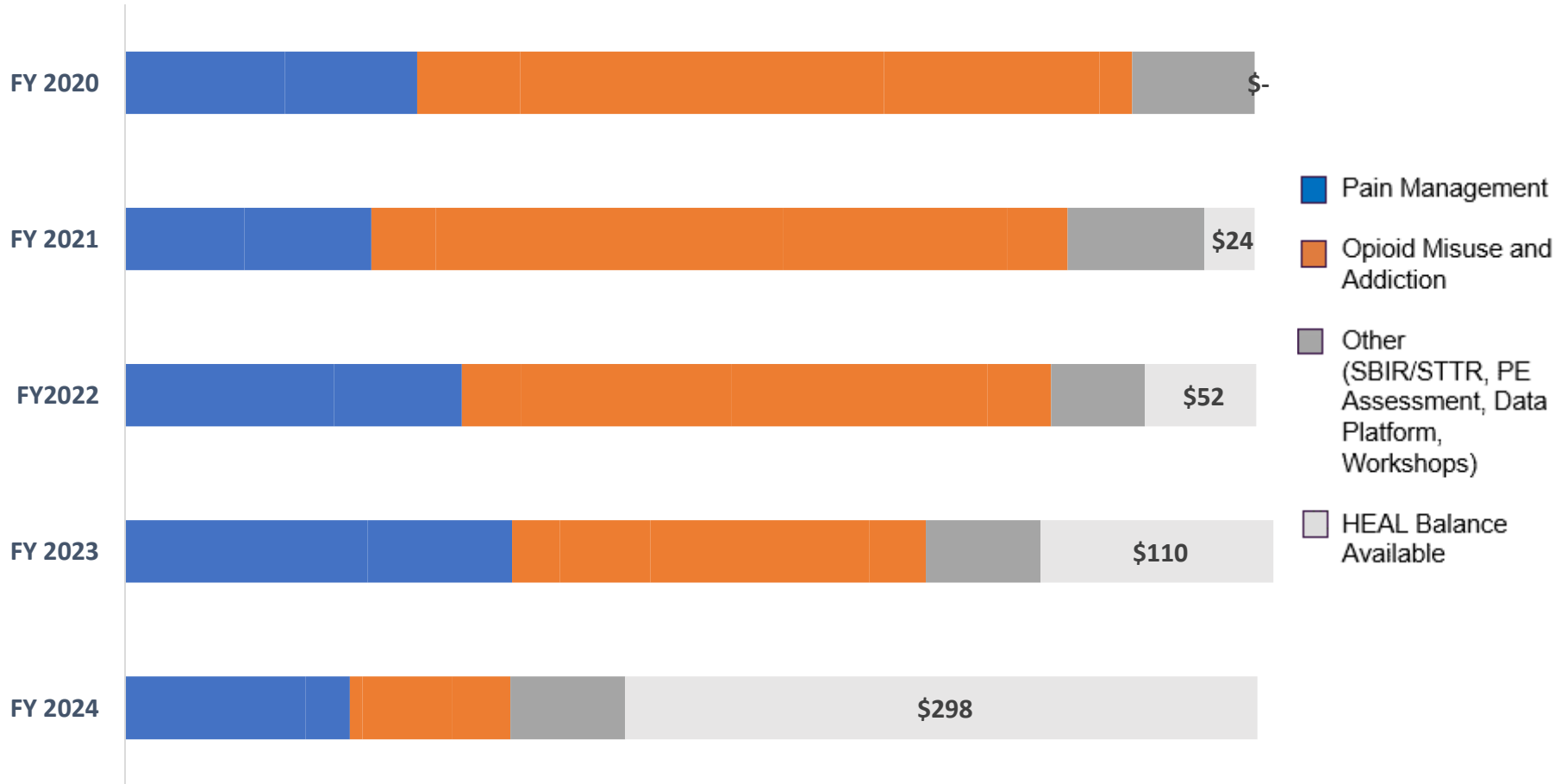
- **\*Concept 1:** A Coordinated Suite of Funding Opportunities Supporting Early-Phase Therapeutic Development for Pain
- **Concept 3:** HEAL Studies to Enhance Phenotyping of Study Participants with Chronic Overlapping Pain Conditions
- **Concept 4:** Managing comorbid chronic pain and OUD
- **Concept 6:** Optimizing multi-component service delivery interventions for people with opioid use disorder, co-occurring conditions, and/or suicide risk
- **Concept 8:** HEALthy Brain and Child Development Study
- **Concept 9:** Comparative-effectiveness trial for the pharmacological treatment of neonatal opioid withdrawal syndrome
- **Concept 10:** Fast-track the discovery and development of medications to treat opioid use disorders

# HEAL Initiative Budget: Future Funding Framework



Available funds to be divided evenly between pain and addiction focused research

# HEAL Initiative Budget: Future Funding Framework



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## Future Opportunities

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# FY 2020 HEAL Workshops

Interventions for Managing Comorbid Chronic Pain & OUD/Physical Dependence	June 1-2, 2020
Towards the Use of Buprenorphine in Infants: Scientific and Practical Considerations	August 24-25, 2020
Research Priorities for Addressing Social and Economic Determinants of Opioid-Related Health Disparities- Expert Panel Workshop and Planning Meeting	September 9, 2020
Workshop on the structural and dynamic imaging of myofascial tissues: potential impact on musculoskeletal pain research	September 16-17, 2020
Navigating pediatric to adult health care: Lost in health care transition	September 30-October 1, 2020
Developing meaningful endpoints for pain clinical trials	October 8 & October 15, 2020
Target Validation for Non-Addictive Therapeutics Development for Pain - Strategic Approaches and Best Practices	February 2021

# MDWG Topics of Interest

- Impact of COVID 19
- Ongoing budget outlook
- Special Populations
- Individuals with OUD and Mental Health Conditions
- Older Adolescents and Young Adults
- Justice Involved Individuals
- Infants and Children with NOWS



