

# Programs for Neuroscience Translational Research



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# Disclaimer

- Opinions are my own and not necessarily those of the Government.
- No financial conflicts of interest to report

# Agenda

- Introduction to NIH Neuroscience
- NINDS Division of Translational Research
  - IGNITE
  - CREATE Bio (biologics)
  - BPN (small molecule)
  - Translational Neurodevices
  - Clinical Resources at NINDS
- NIH Services for Translational Neuroscience
- General Consideration when applying to NIH

# Introduction to NIH Neuroscience

# National Institutes of Health



NIH seeks fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce the burdens of illness and disability.

# The National Institutes of Health

There are **27** different Institutes and Centers (ICs), **24** of which award grants.

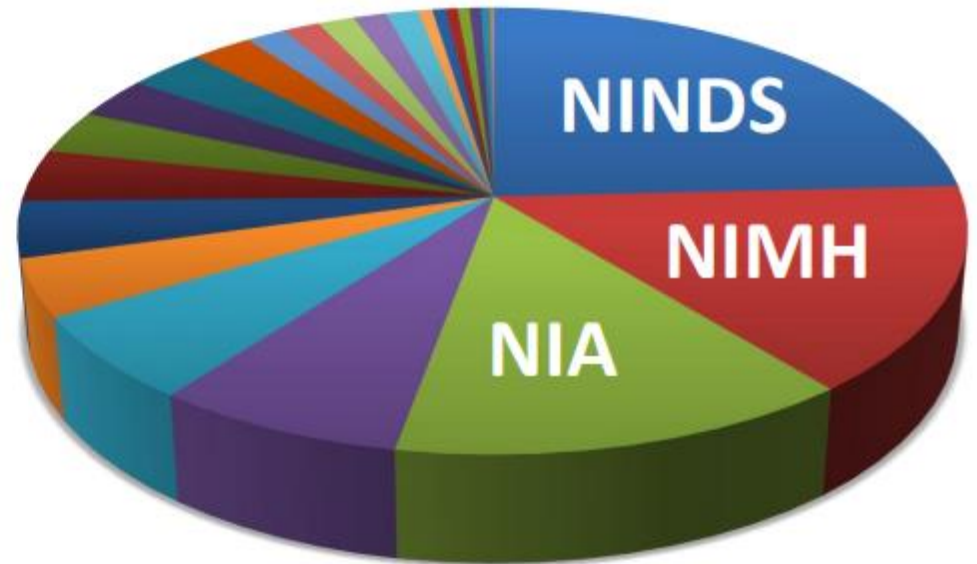
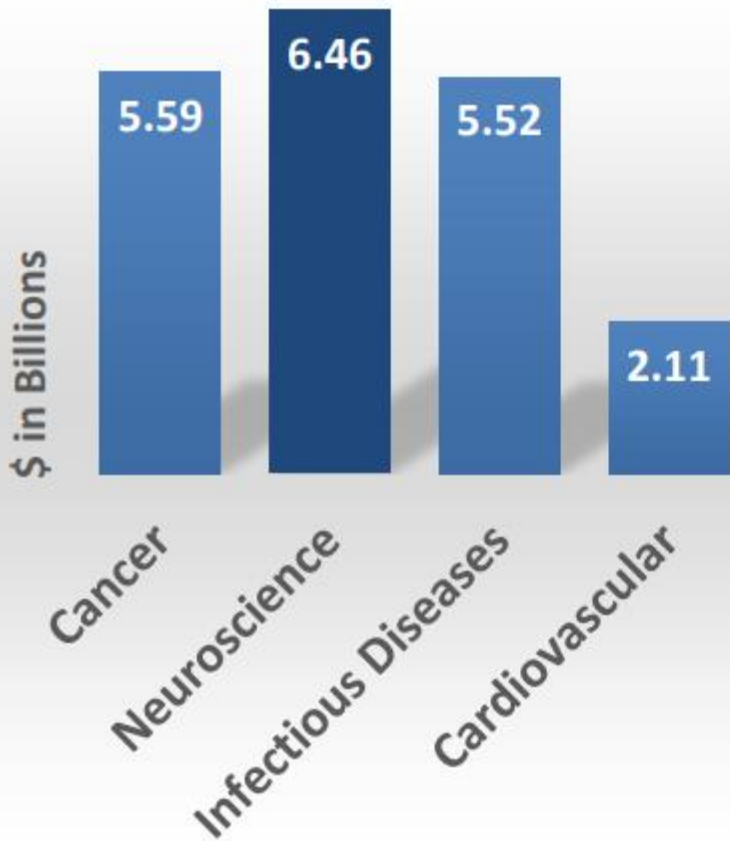
Each one has:

- Different missions
- Different funding priorities
- Different budgets
- Different types of grants they support
- Different procedures for making funding decisions
- Different funding strategies



Important to know you primary indication area

# 2016 NIH Neuroscience Funding



# Types of NIH Grant Programs: U versus R mechanism

- **R= Research Grants**, includes R01s, the most common grant program used to support a discrete, specified, circumscribed research project
- **U= Cooperative Agreement**, an assistance mechanism in which substantial NIH scientific and/or programmatic involvement with the awardee is anticipated during the performance of the activities
  - U44- Small Business Innovation Research (SBIR) Cooperative Agreements



# Types of Mechanisms

- Funding Opportunity Announcements (FOAs)
  - Read the each FOA carefully
    - PA vs PAR vs RFA: Each one can have different requirements, review criteria, eligibility etc.
    - Is it a Cooperative Agreement (U-grant vs. R-grant)?
    - Is it milestone based?
    - Is it an SBIR mechanism?
  - Follow the instructions in the FOA
    - Failure to do so may result in your application being withdrawn from consideration prior to review.

