



National Institute of
Neurological Disorders
and Stroke

OPEN STAGE

webinar series

Office of Programs
to Enhance the
Neuroscience Workforce

NIH HEAL Initiative Programs and Funding Opportunities at NINDS

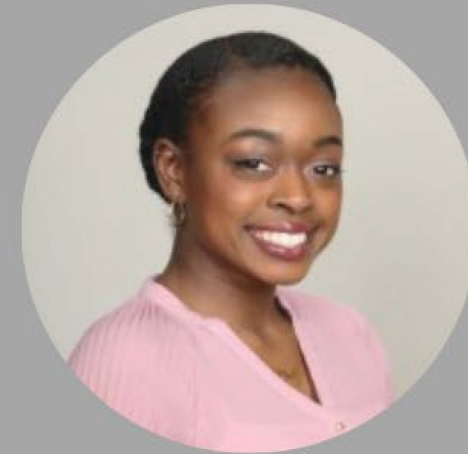
with invited speakers:



**JACOB
COVERSTONE, FACEHP**
PURPOSE NETWORK



**JOHN
PADERI, PHD**
IHP THERAPEUTICS



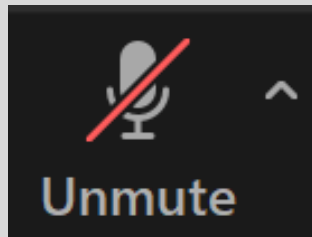
**KENNEDY
GOLDSBOROUGH, PHD**
EMORY UNIVERSITY

JUNE 25, 2024 | 1:00-2:30 PM ET

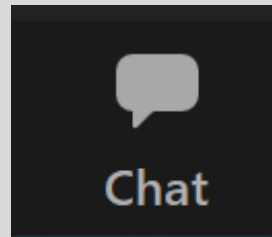
Register: <https://go.nih.gov/yA391Rm>

Meeting Reminders

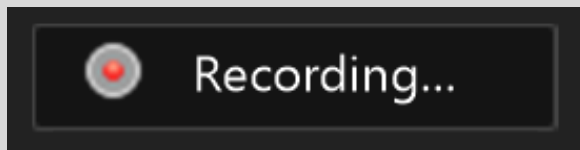
Attendees are muted



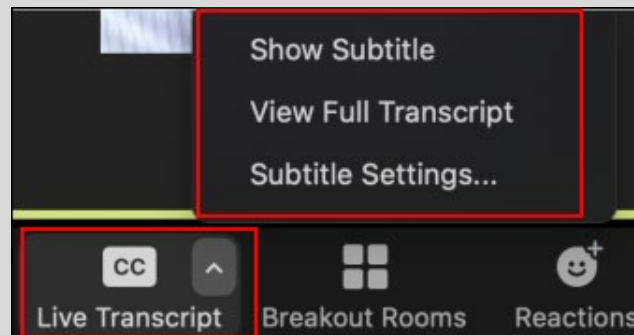
Submit questions in the chat



Presentation is being recorded



Live transcript available



Stay Connected



Twitter:
[@NINDSDiversity](https://twitter.com/NINDSDiversity)

Podcast:
ninds.buzzsprout.com



Listserv:
<http://go.usa.gov/xkpN6>

Email:
NINDSOPENStage@ninds.nih.gov



OPEN STAGE

Webinar Series

NINDS' Role in HEAL Initiative:

Enhancing the Workforce in Pain Research & Management

D.P. Mohapatra, PhD

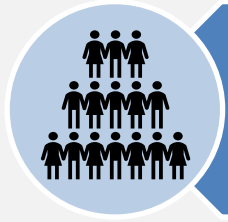
Program Director

Systems and Cognitive Neuroscience



National Institute of
Neurological Disorders
and Stroke

Pain – A Public Health Crisis



51.6 million
Americans have
CP (3+ months)



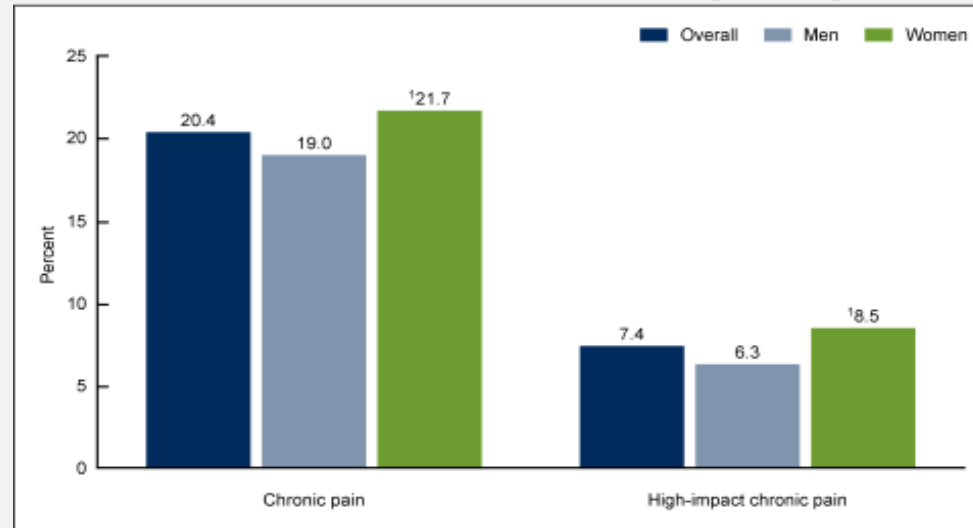
17.1 million
individuals have
high impact CP



\$635 billion*
annual costs

- Pain is the most common reason people seek medical care
- More new cases of chronic pain than for diabetes, depression, and high blood pressure
- More rural than urban dwellers report pain
 - 28% of rural & 16% of urban residents with chronic pain
 - 11% of rural & 6% of urban residents with high impact chronic pain

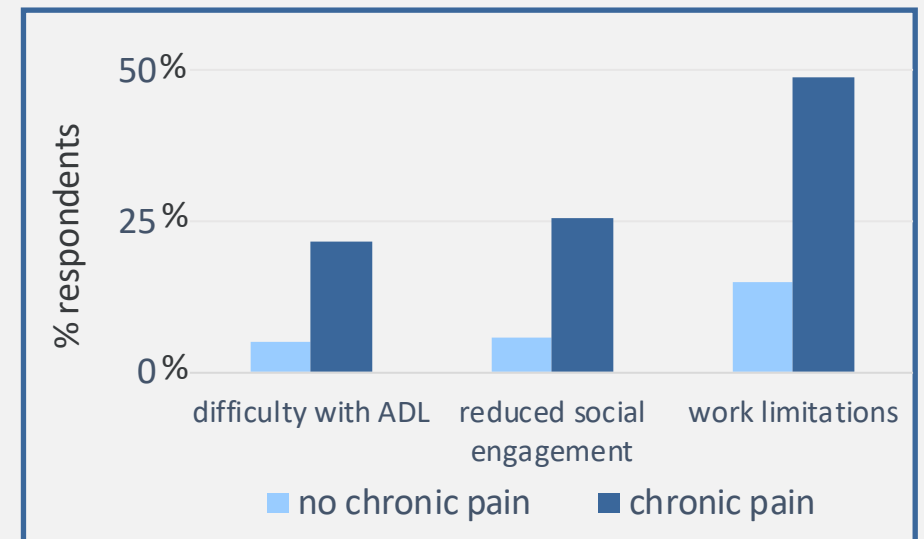
More women than men report pain



*high impact chronic pain = pain lasting more than 3 months that interferes with life (school, work, social life, etc.)
<https://www.cdc.gov/nchs/products/databriefs/db390.htm>

National Center for Health Statistics: NHIS 2019, *Pain and Therapy*, Vol. 10, pp: 287–314 (2021)

Chronic pain interferes with life



NINDS' Mission on Pain Research & Management

- NINDS is the lead institute for pain research at NIH and supports basic, translational, and clinical pain research to develop new and innovative advances in the pain field
- NINDS leads the Executive Committee of the NIH Pain Consortium, which includes 21 NIH ICOs
- NINDS, alongside NIAMS and NCCIH, leads the HEAL Initiative's efforts to enhance pain management

Pain conditions within NINDS' mission include, *but are not limited to:*

- Pain associated with neurological disorders - acute pain, chronic pain, headache, migraine, Alzheimer's disease and other dementias, Parkinson's disease, spinal cord injury, traumatic brain injury, complex regional pain syndromes, and post-stroke pain.
- Neuropathic pain (not associated with cancer treatments or diabetes), amputation pain, and neuromas.

NINDS supported research has led to:

- Discoveries of several ion channels, receptors, and neurotransmitters for pain
- Identification of ascending & descending pain modulation circuits in brain & spinal cord
- Two FDA-approved pain therapeutics
 - Ziconotide (Cav2.2 blocker)
 - CGRP antibodies
- In trial - several analgesic therapeutic agents and nerve stimulation/neuromodulation devices

The Nobel Prize in Physiology or Medicine 2021 was awarded jointly to Dr. David Julius and Dr. Ardem Patapoutian "for their discoveries of receptors for temperature and touch"



The Brain Prize 2021 winner Dr. Michael Moskowitz showed that a migraine attack is triggered when trigeminal nerve fibers release neuropeptides (e.g., CGRP) and proposed that blocking the action of released neuropeptides could be a new approach to treating migraine.



NIH Helping to End Addiction Long-term (HEAL) Initiative: Pain Research Priorities

Mission: HEAL pain research aims to reduce pain and the risk of opioid use disorder by developing safe and effective pain treatment and prevention strategies to improve quality of life for all people.