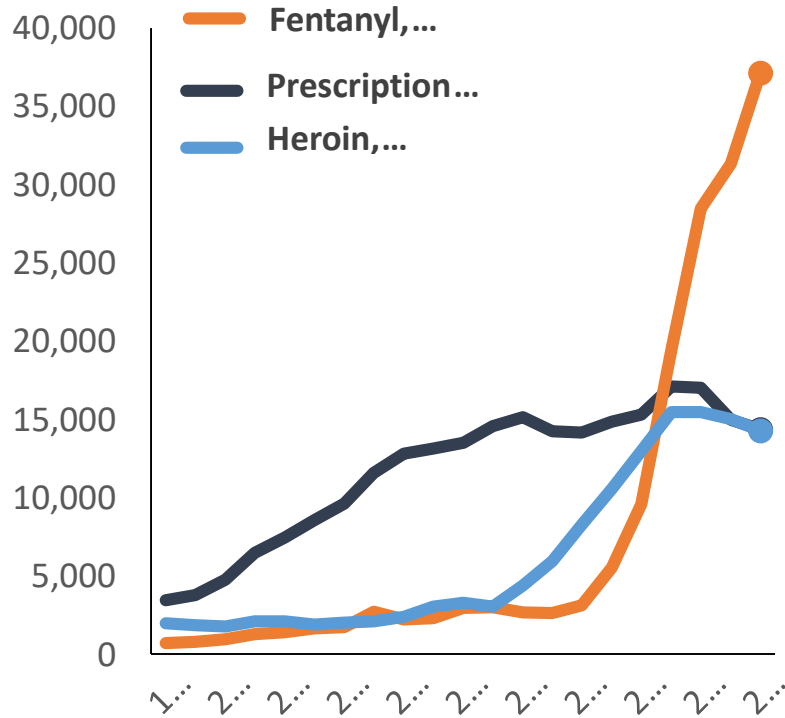


## Emerging Issues in the Opioid Crisis: Collision of COVID-19 on Opioid Overdose and Treatment

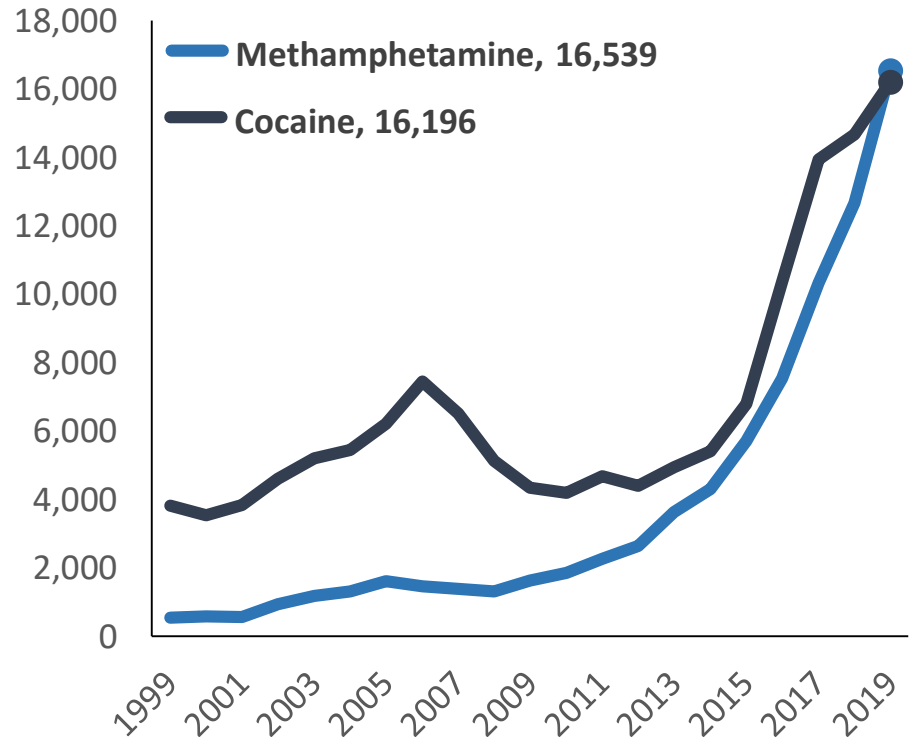
Nora D. Volkow, M.D., Director, National Institute on Drug Abuse

# Overdose Deaths in 2019 Increased by 4.6%

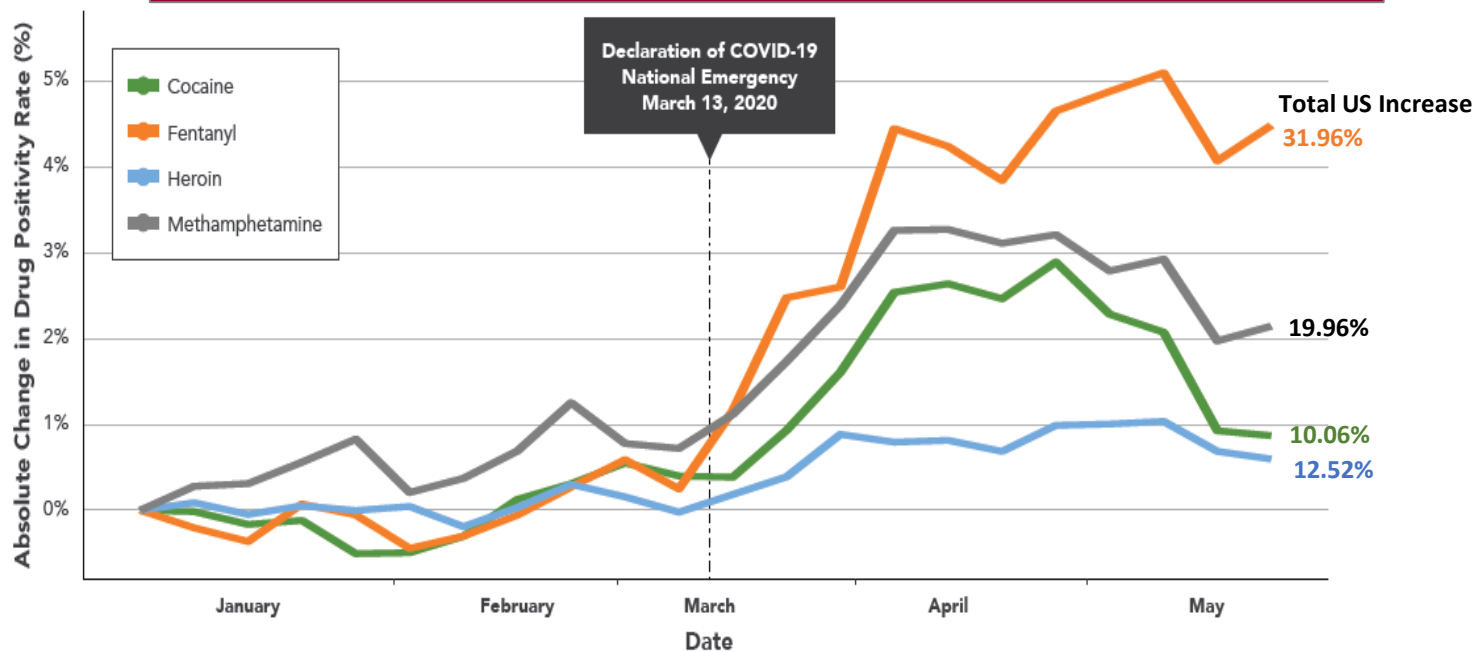
Number of Deaths



Number of Deaths



# Drug Use Increase During COVID

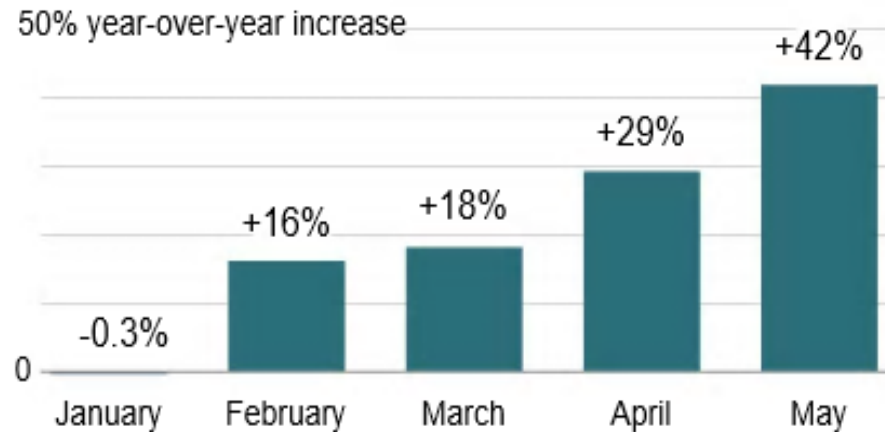


## Total Study Population Change in Unadjusted Positivity Rate for Cocaine, Fentanyl, Heroin and Methamphetamine

Millennium Health Signals Report™ COVID-19 Special Edition: Significant Changes in Drug Use During the Pandemic Volume 2.1 | Published July 2020

# Overdoses Grew Dramatically During COVID Pandemic

Overdoses increased up to 42% per month during the pandemic, as compared to the same months in 2019.