# NIH Provides a Wealth of Information Online



**Grants & Funding**  
NIH's Central Resource for Grants and Funding Information

Entire Site  Search this Site

[eRA](#) | [NIH Staff](#) | [Glossary & Acronyms](#) | [FAQs](#) | [Help](#)

- HOME
- ABOUT GRANTS
- FUNDING
- POLICY & COMPLIANCE
- NEWS & EVENTS
- ABOUT OER

Doing human subjects research?  
New NIH policies impact you.

Learn More






-  Find Funding
-  How to Apply
-  Explore NIH Funded Research (RePORT)



### About Grants

Navigate the NIH grants process from finding a funding opportunity to monitoring your award.

- Grants Process Overview 
- Get Started 
- How to Apply 
- Application Referral and Review 
- Pre-Award and Post-Award Processes 
- Forms Library 

[Learn More](#)



### Policy and Compliance

Learn about the policy and compliance obligations of your grant award and find helpful resources on select policy topics.

- NIH Grants Policy Statement 
- Notices of Policy Changes 
- Compliance and Oversight 
- Select Policy Topics 

[Learn More](#)



### Information for...

Find key resources just for you.

- Researchers 
- Research Administrators 
- Reviewers 
- Small Businesses 
- Foreign Applicants 
- Media and the Public 
- NIH Staff  

# Who at NIH Can Answer Your Questions?

## Before You Submit Your Application

- A Program Officer at an NIH Institute or Center
- Scientific Review Officer

## After You Submit

- Your Scientific Review Officer

## After Your Review

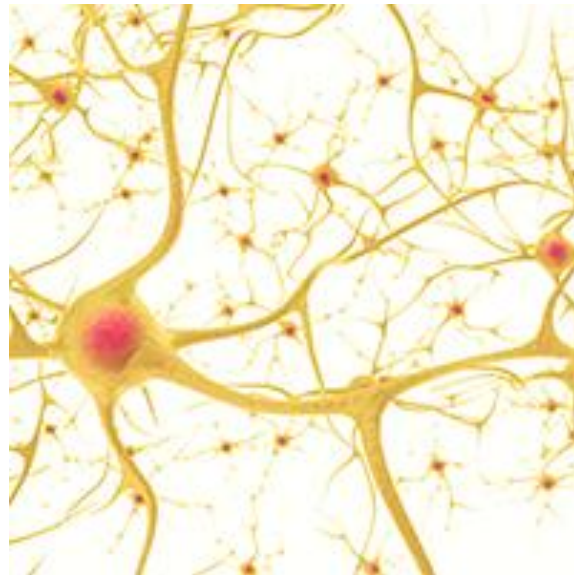
- Your Assigned Program Officer



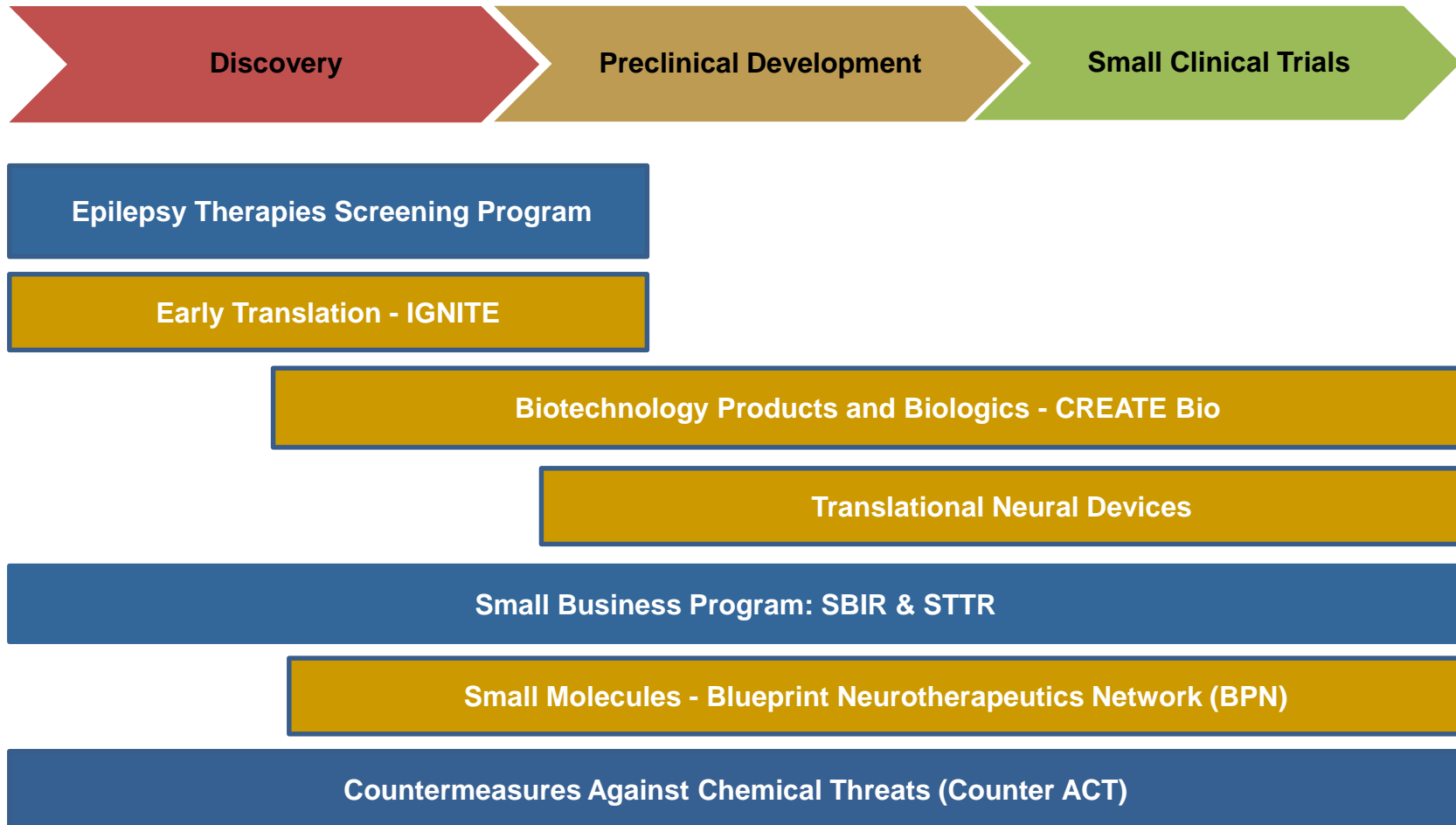
# NINDS Division of Translational Research