Enhance Pain Management



- Understand the biological underpinnings of chronic pain
- Accelerate the discovery and pre-clinical development of non-addictive pain treatments
- Advance new non-addictive pain treatments through the clinical pipeline
- Inform best practices for effective pain management while minimizing risk of addiction

HEAL has invested over \$1.25B on Pain and Cross-Cutting Research from 2018-2023

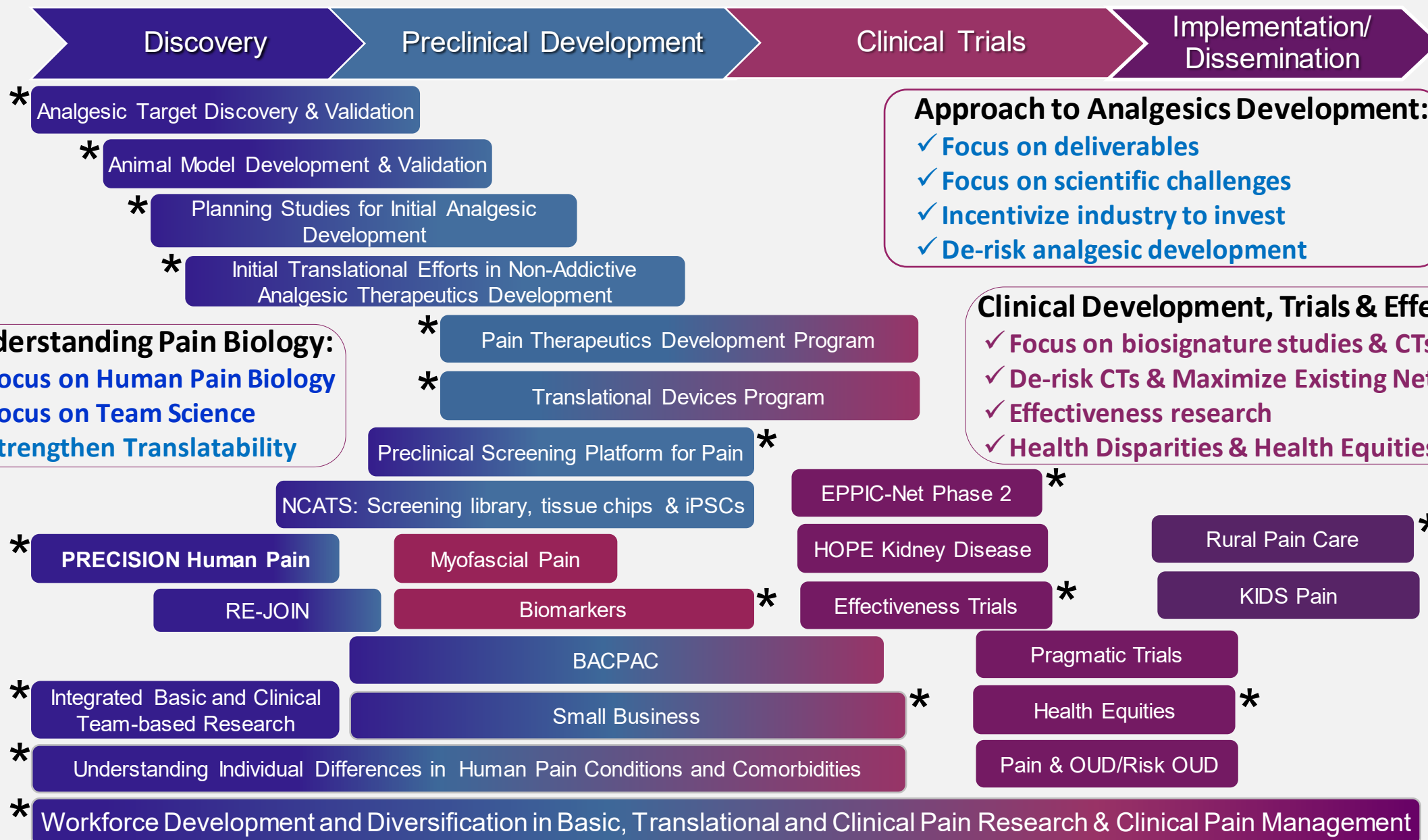
Discovery

Preclinical Development

Clinical Trials

Implementation/
Dissemination

HEAL Pain Program Overview



*NINDS as Lead IC

Incorporation of ‘Plans to Enhance Diverse Perspectives (PEDP)’ As Required Grant Application Component

- **What is a PEDP?** A summary of strategies to advance the scientific and technical merit of the proposed research & project through diversification and inclusivity.
 - To capitalize on innovative ideas, distinct perspectives, variety of experiences, training, backgrounds, and skillsets
- Definition of “diverse perspectives” is broad

WHO DOES the research

Investigators/trainees who are:

- historically underrepresented in the biomedical research workforce ([NOT-OD-20-031](#))
- from different scientific disciplines
- at varying career stages
- with varied skills, experience, and expertise

WHO PARTICIPATES in the research

- Recruit diverse participants for human studies.
- Use of specimens derived from varied ancestries.
- Any projects involving human participants or samples derived from humans should be collected in an ethically sound manner and consented appropriately

WHERE research is done

- Participation of researchers from diverse organizations and institutions (e.g., research intensive & active, undergraduate, minority-serving, community-based, etc.).

PEDP is assessed under “**all 5**” review criteria for grant applications
(Significance, Investigator, Innovation, Approach, and Environment)

Community Engagement

HEAL Community Partner Committee

- People with lived experience, advocates, community advisors, family members
- Input on key issues faced by individuals affected by pain and substance use
- Identify, refine, and prioritize engagement activities linked to HEAL science
- Supported by the NIH Patient Engagement Workgroup



Strategy

Survey the research community to learn and improve

Funded supplements to 14 awards

Contact: Linda Porter and Janelle Letzen

Health Equity in Pain Management

**FOCUS ON POPULATIONS
THAT EXPERIENCE HEALTH
DISPARITIES**

COMMUNITY ENGAGEMENT

**MULTI-LEVEL
INTERVENTIONS**

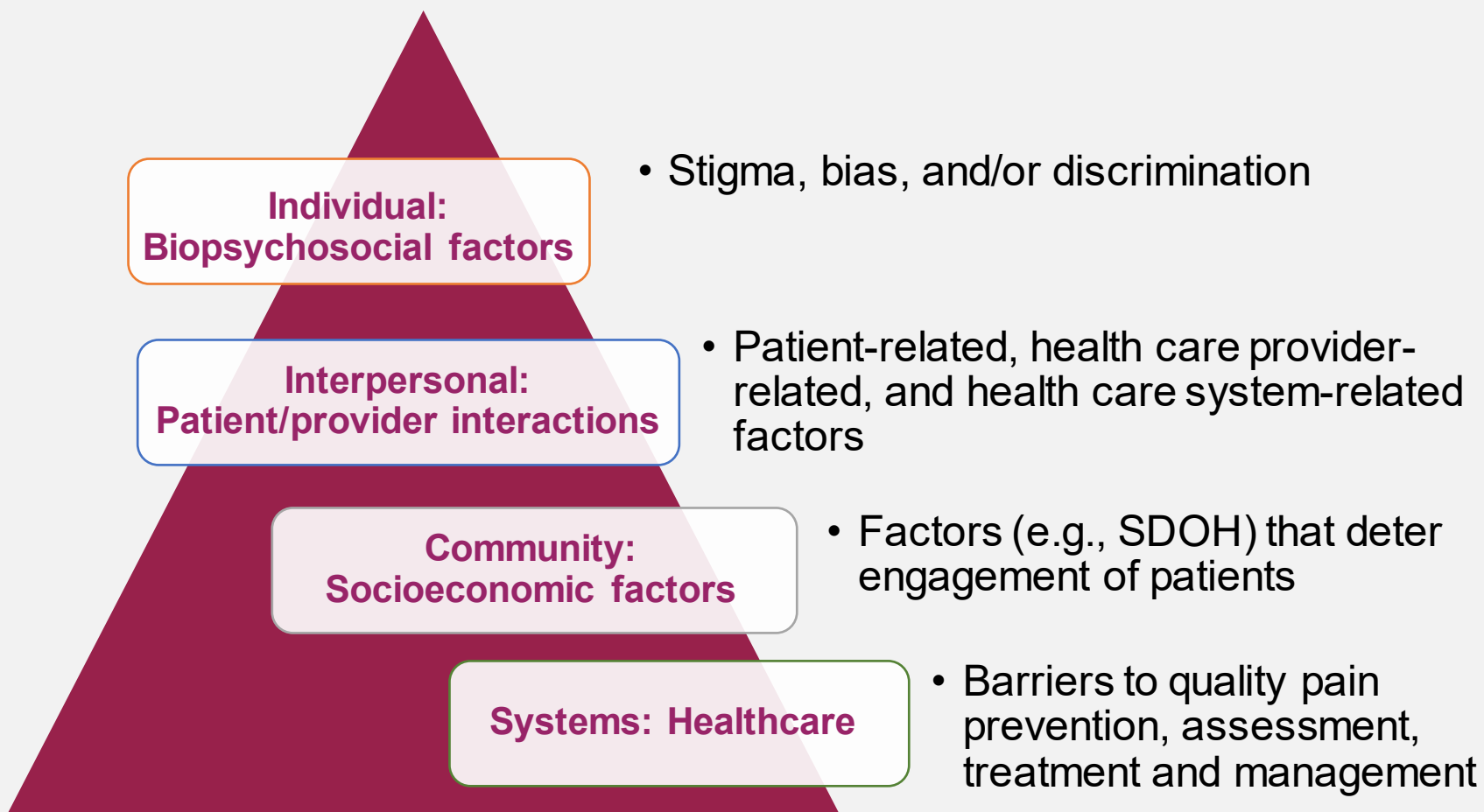
NIH-DESIGNATED POPULATIONS THAT EXPERIENCE HEALTH DISPARITIES

- Racial/Ethnic Minoritized Populations
 - Blacks/African Americans
 - Hispanics/Latinos
 - American Indians/Alaska Natives
 - Asian Americans
 - Native Hawaiians and other Pacific Islanders
- Socioeconomically disadvantaged populations
- Underserved rural populations
- Sexual and gender minorities