Note: Percent growth references the 1,201 agencies reporting to ODMAP by January

Source:  ODMAP  
OVERDOSE DETECTION  
MAPPING APPLICATION PROGRAM

ALYSSA FOWERS/THE WASHINGTON POST

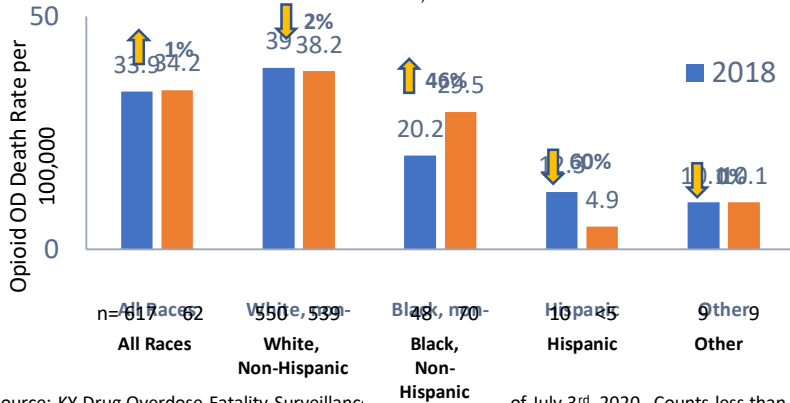




# Overdose Deaths in HEALing Communities States

### Kentucky Opioid Overdose Deaths by Race/Ethnicity:

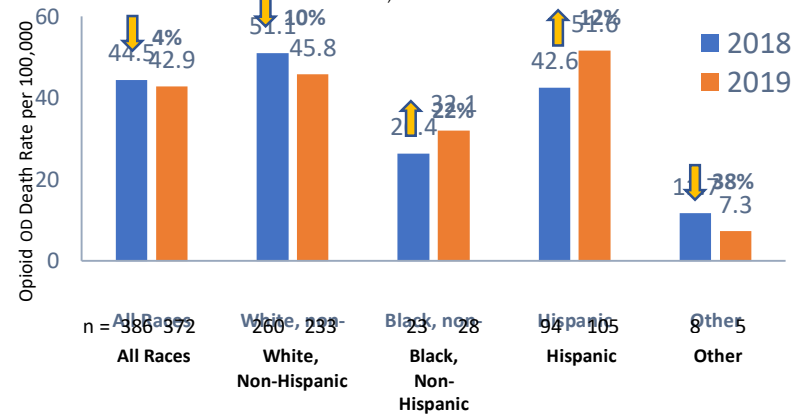
2018-2019, N=16 Communities



Source: KY Drug Overdose Fatality Surveillance, 2018-2019. Counts less than 5 suppressed by state data reporting policy. Produced by the Kentucky Injury Prevention and Research Center, University of Kentucky. of July 3<sup>rd</sup>, 2020.

### Massachusetts Opioid Overdose Deaths by Race/Ethnicity:

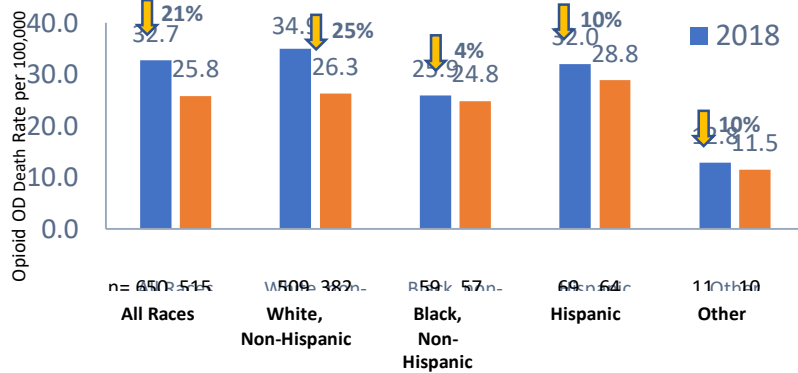
2018-2019, N=16 Communities



Source: MA Registry of Vital Records and Statistics

### New York Opioid Overdose Deaths by Race/Ethnicity:

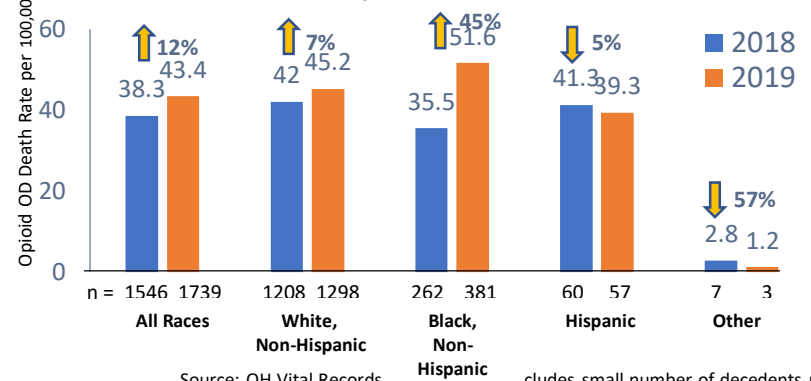
2018-2019, N=16 Communities



Data and analysis provided by New York State Department of Health July 27, 2020

### Ohio Opioid Overdose Deaths by Race/Ethnicity:

2018-2019, N=16 Communities

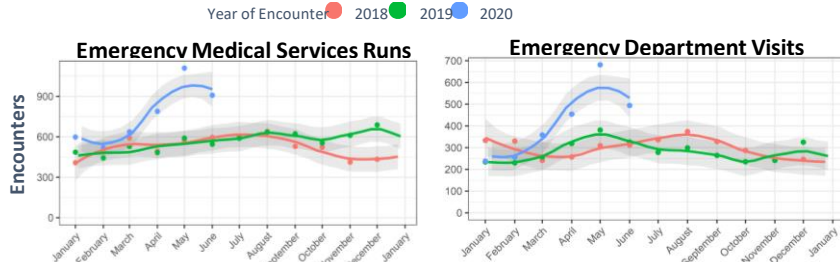


Source: OH Vital Records

includes small number of decedents missing race/ethnicity)

# Overdose Encounters in HEALing Communities States

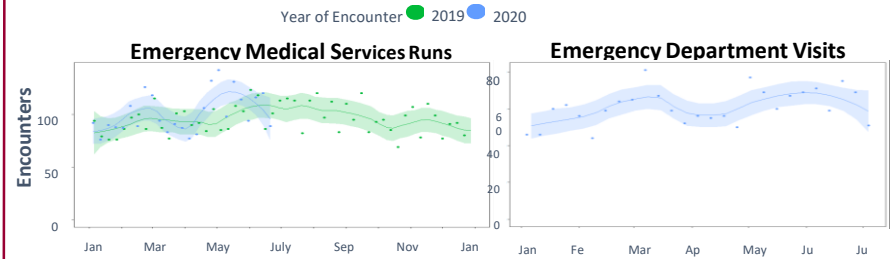
**Kentucky HCS Opioid Overdose-related Encounters:**  
2018-2020, N=16 Communities



Data Sources: Kentucky Board of Emergency Medical Services data and Syndromic surveillance of emergency department visits

Solid lines represent LOESS Regression of Opioid Overdose Encounters. Points represent raw counts of records.

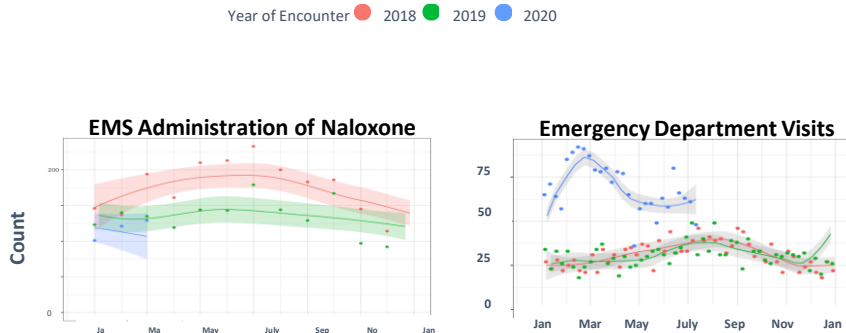
**Massachusetts HCS Opioid Overdose-related Encounters:**  
2019-2020, N=16 Communities



Data Sources: MA Department of Public Health; MA Ambulance Trip Information System and Syndromic Surveillance data

Solid lines represent LOESS Regression of Opioid Overdose Encounters. Points represent raw counts of records.