# NINDS Division of Translational Research (DTR)

- **Mission:** *To accelerate basic research findings towards patient use for neurological disorders and stroke by provide funding, expertise, and resources for the research community*



# Translational Funding Opportunities



**IGNITE: Innovation Grants to Nurture Initial Translational Efforts**

**CREATE: Cooperative Research to Enable and Advance Translational Enterprises**

# Focusing on Early Translational Efforts

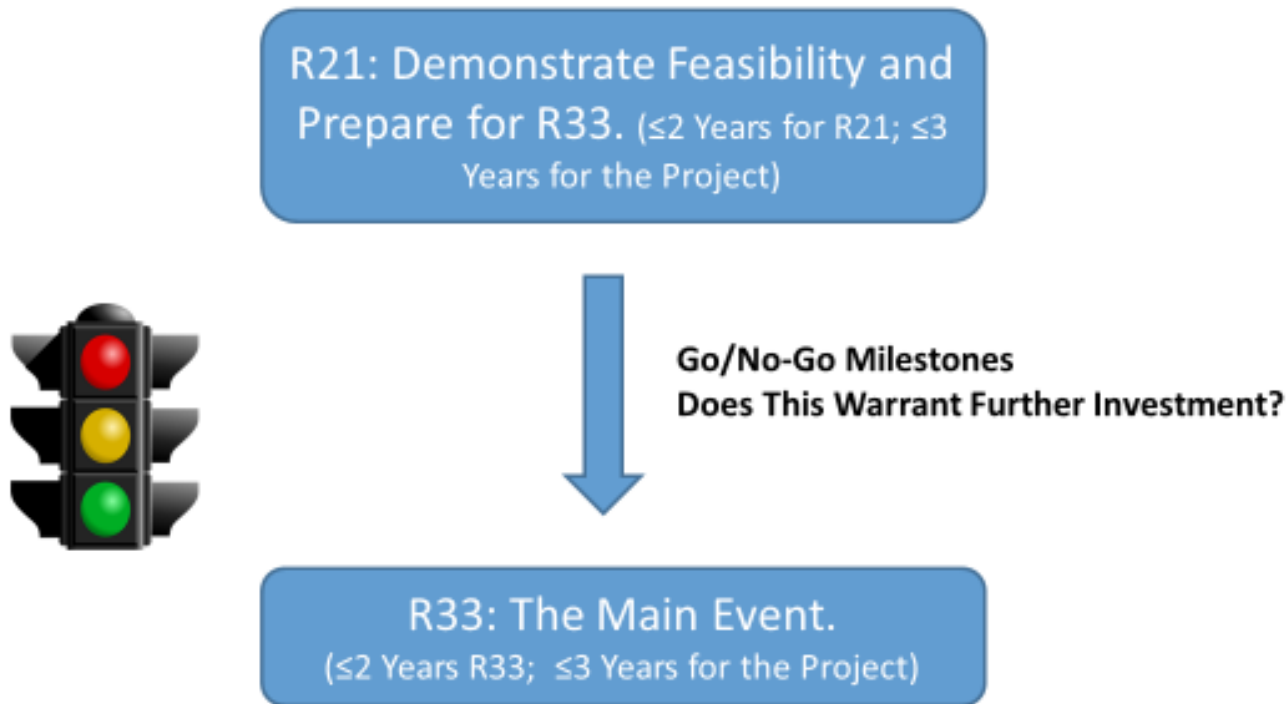


- **PAR-15-070:** Assay Development and Therapeutic Agent Identification and Characterization
- **PAR-15-071:** Pharmacodynamics and In vivo Efficacy Studies
- **RFA-NS-16-013:** Development and Validation of Translational Model Systems for Drug Discovery

Contact: [mary.pelleymounter@nih.gov](mailto:mary.pelleymounter@nih.gov)

***Purpose of IGNITE is to get preliminary data for entry into CREATE and BPN***

# IGNITE is an R21/R33 Mechanism



**Extremely Clear, Quantitative and Definitive Milestones are *Essential*.**  
**Only 1 Go/No-Go Point**  
**Transition to R33 via Administrative Review**

Budget is \$250,000/yr; \$750,000/project



# CREATE BIO (Funding for biologics)

## Funding Promising Therapeutic Biologics

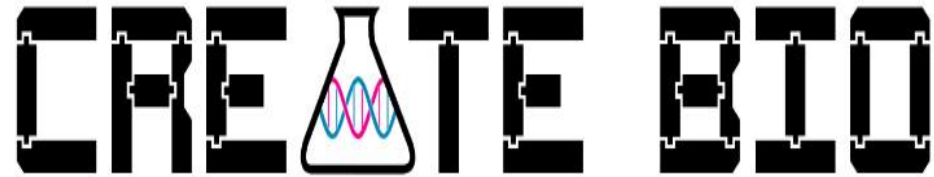
**Modalities: Peptides, Proteins,  
Oligonucleotides, Gene and Cell  
Therapies**

### Purpose

- Optimization: Optimization of therapeutic leads
- Development: IND-enabling studies/Early phase clinical trials