Program Lead/Contact:
Cheryse Sankar, Ph.D. (NINDS) - Cheryse.Sankar@nih.gov

Factors Contributing to Health Disparities in Pain



Program Lead/Contact:
Cheryse Sankar, Ph.D. (NINDS) -Cheryse.Sankar@nih.gov

OPEN Stage: HEAL Pain Workforce Efforts

Laura D. Wandner, PhD

Program Director

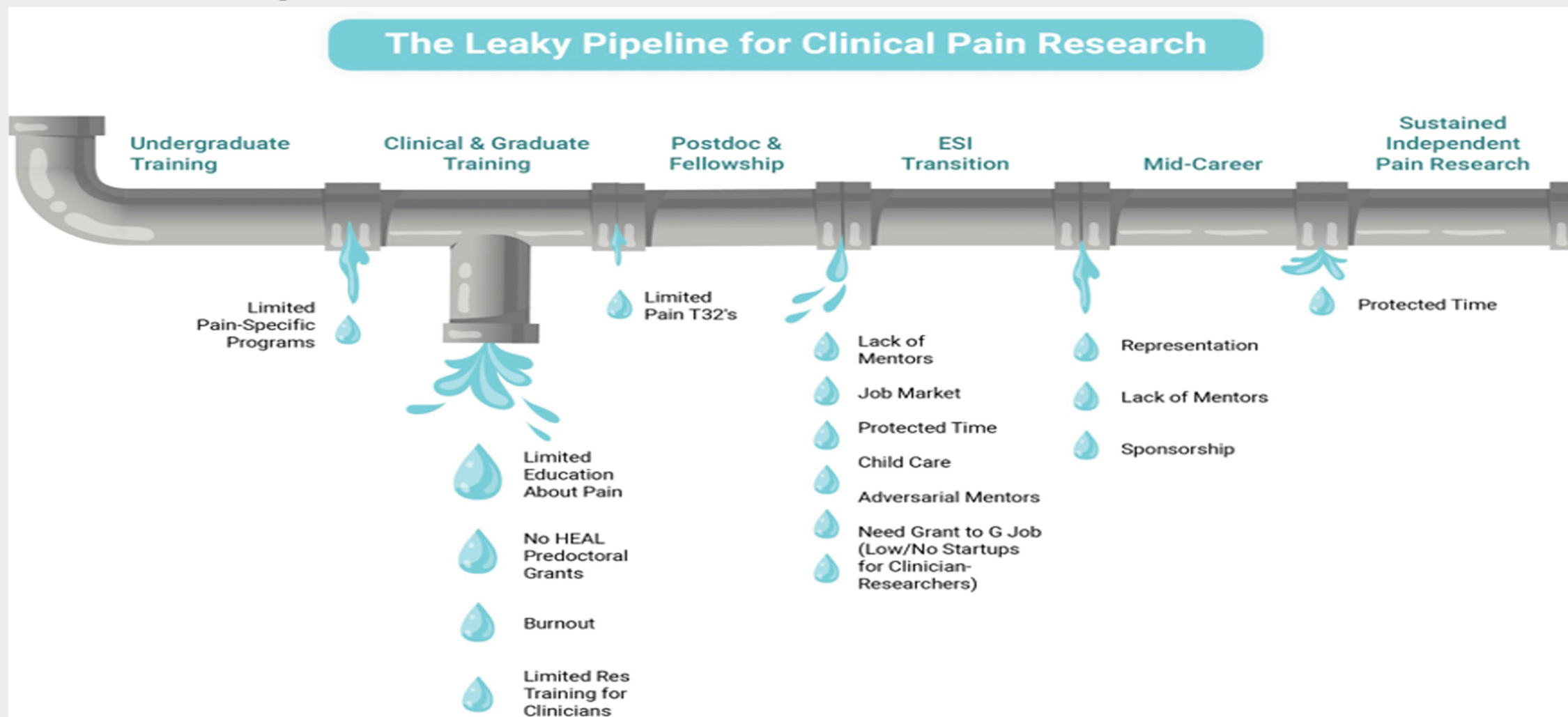
Office of Pain Policy and Planning

National Institute of Neurological Disorders and Stroke

How is HEAL Research Helping to Improve Pain Management



Enhancing the Pain Research Workforce



Enhancing the Pain Research Workforce

The Pain Crisis: All Hands on Deck

A formidable and rapidly evolving crisis demands a uniquely powerful response.

We must ensure an expanded, enduring, and diverse pool of highly trained scientists to perform high quality pain research in the face of a diminishing community and expanding research opportunities.





HEAL Pain Workforce Workgroup Mission

The HEAL pain workforce workgroup aims to cultivate a diverse and innovative pain research workforce and community capable of meeting the dynamic challenges of studying and treating people with lived pain experience and comorbid conditions from a biopsychosocial perspective. By recruiting, retaining, and educating basic, translational, and clinical pain researchers from diverse backgrounds, the NIH HEAL workforce workgroup aims to enrich the field with varied perspectives and skills. The goals of this group are to:

- 1) provide workforce opportunities for pain researchers across the spectrum of pain research (i.e., preclinical, translational, and clinical research) and at all career stages
- 2) attract and retain talented pain researchers from diverse professional backgrounds, sociodemographic backgrounds, regions on the country, and across the spectrum of pain research to build and retain a pipeline of pain researchers
- 3) attract researchers from non-traditional pain research backgrounds to expand the pain research field and enhance the innovation of pain research



HEAL Pain Workforce Workgroup

Mission to enhancing pain education and/or continuing education at all career stages

- 5) support the professional development of pain researchers at all career stages through structured training and mentorship programs
- 6) foster a collaborative and supportive community among pain researchers that encourages innovation and shared learning;
- 7) promote an inclusive culture within the pain research workforce that values and utilizes the contributions of researchers from all backgrounds

By achieving these goals, the NIH HEAL pain workforce workgroup will enhance the capacity of the pain research community to address the critical challenges of improving pain management care for those people with pain, identifying and developing new and effective non-opioid treatments to manage pain, and ultimately improving patient care and outcomes.

Workforce Co-Chairs: Laura Wandner (NINDS) and Steven Pittenger (NCATS)

HEAL Efforts to Enhance the Pain Workforce (FY21-FY24)



- ❖ 40 awards in total
- ❖ 14 states funded within the pain workforce initiative
- ❖ Grants have been awarded to investigators at all career stages from postdoctoral trainees through senior investigators

NIH Workforce Efforts

Problem: Need to diversify the pain research workforce

- *Solution: Supplemental funding for HEAL awardees to recruit a diverse individual into their project.*

- Diversity Supplements to Encourage Eligible NIH HEAL Initiative Awardees to Apply for Supplements to Promote Diversity in Health-Related Research

- Please monitor the HEAL website for the funding opportunity.

- *Solution: Supports small-scale research projects at educational institutions that provide baccalaureate or advanced degrees for a significant number of the Nation's research scientists but have not been major recipients of NIH support.*

- R15 award - Promoting Diversity in the Pain Workforce

- Please monitor the HEAL website for the funding opportunity.



Approved
Concept



Approved
Concept

NIH Workforce Efforts

Problem: Not enough early-career researchers to replace those leaving the field

- *Solution:* Supplements to train novice researchers and investigators new to pain research

- HEAL training supplement

- Please contact a HEAL investigator to ask to submit a supplement as part of their HEAL award.

- *Solution:* Released a national scholar grant where researchers will receive enhanced mentorship for 2-3 years. The aim is to fund researchers who are not yet ready for an independent NIH grant. Scholar cohorts are meant to be multidisciplinary and diverse.

- HEAL National K12

Approved
Concept

Scholar
applications
due winter
2025

Program Contacts: Rebecca Hommer – rebecca.hommer@nih.gov (NINDS)

Laura Wandner – laura.wandner@nih.gov (NINDS)



NIH Workforce Efforts

Problem: Not enough early-career researchers to replace those leaving the field

Postdoc applications due Fall 2024/Winter 2025

- *Solution:* HEAL Initiative Partnerships to Advance Interdisciplinary (PAIN) Training in Clinical Pain Research: The HEAL Pain Cohort Program (T90/R90 Independent Clinical Trial Not allowed)
 - T90/R90 postdoctoral centers have been funded. Check the HEAL website to see if there is a postdoctoral training program you would like to apply to. Each center will be sending out a call for applications in the fall/winter of 2025.
- *Solution:* HEAL Initiative PainCare Clinical Training Program (PCTP)
 - HEAL plans to fund career development awards (K23s and K08s) for those people who are clinical pain researchers.
 - Please monitor the HEAL website for the funding opportunity.

Approved Concept



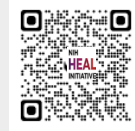
K99/R00 Advanced Postdoctoral-to-Independent Career Transition Awards in Pain and Substance Use Disorder Research



Standard Awards:

K99/R00 Independent Clinical Trial Not Allowed [RFA-NS-22-022](#)

Independent Basic Experimental Studies with Humans Required [RFA-NS-22-023](#)



Goal: to support a cohort of new and well-trained independent investigators conducting Pain and/or SUD research, in order to increase the independent investigator workforce in research areas supported by the NIH HEAL Initiative

Diversity:

K99/R00 Independent Basic Experimental Studies with Humans Required [RFA-NS-22-024](#)

K99/R00 Independent Clinical Trial Not Allowed [RFA-NS-22-025](#)



Goal: to support a cohort of new and well-trained, independent investigators from **diverse** backgrounds (e.g. see [NOT-OD-20-031](#), Notice of NIH's Interest in Diversity) conducting Pain and/or SUD research, in order to **promote a diverse pool of available independent investigators** working in research areas supported by the NIH



HEAL Initiative

Program Leads:

DP Mohapatra (NINDS) DP.Mohapatra@nih.gov

Elizabeth Sypek (NINDS) Elizabeth.Sypek@nih.gov

Multiple Receipt Dates through 2025

NIH Workforce Efforts

Problem: Need to increase contact with mentors, increase opportunities to collaborate with pain researchers across the spectrum of pain research (e.g., preclinical, translational, and clinical pain research), and centralize resources and trainings.

- **Solution:** Establishing a network to increase mentorship and career development throughout the year; organize an annual meeting; facilitate communication across the spectrum of pain research
 - HEAL coordinating center R24, also called the PURPOSE network



Contact: Laura Wandner – laura.wandner@nih.gov (NINDS)



- **PURPOSE** stands for “Positively Uniting Researchers of Pain to Opine, Synthesize, & Engage”
- *Goal of the network:* Connect pain researchers across the continuum of pain research, from all disciplines and at all career stages.
 - Establish and run a digital platform
 - Organize and run an annual meeting

NIH Workforce Efforts

Problem: Researchers have questions about grant mechanisms, open funding announcements, and tips and tricks about how to write a strong grant.

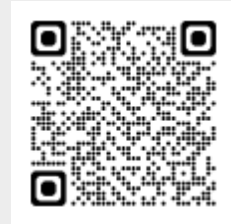
- *Solution: Ran a monthly webinar series to answer PIs questions about grant mechanisms*
 - NIH Pain Consortium Grant Mechanism Webinar Series
- *Solution: The PURPOSE Network has established a monthly “Get to know your IC webinar”*
 - Program Officers from the NIH Institutes discuss the type of pain reach they fund and answer any institute specific questions.



Contact: Laura Wandner – laura.wandner@nih.gov (NINDS)

Relevant HEAL Workforce Websites

- **HEAL Funding Announcement Website**
 - Please monitor the HEAL website for open workforce funding announcements
- **HEAL Workforce Website**
 - Please monitor the HEAL workforce website to see the current and past workforce initiatives
- **University of Michigan HEAL K12 website**
 - Please monitor the HEAL K12 website to check when the next application window will open. There will be a webinar that explains the application processes.
- **PURPOSE website**
 - If you are interested in pain research, please consider joining the PURPOSE network.