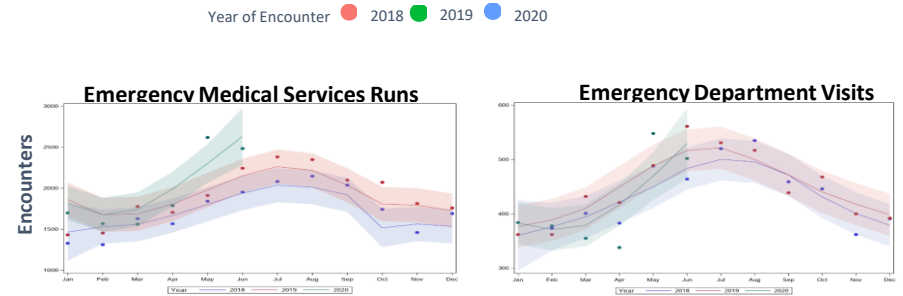
**New York HCS Opioid Overdose-related Encounters:**  
2018-2020, N=16 Communities



Data Sources: New York State Bureau of Emergency Medical Services and Trauma Systems and Syndromic Surveillance of emergency department visits

Solid lines represent LOESS Regression of Opioid Overdose Encounters. Points represent raw counts of records.

**Ohio HCS Opioid Overdose-related Encounters:**  
2018-2020, N=19 Communities

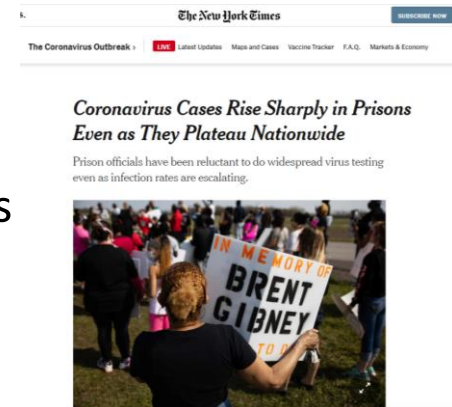


Data Sources: Ohio syndromic surveillance of emergency department visits

Solid lines represent LOESS Regression of Opioid Overdose Encounters. Points represent raw counts of records.

# COVID & The Justice System

- People in jails & prisons are particularly vulnerable to COVID
- Some of the largest outbreaks in U.S. have been in jails or prisons
  - As of August 4th: > 86,000 cases
  - Outbreaks in jails and prisons can spread to the community
- Testing has been limited in prisons and jails (when available infection rates tend to be high; up to 98%).
- Rapid push to reduce incarcerated populations reduced census in jail & prison
  - Limited the ability to connect to community support services (housing, mental health, MOUD)
- Prisoners have limited access to MH and SUD services
  - Telehealth services are being adopted in some jails/prisons



Sources: <https://www.nytimes.com/2020/06/16/us/coronavirus-inmates-prisons-jails.html>; <https://www.vera.org/publications/covid19-jail-population-decline>  
<https://www.themarshallproject.org/2020/05/01/a-state-by-state-look-at-coronavirus-in-prisons>; <https://www.vera.org/projects/covid-19-criminal-justice-responses/covid-19-data>  
<https://www.themarshallproject.org/2020/07/16/prison-populations-drop-by-100-000-during-pandemic>; <https://www.themarshallproject.org/2020/06/01/what-covid-19-prison-outbreaks-could-teach-us-about-herd-immunity>

## Discussion

- How can collaboratives such as the JCOIN and HEALing Communities Study be assets during changing landscape of COVID?
- How can the HEAL Initiative best respond to the changing landscape of drug use during COVID?
- How are other aspects of HEAL affected by COVID and related aspects of the pandemic?



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## Realignment of the Analgesic Development Program

Walter Koroshetz, MD  
Director, NINDS

HEAL Multidisciplinary Working Group; Aug. 31, 2020



**#NIHhealInitiative**

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# Bridging Gaps in the analgesic development pipeline

## ❖ Academics and Small Biotechs:

- Excellent ideas with good scientific premise
- Disease biology expertise

### but often lack:

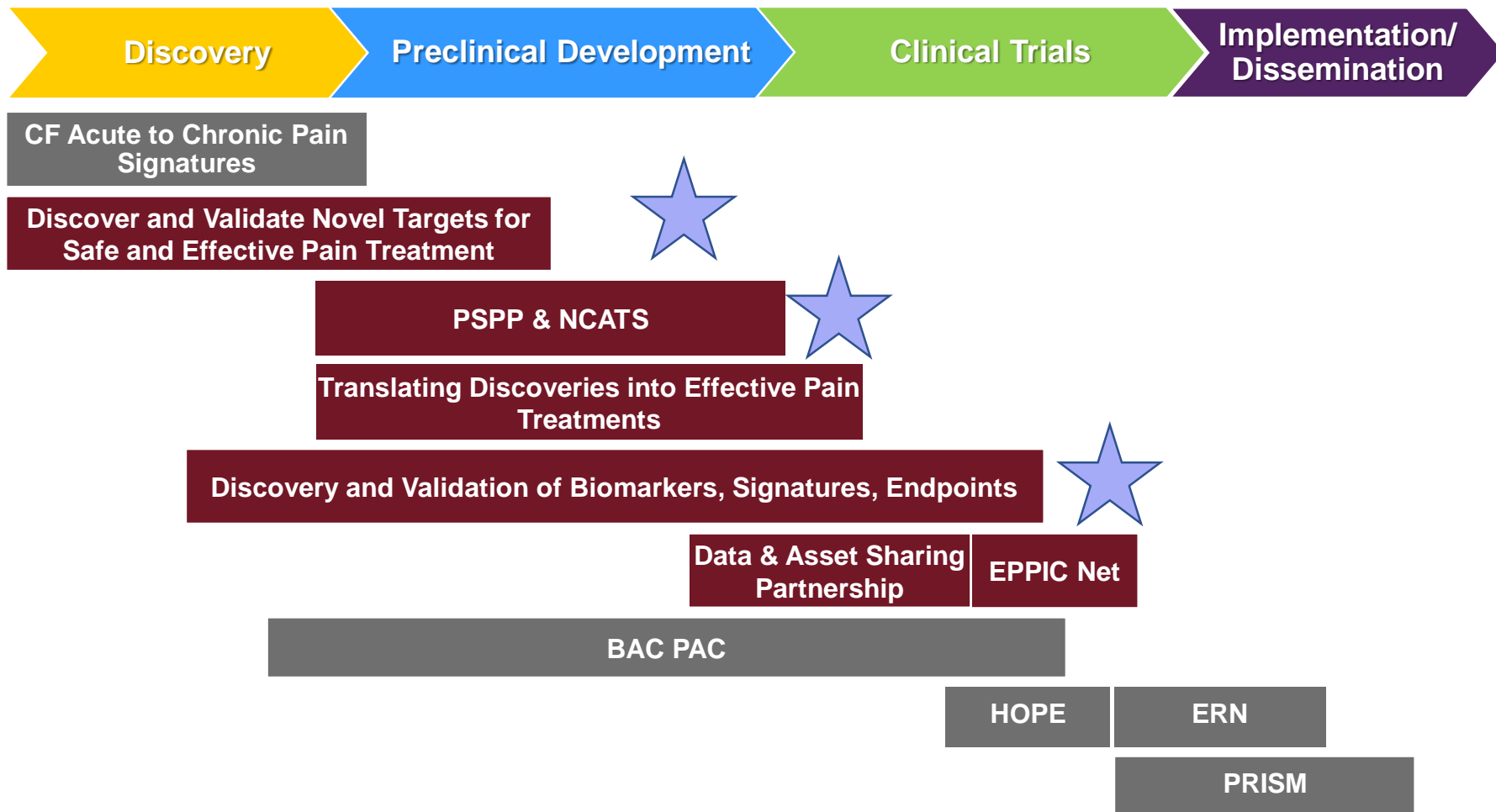
- Resources to advance their ideas
- Complete preliminary data packages
- Screening assays and chemical starting points
- Models for future testing

## ❖ Realigned HEAL program will:

- Provide specialized drug discovery and development planning and expertise
- Provide access to drug discovery infrastructure and testing to advance to clinic
- Preserve investigators' IP
- Combine the strengths of NIH and industry expertise for drug discovery