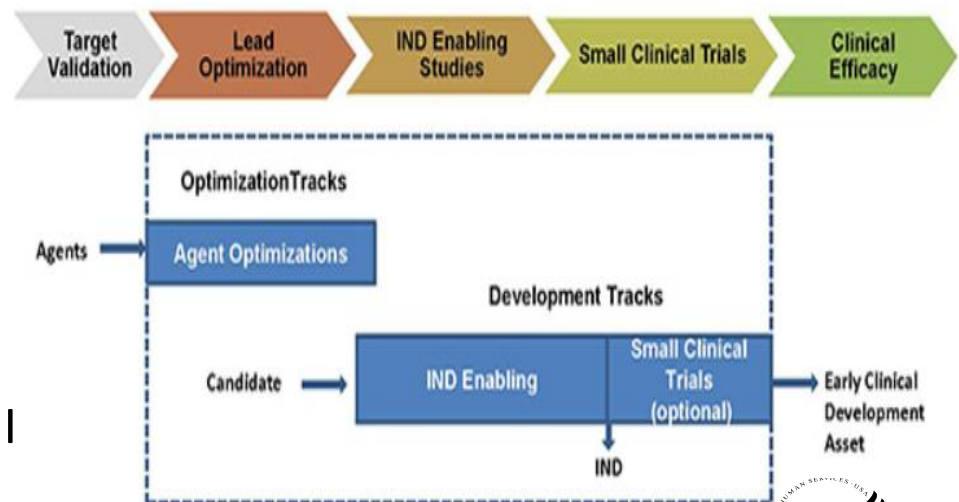
### End Goals

- Optimization: Characterize and select a lead candidate
- Development: Submit an IND application and/or conduct Phase I Trials



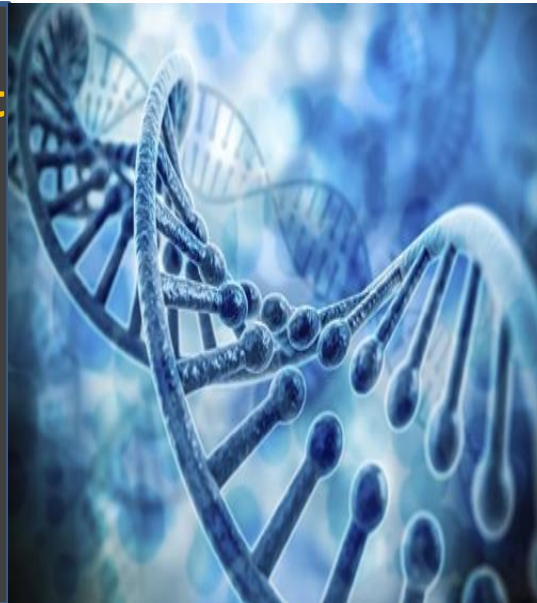
Cooperative Research to Enable and Advance Translational Enterprises for Biologics

### CREATE Bio Program Overview



# CREATE Bio Contract Resources/Consultants

- **Biologic CMC Development Consulting**
- **Biologic Regulatory Affairs Consulting**
- **Statistical Consulting**



## Related Resources

- [Application Support Library](#)
- [NIH Stem Cell Information](#)
- [FDA CBER guidance documents](#)
- [FDA CDER guidance documents](#)
- [FDA Clinical guidance documents](#)

- **PAR-18-543 / PAR-18-542** CREATE Bio Development Track: Nonclinical and Early-Phase Clinical Development for Biologics U01 / U44 (Small Business)  
**Next Application Date: February 20, 2018**
- **PAR-17-456 / PAR-17-457** CREATE Bio Optimization Track for Biologics U01 / U44 (Small Business)  
**Next Application Date: February 13, 2018**

# Blueprint Neurotherapeutics Network (BPN) - small molecules

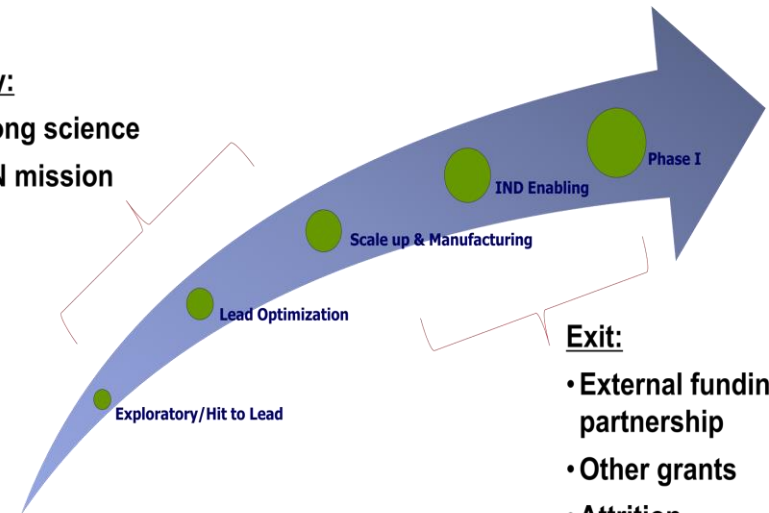
## Program Goals

- To provide funding and necessary resources (CRO access and drug discovery expertise) for drug discovery.
- To maintain the IP of the grantee
- To de-risk potential therapeutics to the point that industry invests and advances the new drugs towards patients efficiently.