NIH Research Training and Career Development Resources

- Overview of all NIH Training Programs – <https://researchtraining.nih.gov/career-path>
- Individual Fellowships - <https://researchtraining.nih.gov/programs/fellowships>
- NIH Institutes Training Program Matrix – (Overview of all NIH Institutes and Centers with research training programs) - <https://researchtraining.nih.gov/institute>
- Other Training Related Programs - <https://researchtraining.nih.gov/programs/other-training-related>
- How to Apply-Application Guide (Preparing, Writing and Submitting Applications) – <https://grants.nih.gov/grants/how-to-apply-application-guide.html#data#>
- Information for Applicants and Awardees (FAQ's, Grant-writing tips, forms) – <https://researchtraining.nih.gov/resources/information>
- How Trainees Get Accounts in eRA Commons - <https://youtu.be/BLgxNNaphKQ>
- Frequently Asked Questions about Research Training and Career Development - <https://researchtraining.nih.gov/resources/faq>
- Clinical Trial Requirements for Grants and Contracts - <https://grants.nih.gov/policy/clinical-trials.htm>
- NIH Clinical Trial Policies - <https://grants.nih.gov/policy/clinical-trials/training-resources.htm>
- NIH Peer Review YouTube Play List (Includes NIH processes, a Mock Study Section, and tips for success): <https://www.youtube.com/playlist?list=PLOEUwSnjvqBKWjASuPFjwWPYKXGjsC4wj>
- NIH Grants YouTube Channel: <https://www.youtube.com/user/NIHgrants/featured>
- NIH Podcasts
 - “All about grants” run by the Office of Extramural Research
 - “NINDS building up the Nerve” run by the National Institutes of Neurological Disorders and Stroke
- Subscribe to “Open Mike” Blog - (Dr. Michael Lauer’s blog - NIH's Deputy Director for Extramural Research, serving as the principal scientific leader and advisor to the NIH Director on the NIH extramural research program). <https://nexus.od.nih.gov/all/category/blog/open-mike/>

Shape HEAL Research Priorities

The NIH HEAL Initiative wants to hear from you!

HEAL is seeking public input to help shape strategic research priorities that will guide the initiative's future efforts to find scientific solutions to the public health crises of overdose, opioid use disorder, and chronic pain.

Submit feedback by **July 31, 2024**, to HEALquestion@od.nih.gov with "HEAL RFI" in the subject line.

go.nih.gov/mcoqY3J



Invited Speaker



Jacob Coverstone, FACEhp
PURPOSE network

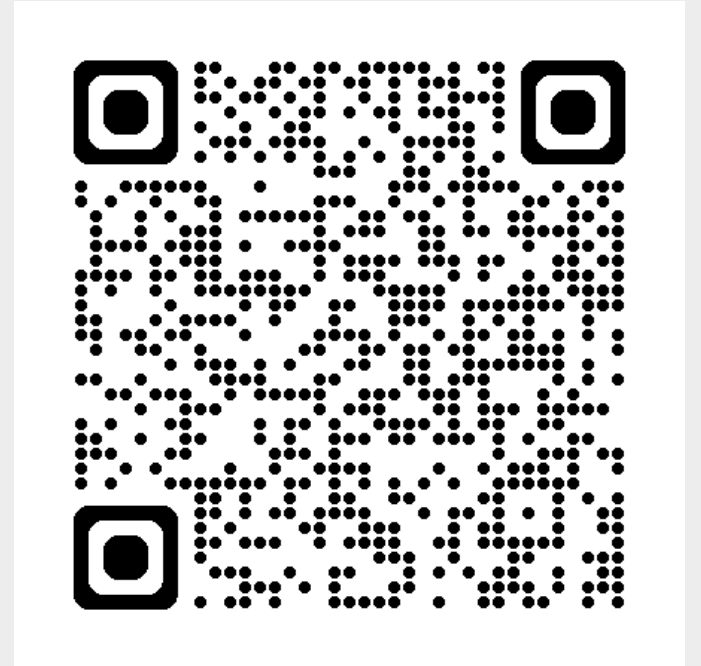
PURPOSE Network

<https://painresearchers.com/>

An NIH-funded platform with tools for collaboration, funding information, and dissemination of research.

Breaking-down silos

Empowering researchers with tools, training, and resources



PURPOSE Network

<https://painresearchers.com/>

An NIH-funded platform with tools for collaboration, funding information, and dissemination of research.

- Funding Opportunities
- Researcher Directory
- Organization Directory
- Community Groups
- Event Aggregator
- Collaboration Space
- Media Center
- Webinars



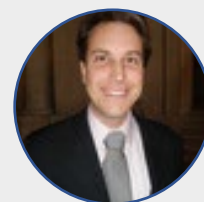
PURPOSE Annual Meeting

Free to all

- Feedback from NIH program officers
- Structured networking with peers & mentors
- Research skill development
- Leadership training
- Tailored feedback on proposals & presentations
- Engagement with PWLE



Honestly, this was one of the best meetings I have ever been. Focused, organized and fun. Thank you!



Luiz Fernando Ferrari, DDS, MS, PhD
Assistant Professor, Taylor Lab,
Department of Anesthesiology, School
of Medicine - University of Utah

Collaborate & Communicate

Tools for admins

Discussion groups & forums

Researcher database

Mobile app

The screenshot displays the RE-JOIN website interface. At the top, there is a large group photo of diverse individuals, with a 'Manage group' button overlaid. Below the photo is the 'RE-JOIN' header, which includes a search bar and a '+93 Join' button. A navigation menu lists: Homepage, About, RE-JOIN DCG, Calendar, Platforms and How-To Guides, Publications, Updates, Members, Working Groups and Committees, Forum, and 2024 RE-JOIN Consortium Annual Meeting. The main content area is titled 'RE-JOIN COMMITTEES' and features two sections: 'EXECUTIVE COMMITTEE CALENDAR' with an image of people in a meeting, and 'STEERING COMMITTEE CALENDAR' with an illustration of a meeting. Below this is the 'RE-JOIN WORKING GROUPS' section, which includes three categories: 'KNEE WG' with an image of a knee joint, 'TMJ WG' with an image of a human head and neck, and 'OMICS WG' with an image of a DNA double helix. At the bottom, there are three links: 'Imaging / Tracing WG', 'CCF Task Force Calendar', and 'PUBLICATION WG BOX FILE'.

PURPOSE Network

<https://painresearchers.com/>

Training, teaching & empowering

Accelerating collaborative team science by centralizing resources, and empowering researchers with tools and information



OPEN Stage: HEAL Pain Therapeutics Development Program (PTDP)

Mary Ann Pelleymounter, PhD – Program Director

Matthew Rice, PhD – Presenter / Scientific Program Manager

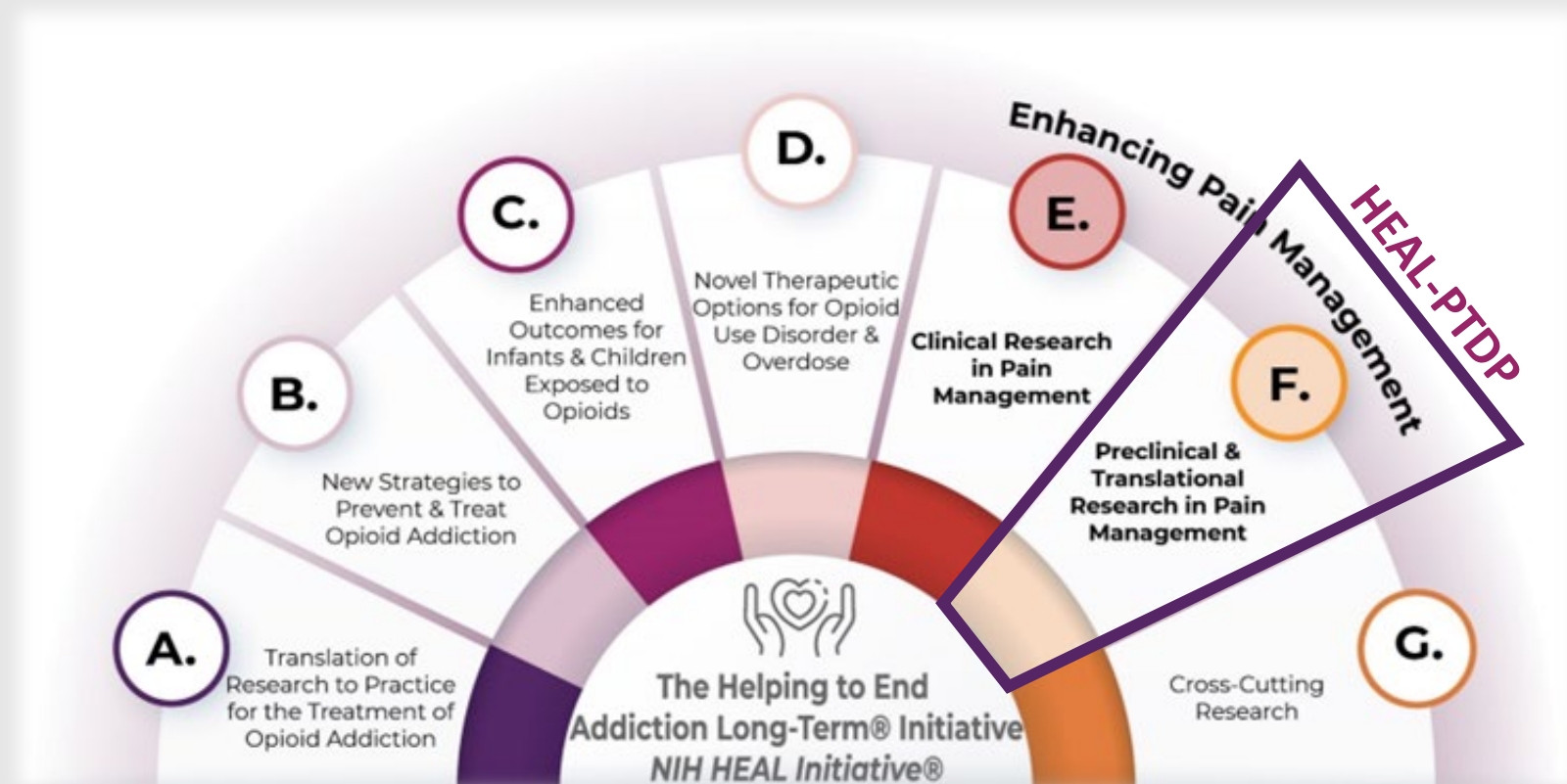
Division of Translational Research (DTR)