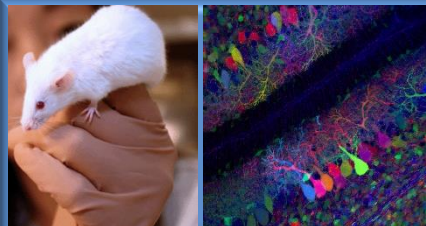
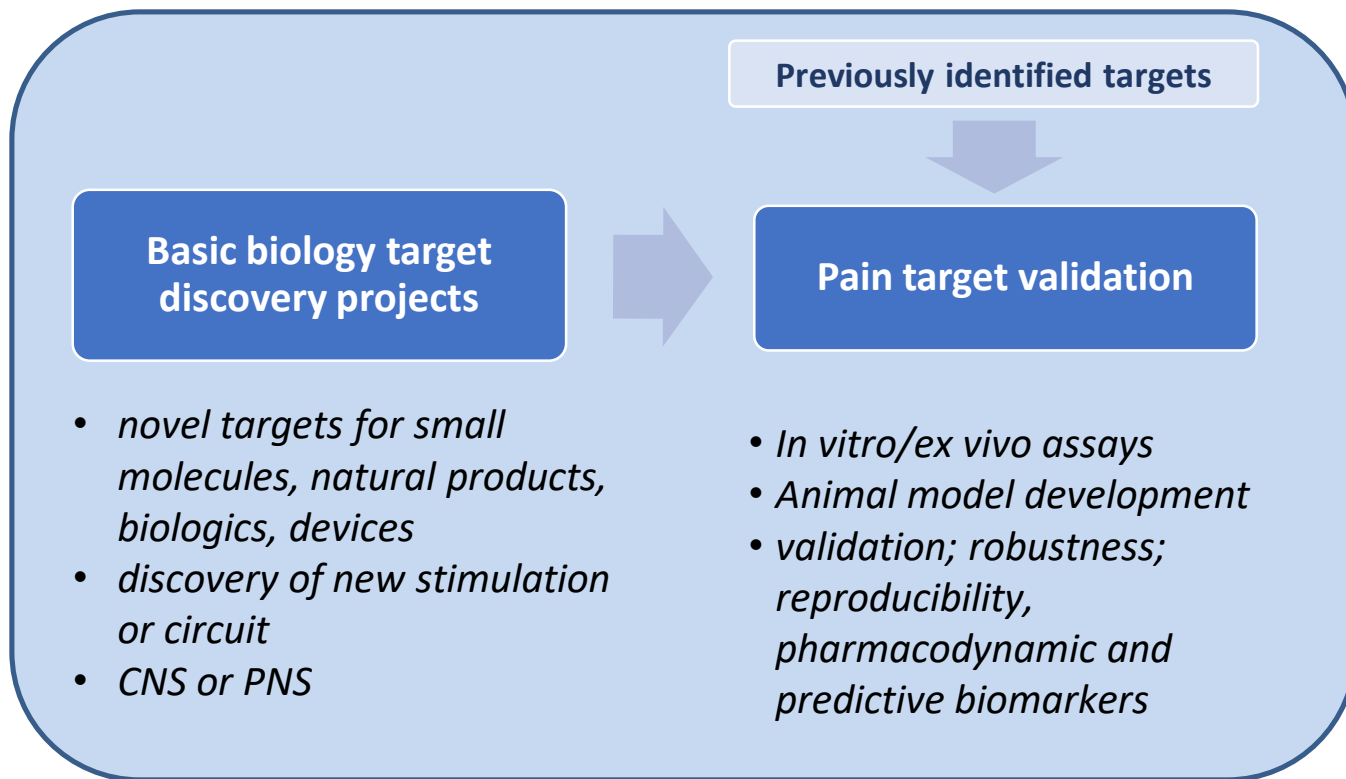
# Current HEAL Programs for Enhancing Pain Management





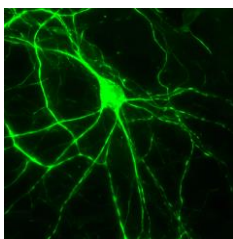
# Current HEAL Programs:

## *Discover and Validate Novel Targets for Safe and Effective Pain Treatment*

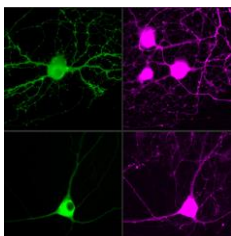


**Enhancing Pain Management**

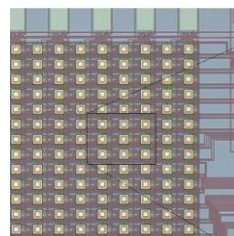
# Current HEAL Programs: *Human Cell-based Screening Platforms*



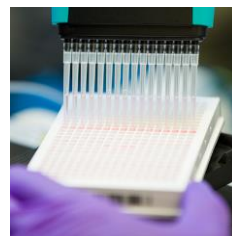
Access to human cell types



Advanced imaging technologies for functional cell characterization



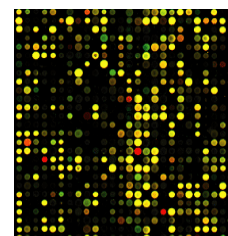
Electrophysiology methods



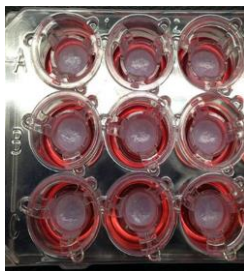
Measurement of signaling pathways, metabolism



Longitudinal tracking of cell behavior



Combined single-cell transcriptomic & proteomic analyses



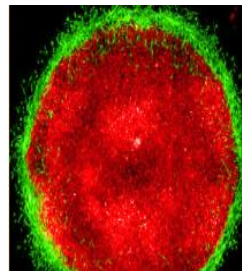
Tissue engineering technologies



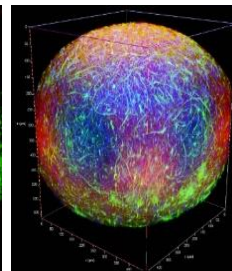
Automated production of iPS cell-derived cells



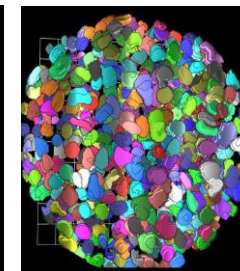
3D bioprinters



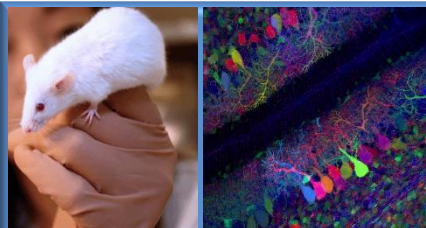
Spatially defined and physiologically relevant tissue models



Validation of 3D organoid cultures



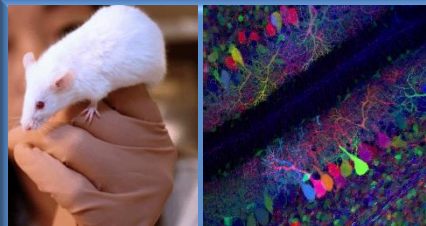
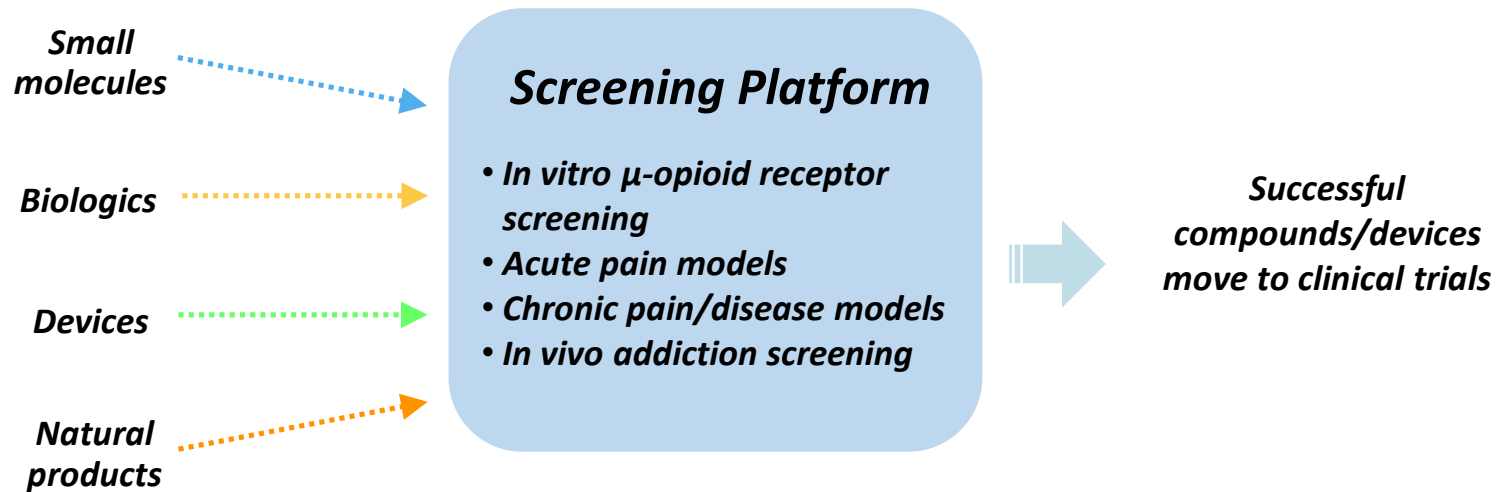
Assays using 3D tissue models