### Entry:

- Strong science
- BPN mission



### Exit:

- External funding/  
partnership
- Other grants
- Attrition



# BPN is a trans-NIH program with 9 ICs participating



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and Stroke

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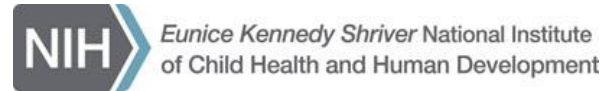
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# BPN Combined Strengths of NIH and Industry Resources

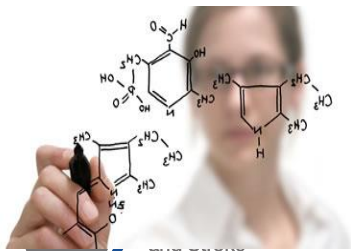
## NIH investigator-initiated ideas

- Small molecule starting point
- Strong disease assays and models
- Novel drug targets



## Industry expertise

- Advisors with extensive pharma experience
- Industry-standard contract services



First in Human Trials

<https://neuroscienceblueprint.nih.gov/bpdrugs/>



# BPN – Projects Can Enter at Any Preclinical Stage



*All Projects Begin with Preparatory Phase*



- Complete entry criteria for SAR or IND-enabling studies
- Conduct due diligence

Not all ICs accept Development Projects

Discovery			Development	
Exploratory	Hit to Lead	Lead Optimization	IND Enabling	Phase I Trial

## General (UG3/UH3) PAR-18-546

UG3: Up to \$300K direct costs x 1 yr

UH3: Up to \$1.5M/yr direct costs x 4 yrs

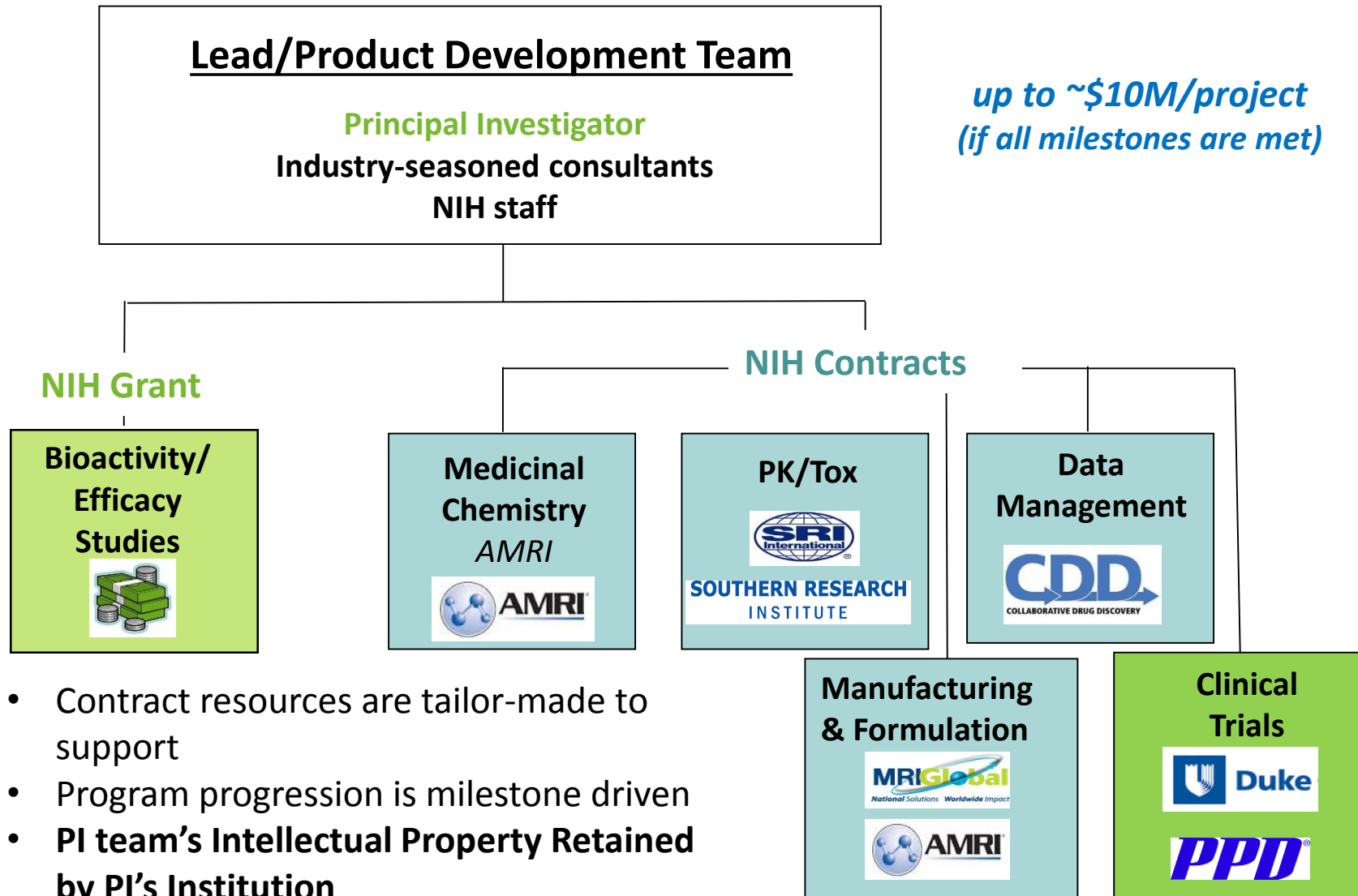
## SBIR (U44-I/II) PAR-18-541

Phase I: Up to \$500K/yr\* (\$700K total across ≤2 yrs)

Phase II: Up to \$1.5M/yr (\$3M total across ≤3 yrs)