National Institute of Neurological Disorders and Stroke (NINDS)

Addressing the Unmet Need for Pain Therapeutics: The Helping to End Addiction Long-term Initiative (NIH HEAL Initiative)

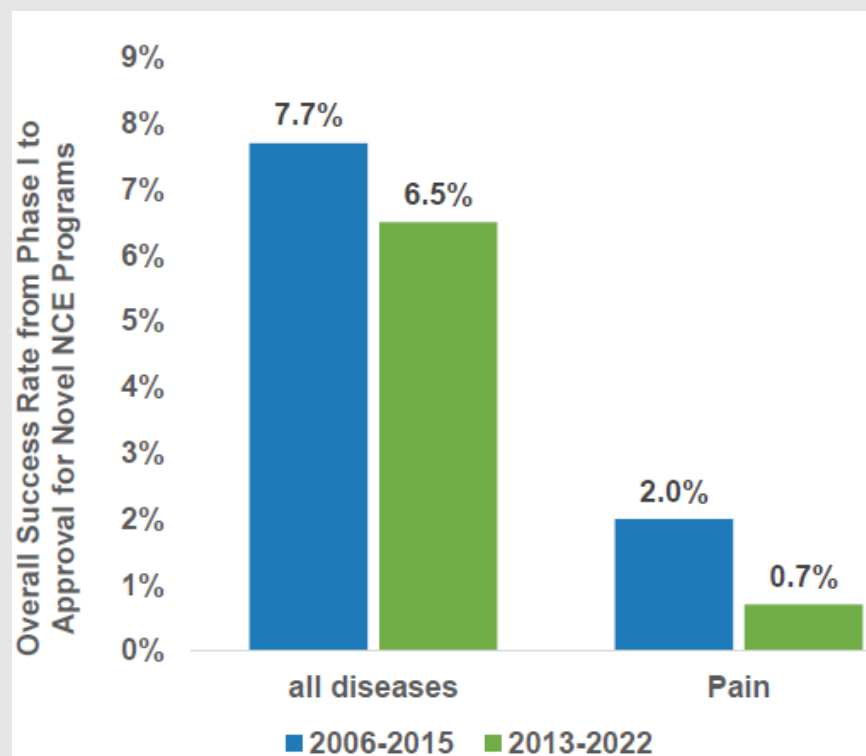
Approach: Enhance Pain Management and Improve Prevention and Treatment of Opioid Misuse and Addiction

- Understand the biological underpinnings of chronic pain
- Accelerate the discovery and pre-clinical development of non-addictive pain treatments
- Advance new non-addictive pain treatments through the clinical pipeline
- Inform best practices for effective pain management while minimizing risk of addiction

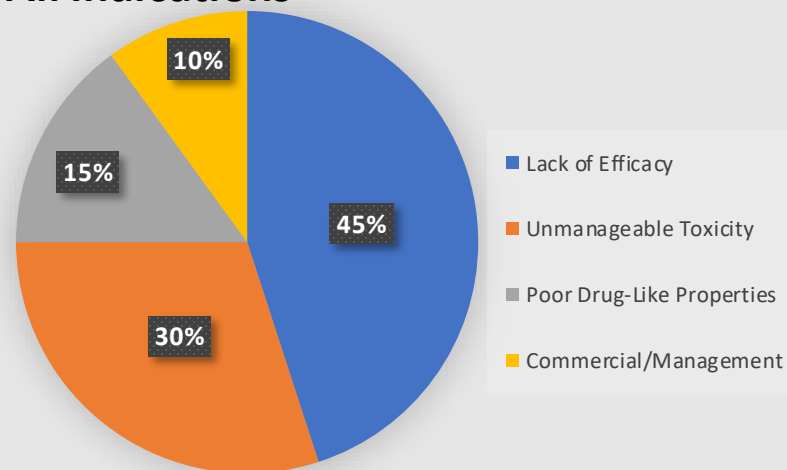


Low Clinical Success Rates in Pain Indications: Reasons for Failures

Clinical Success Rates for Pain Therapeutics Relative to All Other Disease Indications



Reasons for Clinical Failures: All Indications



Reflected in general shrinkage of pain clinical pipeline

Reasons for Clinical Failures: Pain Indications

- ❖ Poor predictive validity of preclinical pain models
- ❖ Heterogeneous patient population within pain conditions
- ❖ Lack of target engagement, predictive or patient selection biomarkers
- ❖ Large placebo effects in clinical trials
- ❖ Therapeutic index challenges

CLINICAL PIPELINE FOR PAIN BY DRUG TYPE, 2017 VS 2022

Innovation Type	2017	2022	% Change
Reformulated/Repurposed	95	49	-48%
Novel Chemical Entity	125	75	-40%
Total	220	124	-44%

HEAL Pain Therapeutics Development Program (PTDP)

Hit/Lead Optimization

Lead Selection/Lead Characterization

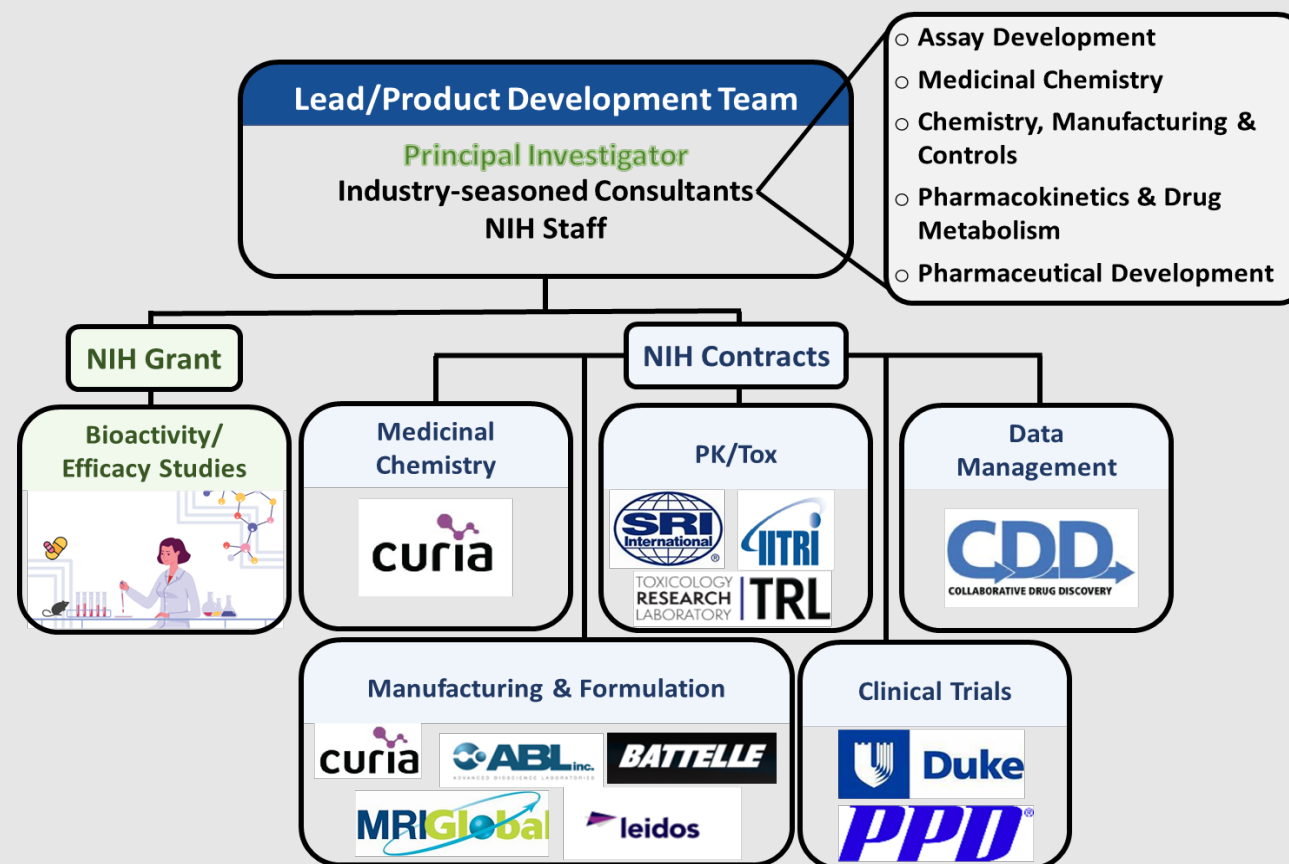
IND Enabling Studies

Phase I Clinical Trial

Virtual Pharma Approach Featuring Industry-Experienced Consultants and NIH Contract Resources

- ❖ Supports biologic, small molecule, and combination product therapeutic development.
- ❖ Grants are milestone-driven
- ❖ **PI team's Intellectual Property Retained by PI's Institution**

- ❖ First grants awarded in 2019
- ❖ 17 Awards made to date
 - 4 Projects in Hit/Lead Optimization
 - 6 Projects in Lead Selection/Characterization
 - 3 Projects in IND Enabling/IND Submission
 - 3 Projects Discontinued
 - 1 Project In-Licensed to Biopharma



Features of the HEAL-PTDP Grant: Funding Opportunity RFA-NS-24-019

Entry Criteria

Discovery

- ✓ A rigorous biological rationale for the intended approach
- ✓ A promising small molecule or biologic starting point for optimization
- ✓ Scientifically sound assays to optimize and test the agent

Development

- ✓ Candidate therapeutic is Identified
- ✓ Strong data package linking modulation of therapeutic target by candidate therapeutic to disease modification
- ✓ Biological activity and ADMET properties of candidate therapeutic are appropriate for intended use

Support & End Goals

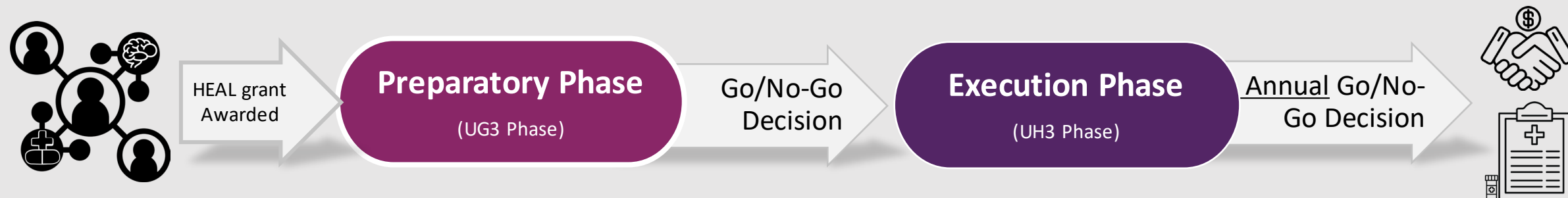
Support

- ✓ Hit to Lead activities
- ✓ Lead optimization, selection, and characterization
- ✓ Biomarker optimization and PK/PD development
- ✓ IND-enabling studies and Phase I trials