Enhancing Pain Management

# Current HEAL Programs: *Preclinical Screening Platform for Pain (PSPP)*

- Promote testing and characterization of non-addictive treatments
- Incentivize academia & industry to accelerate discovery of non-addictive, effective therapies
- Develop or refine animal models of pain conditions
- Generate high quality data to support partnerships, translational programs



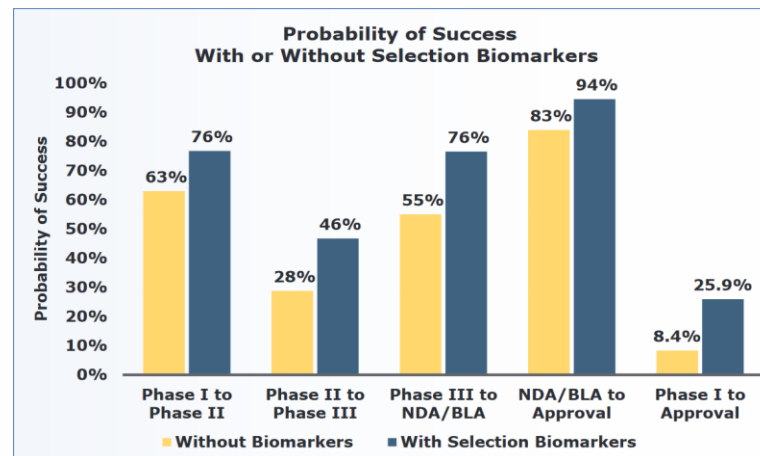
**Enhancing Pain Management**

# Current HEAL Programs: *Biomarker Program*

*Supporting Biomarker Discovery and Validation to Facilitate Clinical Trial Design and Clinical Pain Management Decisions*

## *Discovery of Biomarkers, Biomarker Signatures, and Endpoints for Pain*

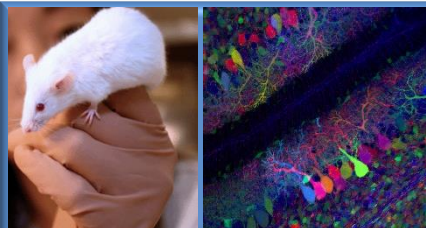
To facilitate discovery of robust biomarkers, biomarker signatures and objective endpoints for pain conditions



Thomas, D. W. et al. Clinical development success rates 2006–2015. San Diego: Biomedtracker/Washington, DC: BIO/Bend: Amplion (2016).

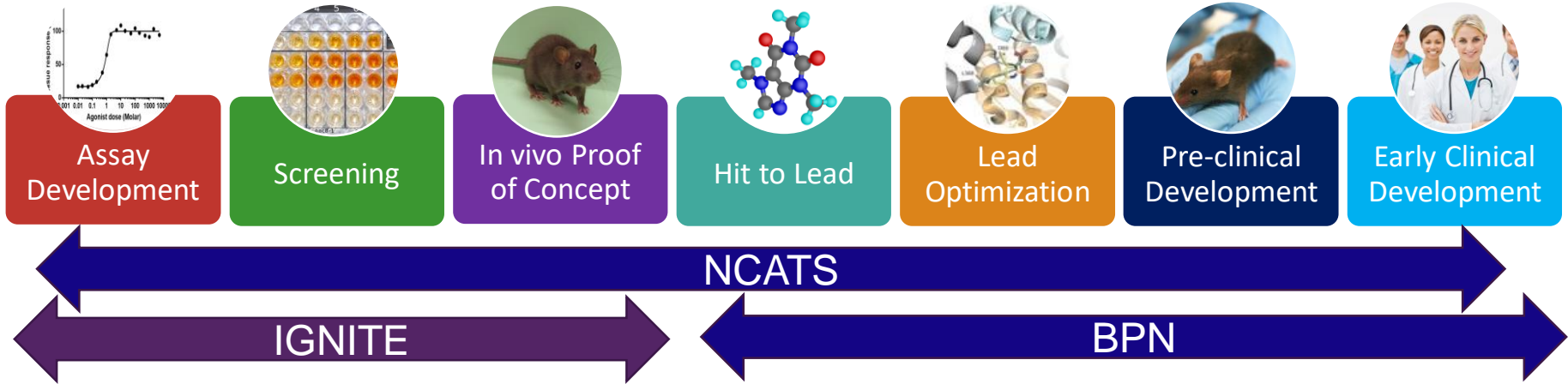
## *Analytical and Clinical Validation of a Candidate Biomarker for Pain*

To support analytical and clinical validation of candidate biomarkers for use in the discovery and development of non-opiate alternatives to the treatment of pain conditions using retrospective and/or prospective methods



**Enhancing Pain Management**

# Therapeutic development programs outside of HEAL: NCATS intramural, NINDS IGNITE and Blueprint Neurotherapeutics are Models to Bridge the Gaps



## Innovation Grants to Nurture Initial Translational Efforts

- End goal is to meet BPN entry criteria
- Milestone-driven grant



## Blueprint Neurotherapeutics Program

- Provides resources (CROs, consultants) in addition to grant support
- Milestone-driven cooperative agreement with goal of IND/IDE



# Proposed HEAL Analgesic Development Program

## Goal

Accelerate development of novel, non-opioid, non-addictive analgesics

## Five-year Benchmarks

- ✓ At least 5 promising projects with appropriate assay(s), model(s), and tools - ready for preclinical lead optimization.
- ✓ At least 3 novel analgesics with an IND and human safety data – ready for clinical efficacy studies through EPPIC-Net or equivalent phase II trial.