# Blueprint Neurotherapeutics Network (BPN)

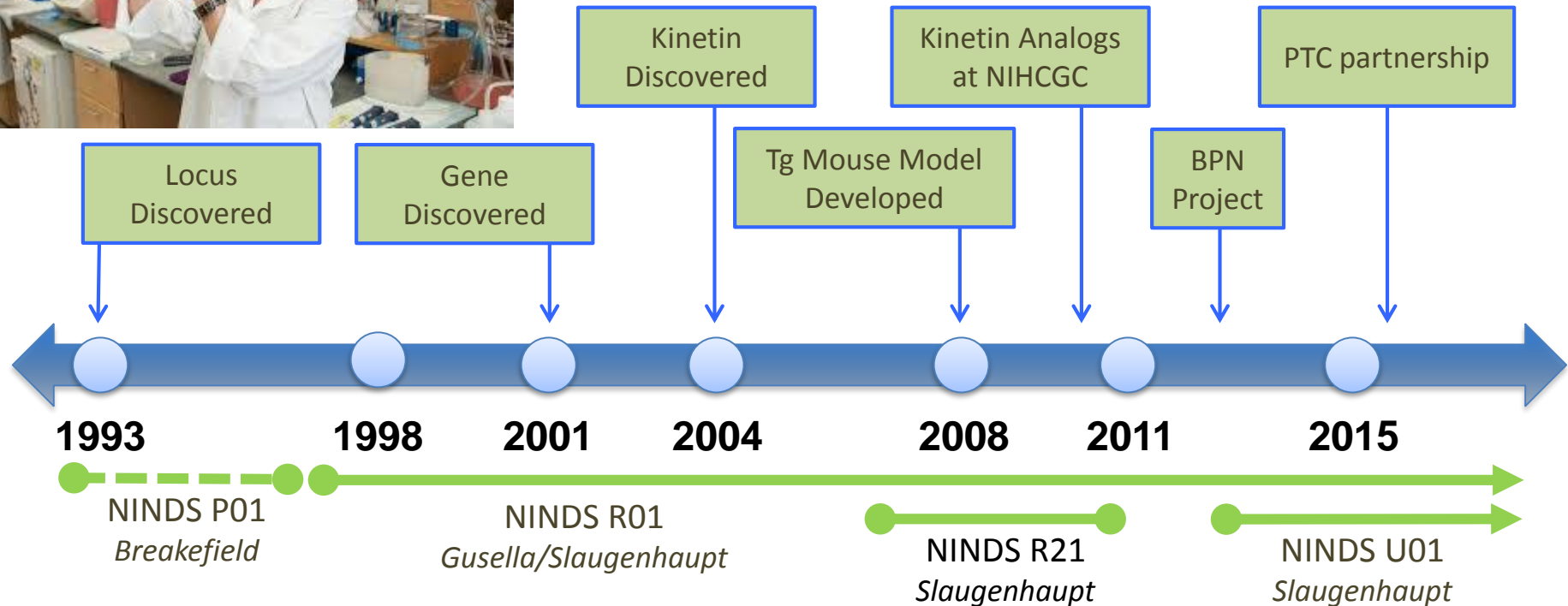
Customized Combo of Infrastructure, Expertise, and Funds



# Support Basic & Translational Activities



## NINDS Support for Familial Dysautonomia Research



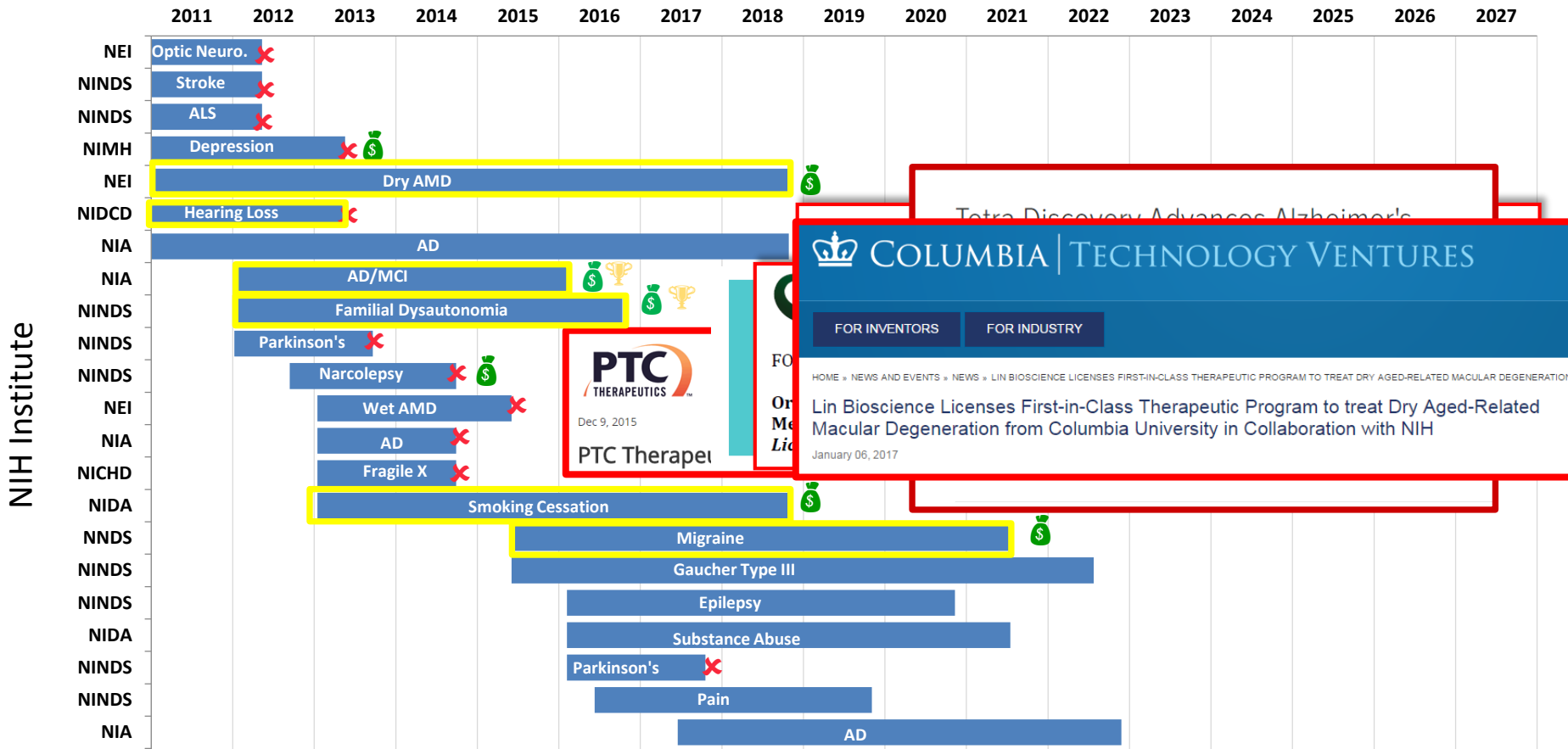
**NIH/NINDS has supported Slaughaupt from Post-doc to Full Professor**