End Goals

- ✓ Identify and fully characterize a lead candidate
- ✓ Identify target engagement biomarker if possible
- ✓ Complete IND enabling studies / File IND
- ✓ Seek partnerships
- ✓ Complete Phase I trial(s)

Two Phase Grant Mechanism: Typical Activities



Preparatory (UG3) Phase

- Optimization using potency and efficacy screens (Discovery)
- Preliminary efficacy and toxicology testing in appropriate animal models for pain (Discovery and Development)
- Characterization and testing for *in vitro* ADME (absorption, distribution, metabolism, and excretion) (Discovery and Development)
- Initial optimization of pharmacodynamic/target engagement biomarkers associated with the therapeutic target or pathway (Discovery and Development)

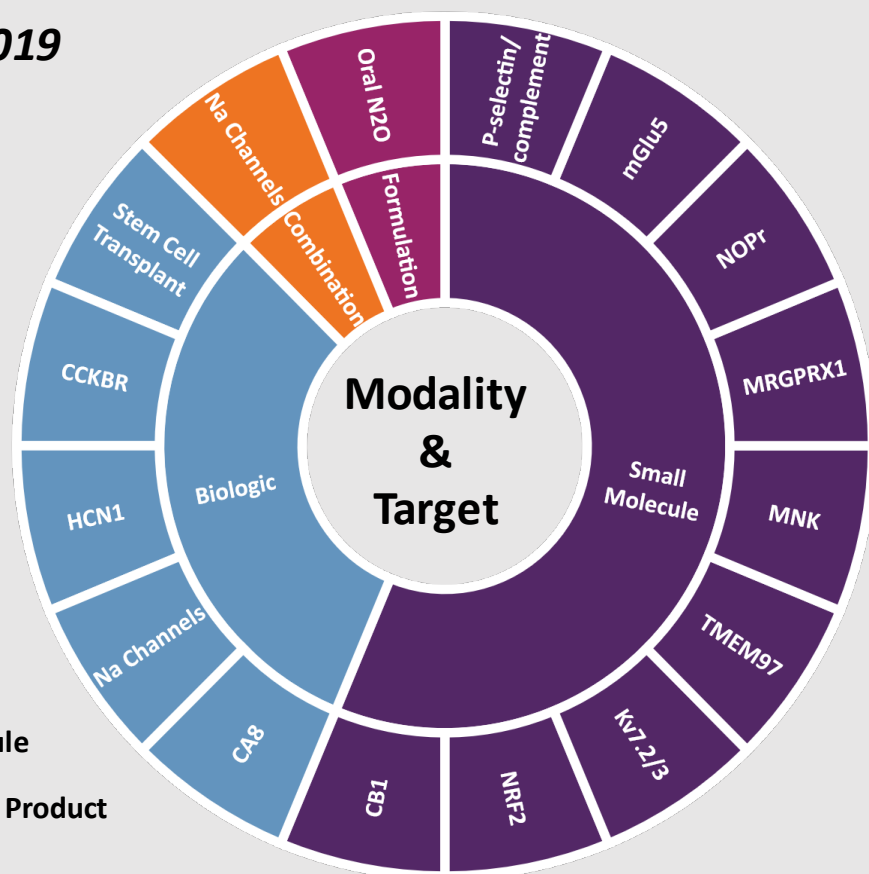
Execution (UH3) Phase

- Any further optimization activities as listed on the left, if needed
- Pharmacokinetics (PK), biodistribution, gene expression, tumorigenicity, and immunogenicity
- Cell bank development and testing
- Formulation and manufacturing for toxicology and human clinical studies
- IND-enabling characterization of the clinical candidate
- Non-GLP and GLP toxicology studies
- IND Submission and Phase I Clinical Testing

Opportunities with the NIH HEAL Pain Therapeutics Development Program (PTDP)

Funded Research

RFA-NS-24-019



NINDS Career Opportunities



Subscribe to our Job Announcements listserv

To stay up to date with all the exciting career opportunities with NINDS, please subscribe to our Job Announcements listserv. Email listserv@list.nih.gov and include this language in the body of your email: **Subscribe NINDS-job-announcements (enter your name).**

Health Program Specialist (HPS)

- Qualifications:
 - Demonstrate expertise, experience and/or educational background in neuroscience or related discipline.
 - A PhD and postdoctoral work is not required but is preferred.
 - Experience in neuroscience and pain therapeutics is a plus but not required.

Questions/Contact Information

Mary Ann Pellemounter PhD, Program Lead: mary.pellemounter@nih.gov

Charles Cywin PhD, Director of Small Molecule Neurotherapeutic Development: charles.cywin@nih.gov

Rakonda Medley, Operations Coordinator: rakonda.medley@nih.gov

IC Representatives

Houmam Araj, PhD NEI
Melissa Ghim, PhD NIDCR
Asif Rizwan, PhD NHLBI
Rachel Altshuler, PhD NCI
Mark Egli, PhD NIAAA
Dana K Andersen, MD NIDDK

Sam Ananthan, PhD NIDA
Hye-Sook Kim, PhD NCCIH
Charles Washabaugh, PhD NIAMS
Helena H Ahn, PhD NICHD
Devon Oskvig, PhD NIA
Edward Andrew Townsend, PhD NIDA

Scientific Program Managers

Mohamed Hachicha, PhD
Pascal Laeng, PhD
Mary Ann Pellemounter, PhD
Oreisa O'Neil-Mathurin, MPH
Shamsi Raeissi, PhD
Ranga Rangarajan, PhD
Matthew Rice, PhD

[Visit PTDP Online!](#)



[Watch our Previous Webinar](#)



2024 and 2025 Receipt Dates (same date for re-submission):
Sept. 24th, 2024 | Jan. 24th, 2025 | May 23rd, 2025 | Sept. 24th, 2025

Invited Speakers



John Paderi, PhD
IHP Therapeutics



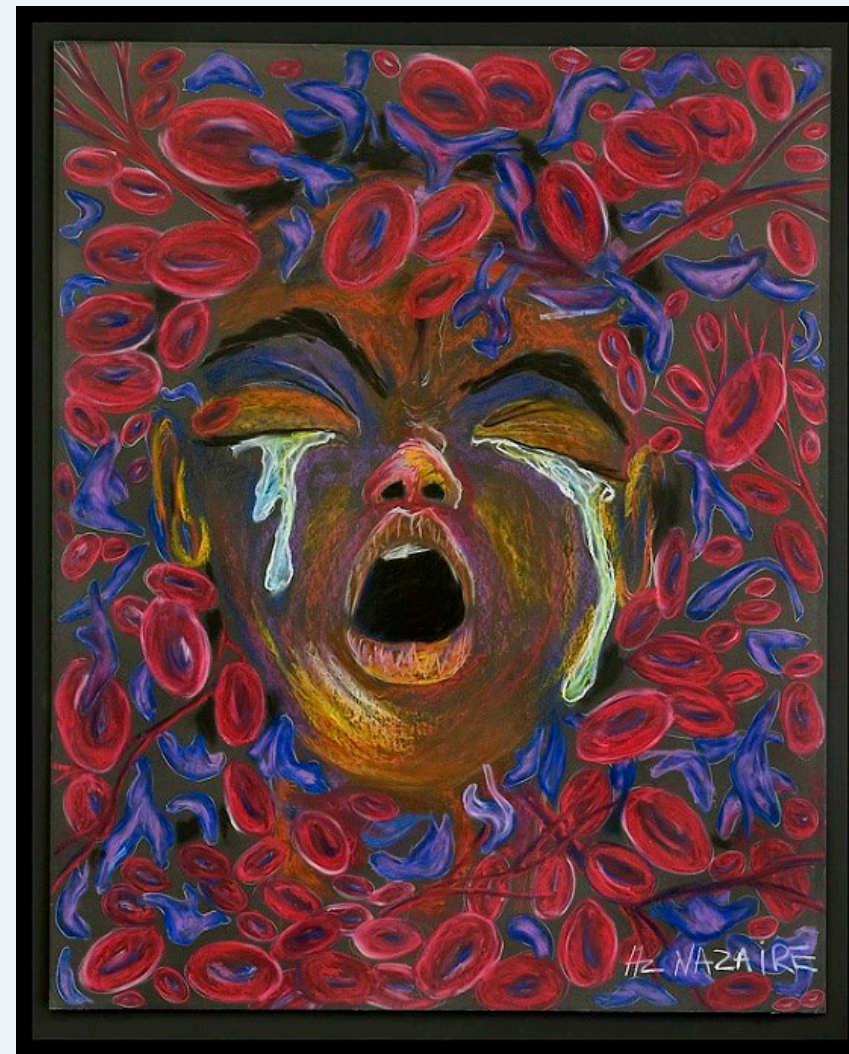
Kennedy Goldsborough, PhD
Emory University



IHP THERAPEUTICS

First home-based rescue
therapeutic for treatment of
acute vaso-occlusive episodes in
sickle cell disease

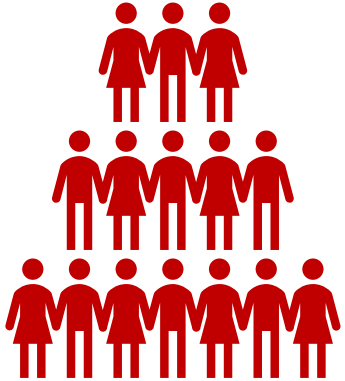
**NIH Open Stage Seminar
June 25, 2024**



Hertz Nazaire - <https://everylifefoundation.org/portfolio-item/te-n-rede-fined/>

Sickle cell pain associated is often described as “worse than childbirth” or “shards of glass flowing in my body”

Sickle Cell Disease (SCD) is a large and growing problem with **major patient impact**



- **7.74M people** WW suffer from SCD (100,000 in the U.S.)
- **376,000 SCD deaths annually**
- Primarily affects people of color



- **“Pain crisis”** or vaso-occlusive episodes (VOE) are the hallmark of SCD
- Described as **“shards of glass flowing in my body”**
- Complication result in **>20-year reduction** in life expectancy
- Caused by “sticky” blood cells that block flow to organs and tissues

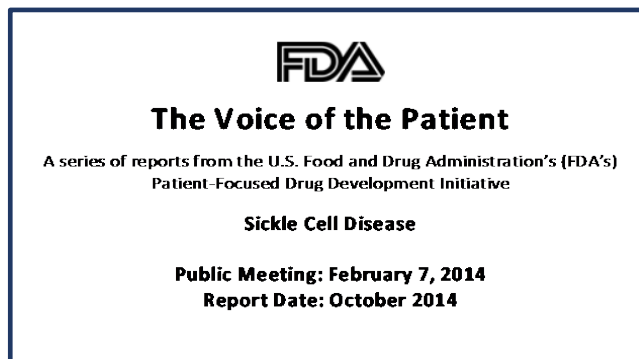
1. Piel, Frédéric B., Martin H. Steinberg, and David C. Rees. "Sickle cell disease." *New England Journal of Medicine* 376.16 (2017): 1561-1573.
2. Thomson, Azalea M., et al. "Global, regional, and national prevalence and mortality burden of sickle cell disease, 2000–2021: a systematic analysis from the Global Burden of Disease Study 2021." *The Lancet Haematology* (2023).