# Realigned Program Strengths

## Enhanced monitoring & evaluation for program progression

- External Panel of Consultants for implementation, selection of models, assays, tools, nomination of candidate & program progress

## Enhanced coordination

- Assist early stage projects to come into the program: planning awards
- Facilitate project advancement through sequential development phases
- Coordinate with Clinical team to advance project to clinical testing
- Facilitate industry partnership for early adoption
- Assure relevance to the program and overall diversity

## Enhanced Participation

- Assist early stage projects to come into the program: planning awards



# Realigned HEAL Analgesic Development Program

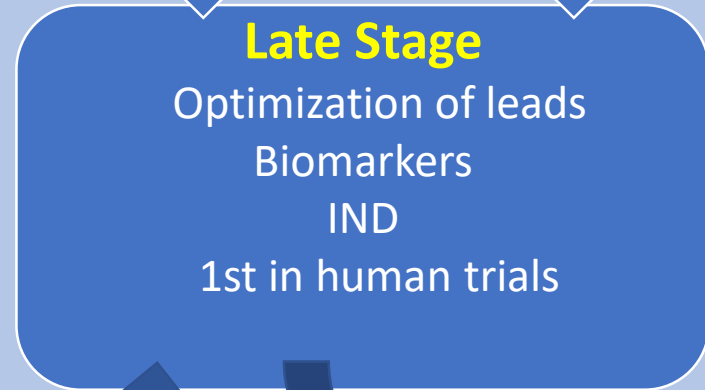
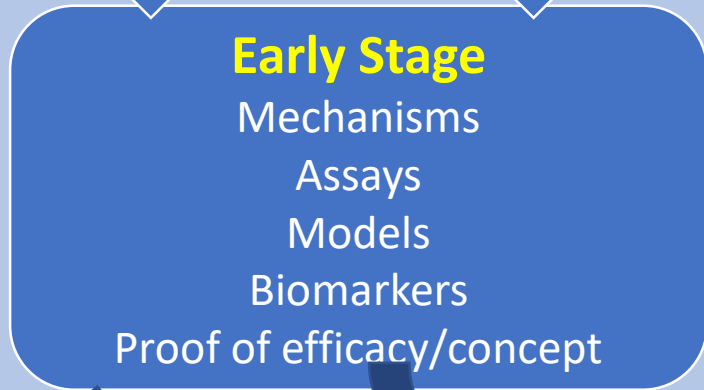
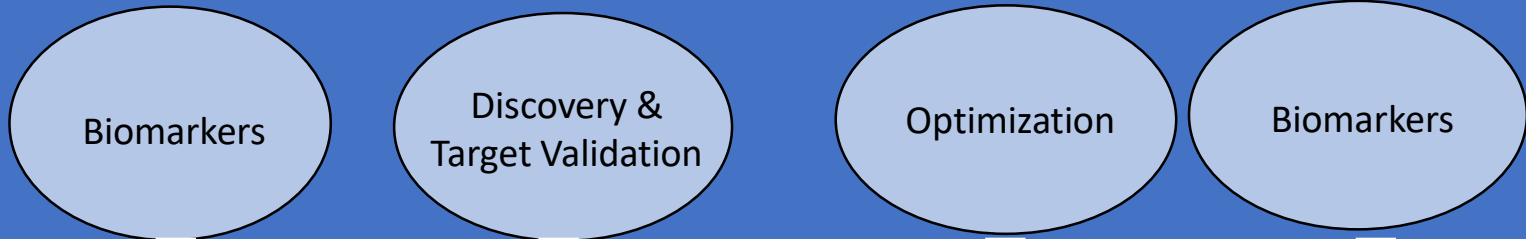


- Realign Programs for Analgesics Development:
- ✓ Focus on deliverables
  - ✓ Focus on scientific challenges
  - ✓ Minimize program complexity
  - ✓ Incentivize industry to reinvest



# Realigned HEAL Analgesic Development Program

## Current programs



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P  
P  
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C  
N  
E  
T

Small molecules  
Biologics

Lead compound

IND approved, phase 1 complete asset

## Proposed program

# HEAL Analgesic Development Program: Early Stage

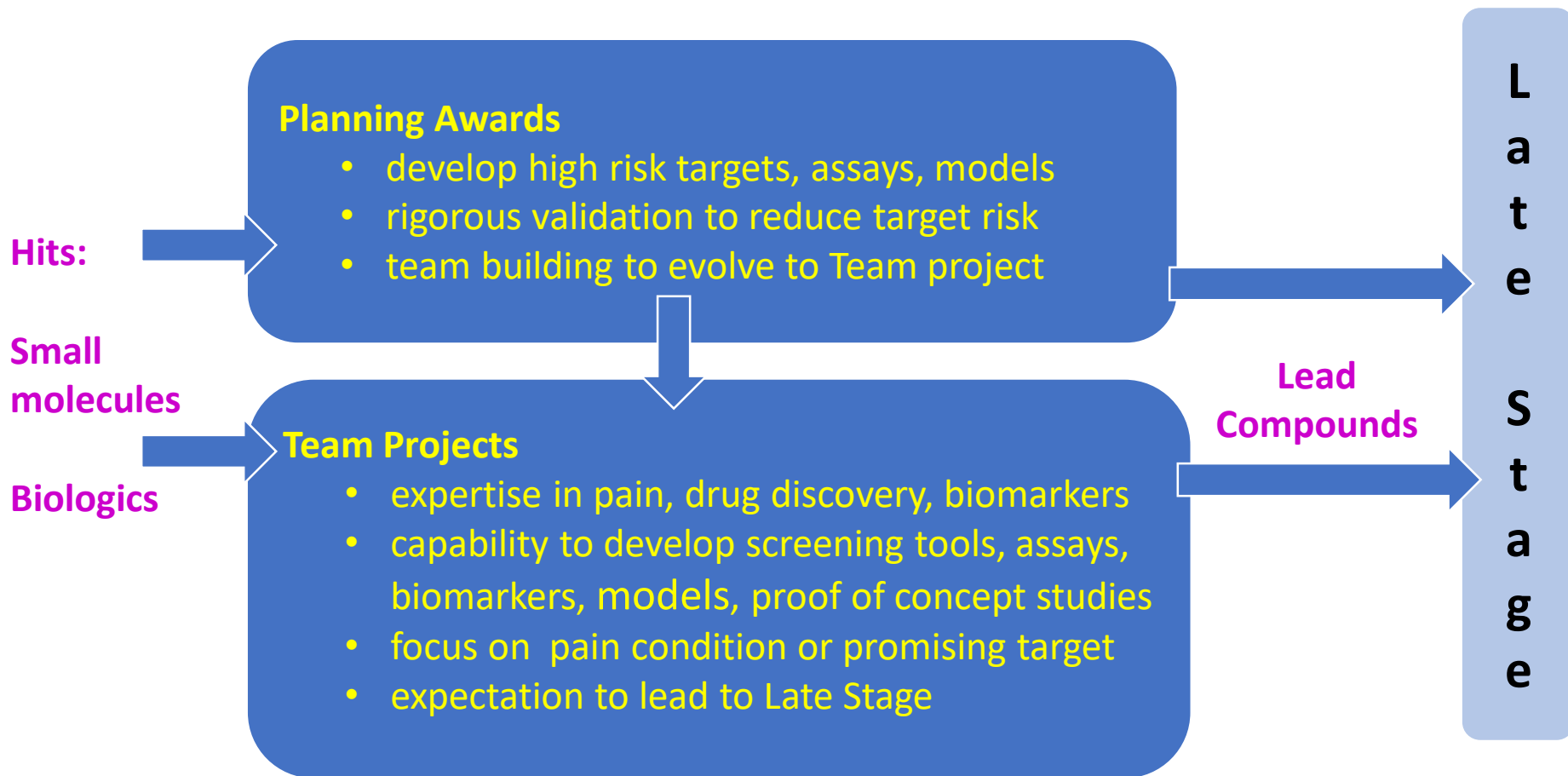


Planning Early Stage

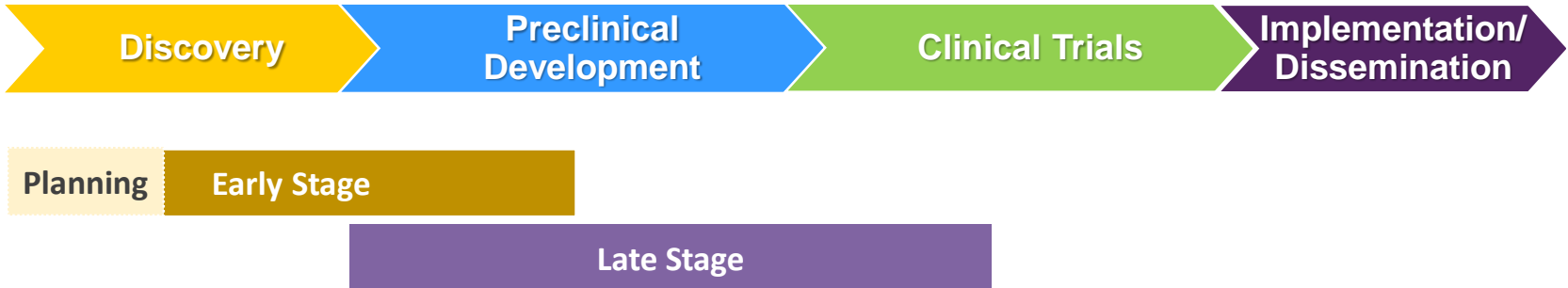
## End Goals and Milestones:

- ✓ Identify assays
- ✓ Validate models and testing tools
- ✓ Identify tools ready for optimization
- ✓ Identify a development path forward
- ✓ Seek partnerships
- ✓ **Ready for Late Stage**

# HEAL Analgesic Development Program: Early Stage



# HEAL Analgesic Development Program: Late Stage



## End Goals and Milestones:

- ✓ Identify clinical candidate
- ✓ File IND
- ✓ Complete phase I trial(s)
- ✓ Identify companion biomarker
- ✓ Seek partnerships
- ✓ **Ready for phase II clinical trial**

# HEAL Analgesic Development Program: Late Stage

## HEAL Pain Therapeutics Program

- Solicit targeted applications
- Confirm assays and studies necessary to initiate optimization or IND-enabling studies
- Conduct lead optimization to identify a development candidate
- Conduct IND-enabling studies and Phase I trials
- Collaborate with expert scientific consultants, CROs, PSPP, and NCATS
- Access to BPN and NCATS resources
- Incorporate biomarker development
- Focus = pain condition or promising target
- Expectation = lead to industry-funded or EPPIC NET/phase II trials

Lead  
Compounds

Phase II ready

E  
P  
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# HEAL Analgesic Development Program: Biomarkers

Early Team  
Projects

## Early stage biomarker development rolled into team projects

- Preclinical markers for validation, proof of concept
- Development and validation completed by team or subcontract

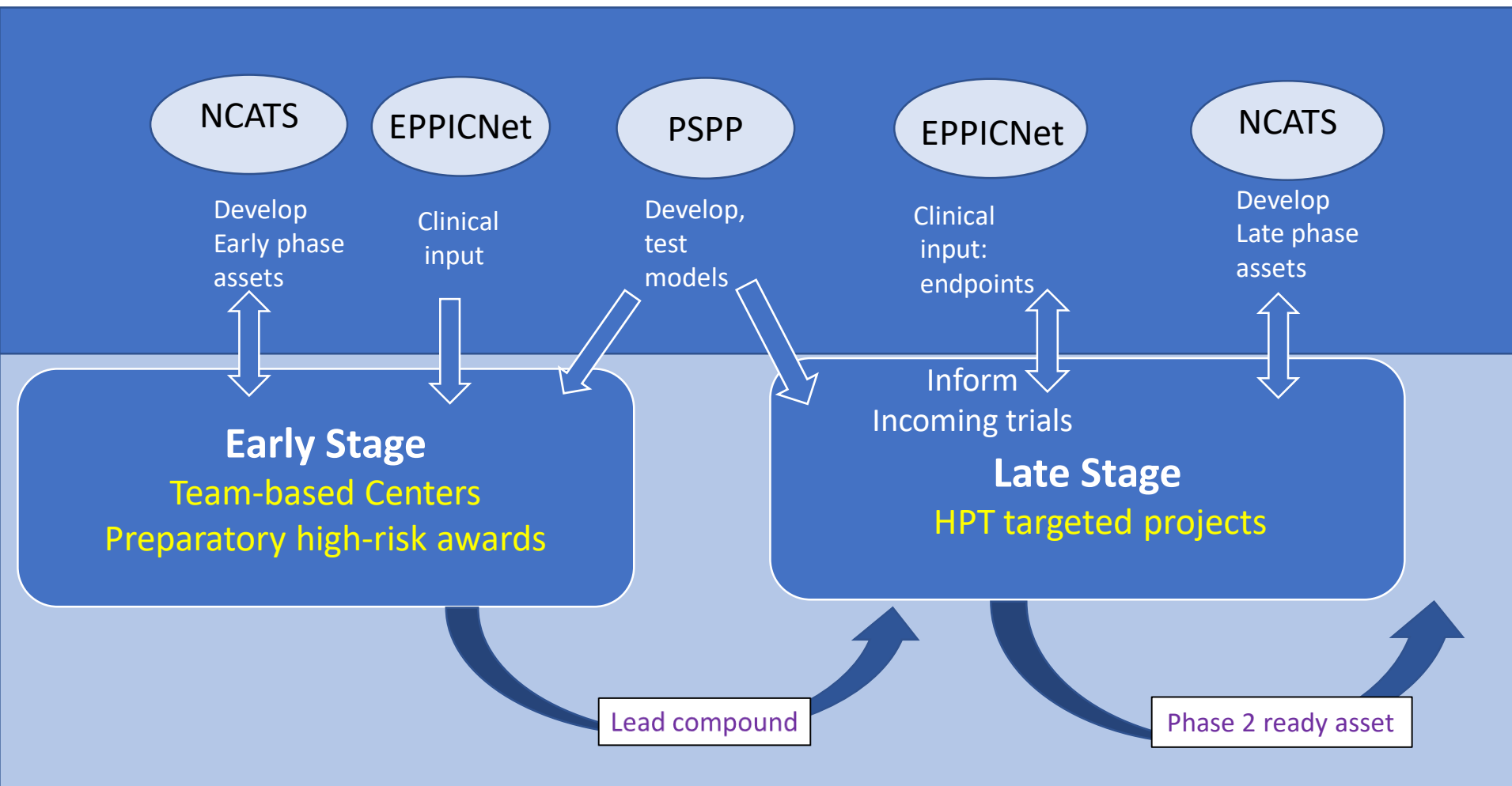
## Access to late stage biomarker development through contracts

- Biomarker development resources for late stage preclinical and early stage human studies

Late Phase  
Projects



# Leveraging other HEAL programs



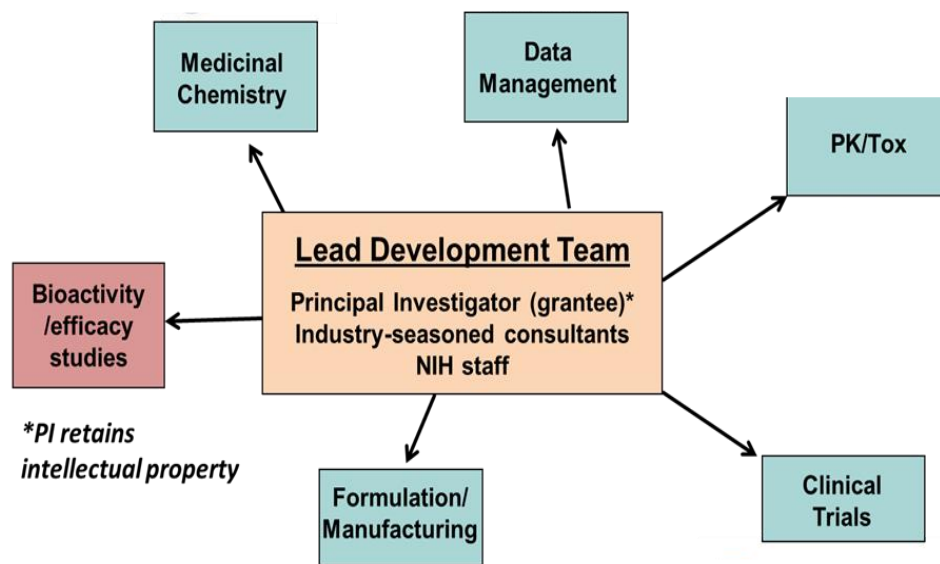
## Early Stage:

### Build Confidence and Get Ready for Preclinical Lead Optimization

- ✓ Study signaling pathway
- ✓ Identify multiple mechanisms that modulate the target
- ✓ Demonstrate target effects on the pathophysiology
- ✓ Demonstrate modulation of target effects the pathophysiology
- ✓ Develop and validate assays and tools specific for analgesic development

## Late Stage:

### Provide Resources Not Readily Available in Academia



**Closed Session**

**Adjourn**