### Additional Public/Private Funding

Dysautonomia Foundation  
Israeli Science Ministry  
Harvard Center for Neurodegeneration and Repair  
US Israel Binational Science Foundation



# BPN Successes



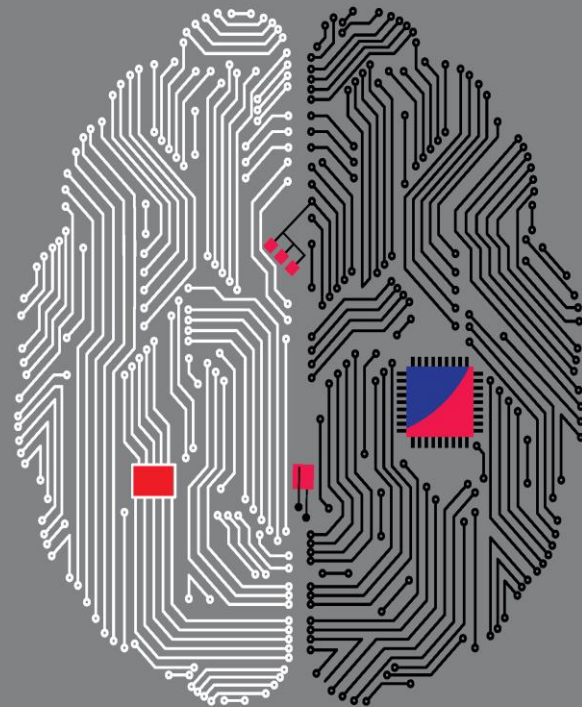
= Graduated   
 = Licensing and outside investment deal announced   
 = Exited

# Translational Neural Devices

- **RFA-NS-18-011:**  
For academic and businesses that are not SBIR eligible
- **RFA-NS-18-012:**  
For small businesses that are SBIR eligible

Supports translational activities to advance the development of therapeutic or diagnostic devices that affect the nervous system or neuromuscular system

## Translational Neural Devices



NIH National Institute of  
Neurological Disorders  
and Stroke

Contact: [nick.langhals@nih.gov](mailto:nick.langhals@nih.gov)



# Small Business Program at NINDS

- The NINDS SBIR/STTR program funds small business concerns to conduct innovative neuroscience research and/or development that has both the potential for commercialization and public benefit
  - Many NINDS SBIR and STTR applications come in through the omnibus solicitations
- All previously mentioned programs are open to small businesses, but only certain opportunities will utilize the small business set-aside
- Applicants who have never received a small business award can apply for the **Applicant Assistance Program (AAP)**
  - Free services intended to help submit a competitive SBIR or STTR application
  - Project must fall within the mission of NINDS, NCI, or NHLBI
  - See more information at: <https://www.dawnbreaker.com/aap/>

Contact: [fertigs@ninds.nih.gov](mailto:fertigs@ninds.nih.gov)

# BRAIN Initiative: Device Development and Tools for Neuroscience Research

For the most up-to-date active funding opportunities, visit:

<https://braininitiative.nih.gov/funding>

## Small Business Opportunities:

- BRAIN Initiative: Next-Generation Invasive Devices for Recording and Modulation in the Human Central Nervous System (U44 Clinical Trial Required), **RFA-NS-18-022**
- BRAIN Initiative: Development Optimization, and Validation of Novel Tools and Technologies for Neuroscience Research (SBIR)(R43/R44 Clinical Trial Not Allowed), **PAR-18-501**
- BRAIN Initiative: Development Optimization, and Validation of Novel Tools and Technologies for Neuroscience Research (STTR)(R41/R42 Clinical Trial Not Allowed), **PAR-18-515**



# Resources for Clinical trials

## NINDS Networks



### [Stroke Trials Network \(NIH StrokeNet\)](#)

Phase III clinical trials as well as early phase trials and biomarker studies preparatory to phase III clinical trials in stroke prevention, treatment and recovery.

Contact: [Scott Janis, Ph.D.](#)



### [NeuroNEXT](#)

Early phase clinical trials and biomarker studies preparatory to phase III clinical trials in neurological disorders.

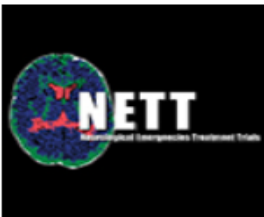
Contact: [Codrin Lungu, M.D.](#)



### [SIREN \(Strategies to Innovate EmeRgENcy Care Clinical Trials Network\)](#)

Clinical trials in neurologic, heart, lung, blood, and traumatic emergencies.

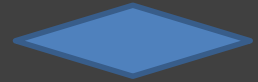
Contact: [Jeremy Brown, M.D.](#)



### [Neurological Emergencies Treatment Trials \(NETT\) Network](#)

Phase III trials of acute injuries and illnesses affecting the brain, spinal cord and peripheral nervous system. \*For new applications requesting network support of emergency care trials see SIREN (above).