IHP-102 uniquely meets needs of the SCD community

Racial stigma and lack of effective treatments have left people treated as an opioid “drug-seeker” while in debilitating pain

“I always dress professionally {when going to the ER during VOE}. It’s crazy that you, as an African-American, have to do this so you aren’t treated like a drug addict.”¹

In 2014 the FDA solicited direct input from the SCD community



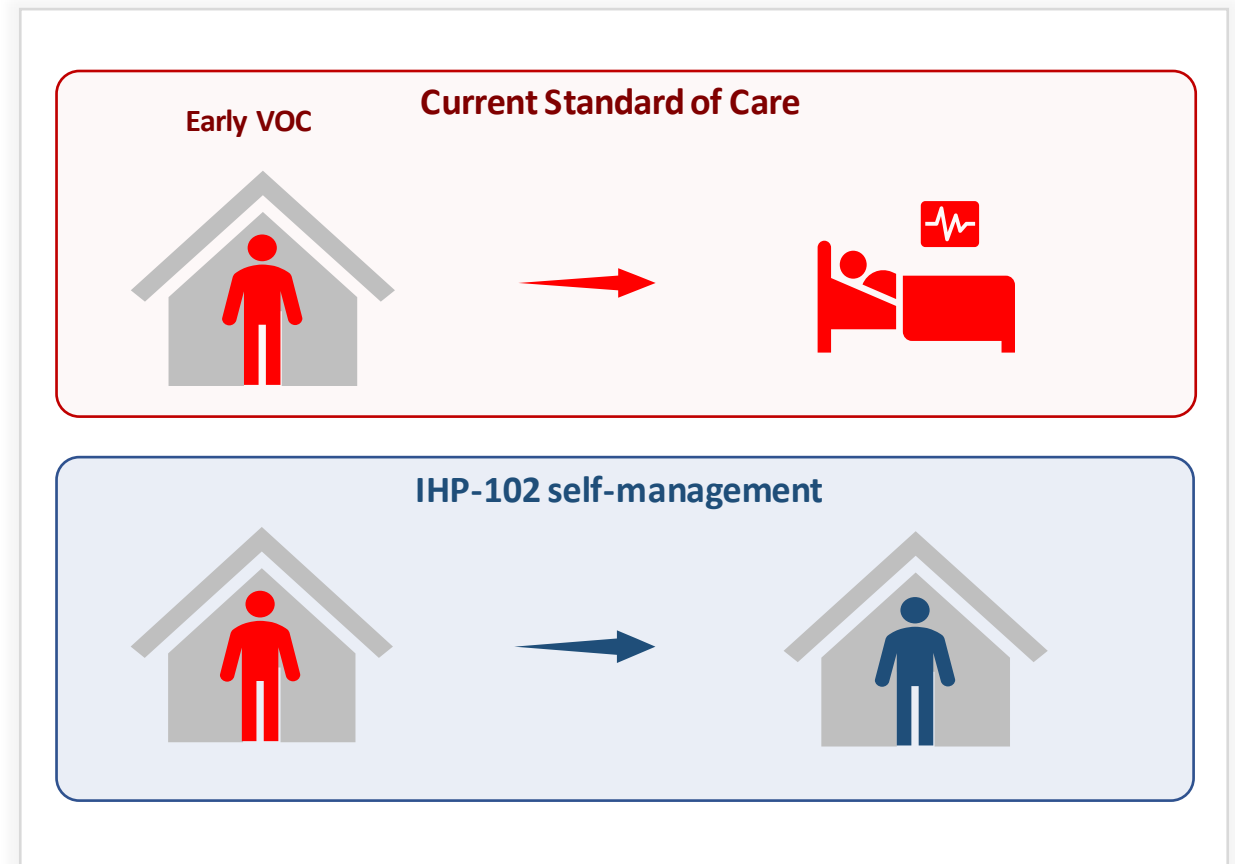
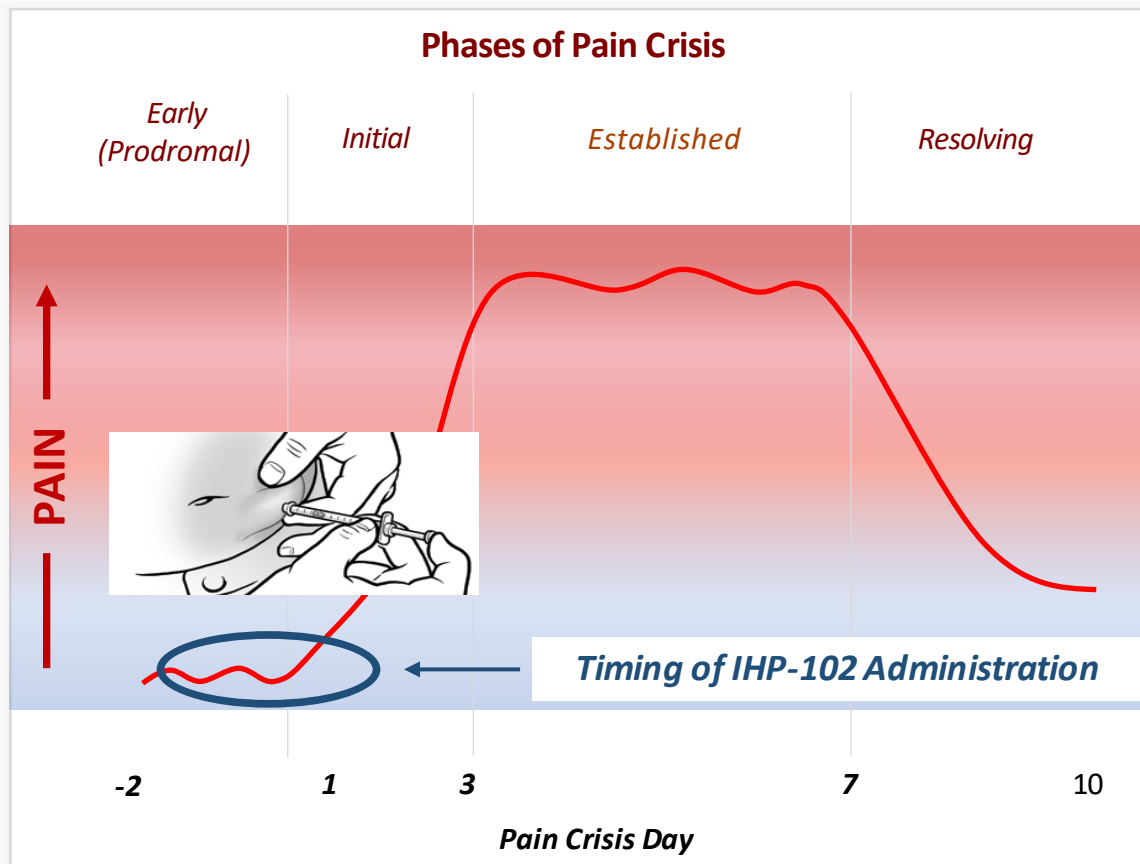
Top Patient-Reported Needs

- ✓ *“Treatments that patients can self-administer”*
- ✓ *“Treatments that stop a pain crisis in its tracks”*

✓ **IHP-102 uniquely meets these needs**

IHP-102 could be administered at the earliest symptom of VOE, thus preventing debilitating pain and life-threatening complications

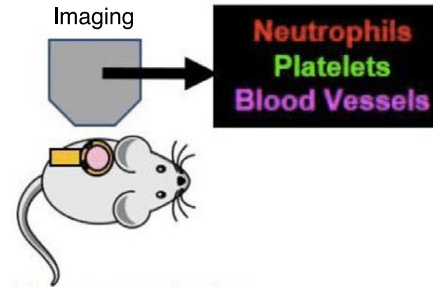
"..if the acute painful crisis is treated aggressively at its beginning, its end would be short with little or no complications."¹



1. Ballas, Samir K., Kalpna Gupta, and Patricia Adams-Graves. "Sickle cell pain: a critical reappraisal." *Blood, The Journal of the American Society of Hematology* 120.18 (2012): 3647-3656

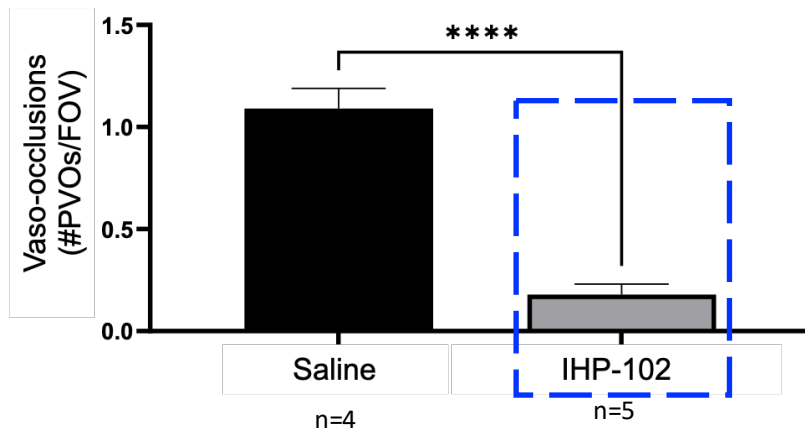
IHP-102 treatment potently reduces vaso-occlusions by >80% in Townes SCD mice

Townes SCD mouse is the gold-standard model for VOC assessment
VOC is stimulated by i.v. oxyHb, representative of hemolysis
IHP-102 is administered by s.c. route

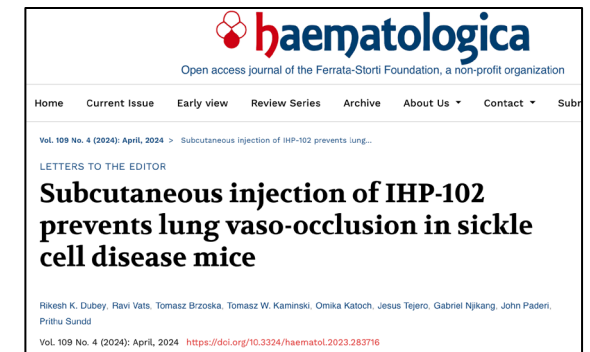


Blood vessel blockages (vaso-occlusions, indicative of VOC) are quantified by imaging

IHP-102 reduces vaso-occlusions by >80% in Townes SCD mice¹



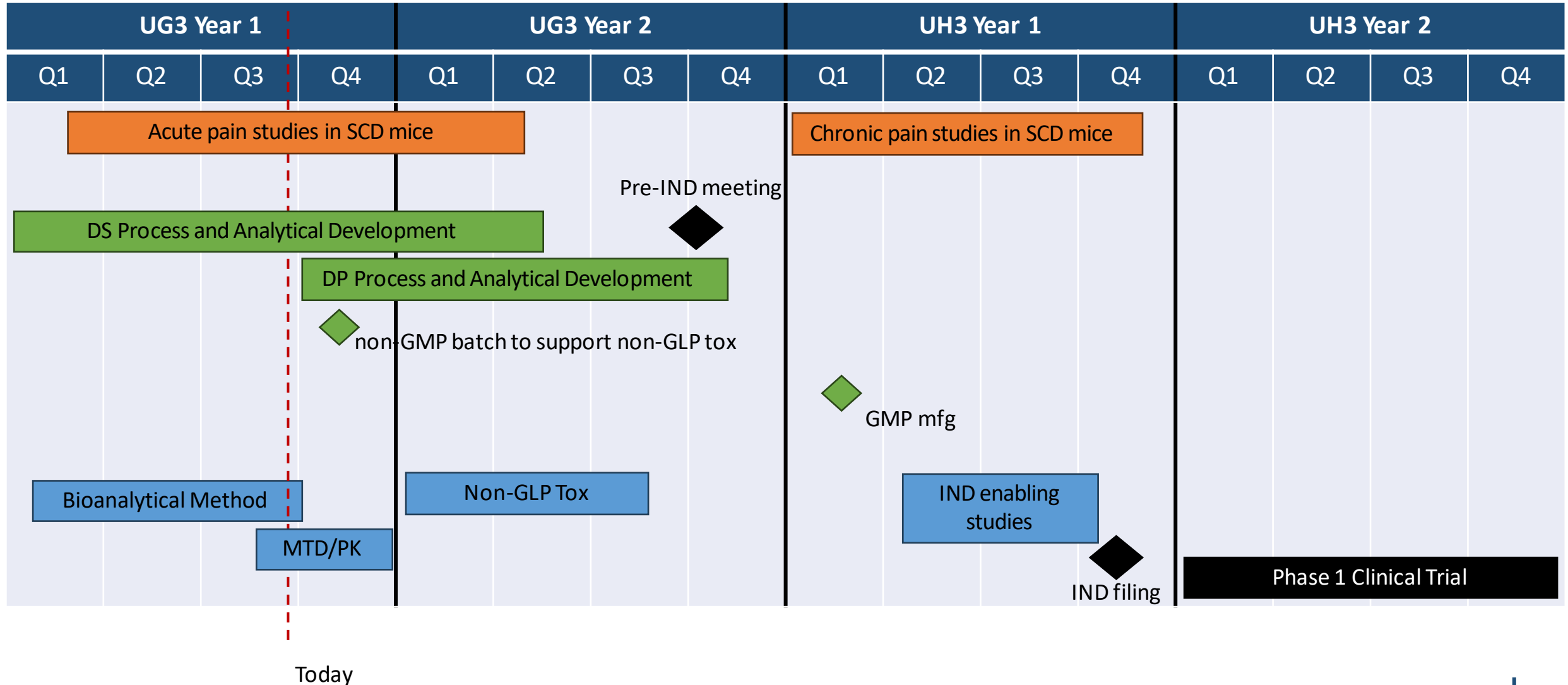
- Data are **best-in-class** in established model and leading academic center
- By comparison, P-selectin inhibition reduces vaso-occlusion by only 50% in this model³



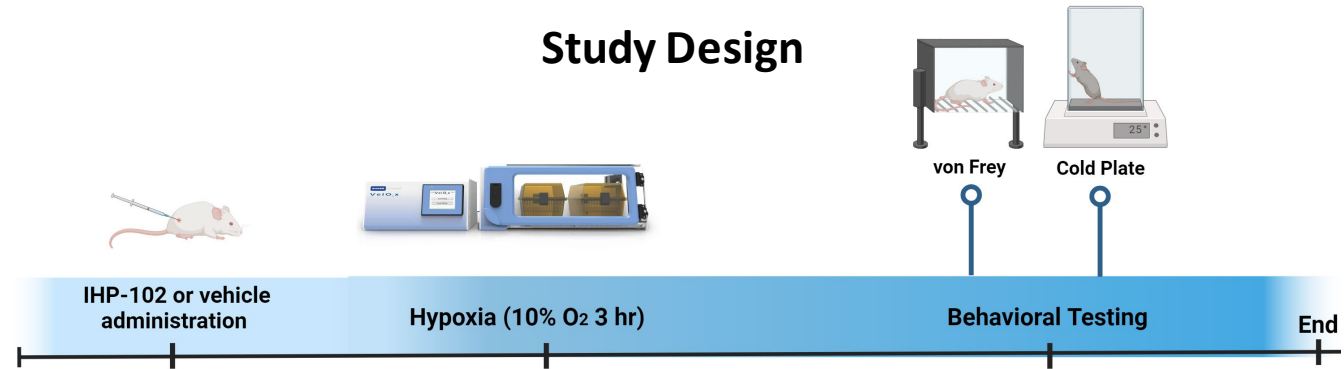
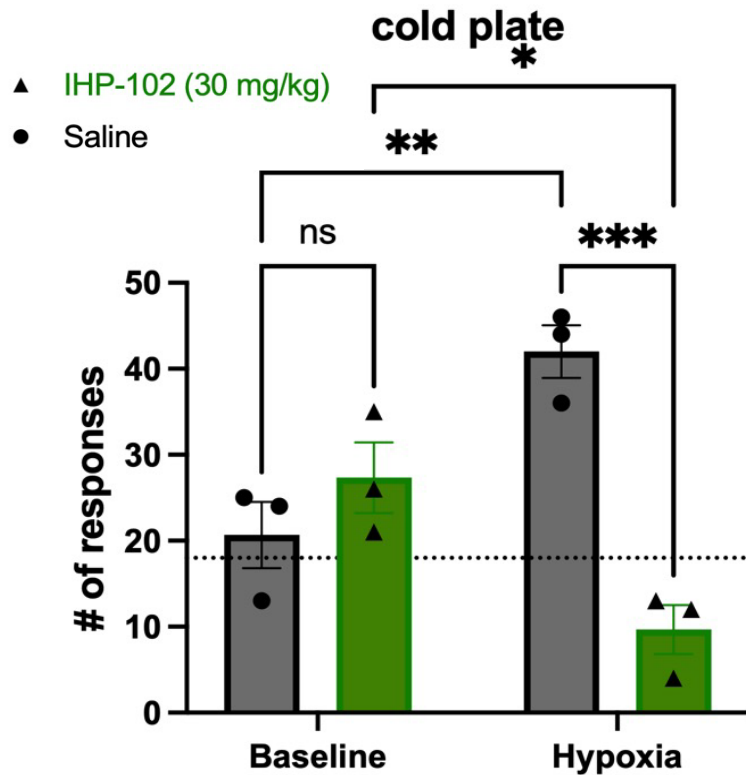
Legend: PVO = pulmonary vessel occlusions; FOV = field of view; IHP-102 dose = 30 mg/kg, SQ; Oxy-Hb challenge = 10 μmol/kg, IV

1. Dubey, Rikesh K., et al. "Subcutaneous injection of IHP-102 prevents lung vaso-occlusion in sickle cell disease mice." *Haematologica* 109.4 (2024): 1259.
2. Paderi, John, et al. "Dual P-Selectin and Complement Inhibition with Subcutaneous IHP-102 Treatment Potently Reduces Lung Vaso-Occlusion in Sickle Cell Disease Mice." *Blood* 142 (2023): 1122.
3. Bennewitz, Margaret F., et al. "Lung vaso-occlusion in sickle cell disease mediated by arteriolar neutrophil-platelet microemboli." *Jci Insight* 2.1 (2017).

Timeline and Milestones Supported by HEAL



IHP-102 Reduces Cold Hypersensitivity in Townes SCD Mice



- IHP-102 (30 mg/kg, s.c.) **reduces cold hypersensitivity by > 75%** compared to saline (vehicle) controls¹
- The decrease observed is reduced below baseline (no hypoxia) suggesting a potent effect beyond the acute vaso-occlusion phase
- Cold sensitivity is observed clinically during VOE²

Additional studies are ongoing, including dose-response and additional MoA

1. Goldsborough, Kennedy N., et al. "Evaluation of IHP-102 for the Treatment of Acute VOE-Like Pain: Study Design." *Journal of Sickle Cell Disease* 1.Supplement_1 (2024).

2. Brandow, Amanda M., et al. "Children and adolescents with sickle cell disease have worse cold and mechanical hypersensitivity during acute painful events." *Pain* 160.2 (2019): 407-416.

Q&A

Breakout Rooms – Feel free to move between the four rooms to meet our speakers!

- **Training & Workforce**

- With DP Mohapatra and Laura Wandner

- **PURPOSE Network**

- With Jacob Coverstone

- **Pain Therapeutics Development Program**

- With Mary Ann Pelleymounter and Matthew Rice

- **Experiences in Drug Discovery**

- With John Paderi, Kennedy Goldsborough, Mohamed Hachicha, and Shamsi Raeissi