Contact: [Robin Conwit, M.D.](#)



## Contact

**Clinton B. Wright,  
M.D., MS**  
[clinton.wright@nih.gov](mailto:clinton.wright@nih.gov)  
**Director, Division of  
Clinical Research**

# NIH Services for Translational Neuroscience

# NIH Services for Translational Neuroscience

## Funding: Preclinical Development

### Alzheimer's Disease Drug Development Program (U01)

- **Support:** Up to 5 years of funding, milestone-driven, must culminate in IND/IDE
- **Participating Institute:** NIA
- **To apply:** PAR-18-174 (U01) Contact: Lorenzo M. Refolo, Ph.D. [refolol@nia.nih.gov](mailto:refolol@nia.nih.gov)

### National Cooperative Drug Discovery/Development Groups (NCDDG) for the Treatment of Mental Disorders, Drug or Alcohol Addiction

- **Support:** Up to 5 years of funding for multidisciplinary teams, Public Private Partnerships
- **Participating Institutes:** NIMH, NIAAA, NIDA
- **To apply:** PAR-17-185 (U01), PAR-17-186 (U19)

Contacts: Linda Brady, Ph.D. [lbrady@mail.nih.gov](mailto:lbrady@mail.nih.gov) (NIMH)

Kristopher Bough, Ph.D. [boughk@mail.nih.gov](mailto:boughk@mail.nih.gov) (NIDA)

Mark Egli, Ph.D. [megli@mail.nih.gov](mailto:megli@mail.nih.gov) (NIAAA)





# NIH Services for Translational Neuroscience cont'd

## Funding: Preclinical Development

### Strategic Alliances for Medications Development to Treat Substance-Use Disorders

- **Support:** Up to 3 years of funding, includes discovery, development, and clinical trials. \$2M per year with expectation of matching funds
- **Participating Institute:** NIDA
- **To apply:** PAR-18-218 (R01) Contacts: Ivan D. Montoya, M.D., M.P.H. [imontoya@mail.nih.gov](mailto:imontoya@mail.nih.gov)

### Grand Opportunities in Medications Development for Substance-Use Disorders

- **Support:** Up to 3 years of funding, milestone-driven, up to \$5M per year
- **Participating Institute:** NIDA
- **To apply:** PAR-18-219 (U01) ) Contacts: Ivan D. Montoya, M.D., M.P.H. [imontoya@mail.nih.gov](mailto:imontoya@mail.nih.gov)



## Services: Pharmacology

### Epilepsy Therapy Screening Program (ETSP) formerly the known as ASP

- **Support:** Screens compounds in animal seizure models
- **To apply:** Contact John Kehne, Ph.D., [john.kehne@nih.gov](mailto:john.kehne@nih.gov)

### Addiction Treatment Discovery Program (ATDP)

- **Support:** Screens compounds in animal models of addiction
- **To apply:** Contact David White, Ph.D., Director ATDP (301) 827-5981

### NIMH Psychoactive Drug Screening Program (PDSP)

- **Support:** Screens novel psychoactive compounds for pharmacological and functional activity at cloned human or rodent CNS receptors, channels, and transporters.
- **To apply:** Contact Jamie Driscoll, [jdrisco1@mail.nih.gov](mailto:jdrisco1@mail.nih.gov)



# NIH Services for Translational Neuroscience cont'd

## Services: Toxicology

### NIMH Toxicological Evaluation of Novel Ligands Program

- **Support:** Provides toxicology, safety, *in vitro* ADME, and pharmacokinetic assessment of promising, target-selective compounds for use as imaging ligands and novel psychoactive drugs.
- **To apply:** Contact Jamie Driscoll, [jdrisco1@mail.nih.gov](mailto:jdrisco1@mail.nih.gov)

### NIDA Toxicology Program

- **Support:** Provides IND-directed toxicology services for substance abuse indications
- **To apply:** Contact Nathan M. Appel, Ph.D., [nappel@nih.gov](mailto:nappel@nih.gov),

### Bridging Interventional Development Gaps (BRIDGs)

- **Support:** Provides synthesis, formulation, pharmacokinetic and toxicology expertise and resources to its collaborators and is open to any disease
- **To apply:** See [ncats.nih.gov/bridgs/about](http://ncats.nih.gov/bridgs/about) for more information



# NIH Services for Translational Neuroscience cont'd

## Services: Chemistry

### Bridging Interventional Development Gaps (BRIDGs)

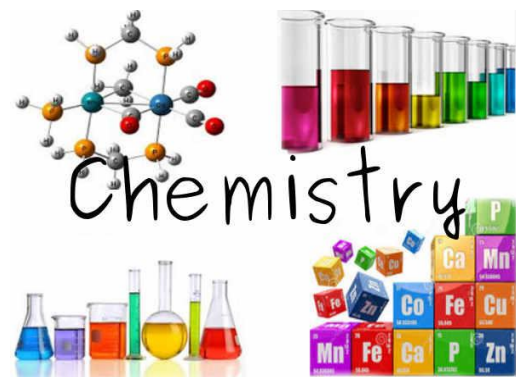
- **Support:** Provides chemical synthesis services, open to any disease
- **To apply:** See [www.ncats.nih.gov](http://www.ncats.nih.gov) for more information

### NIMH Chemical Synthesis and Drug Supply Program

- **Support:** Synthesizes and distributes novel research chemicals, psychoactive drugs, and compounds unavailable from commercial sources. Also supports radiosynthesis, medicinal chemistry, and GMP synthesis for clinical studies.
- **To apply:** Contact Jamie Driscoll, [jdrisco1@mail.nih.gov](mailto:jdrisco1@mail.nih.gov)

### NIDA Chemistry and Pharmaceuticals Branch

- **Support:** Medicinal chemistry, analytical chemistry, metabolism, pharmacokinetics and pharmacodynamics, pharmacogenetics and pharmaceuticals/formulation development aimed at the design, evaluation and development of medications for the treatment of drug addiction
- **To apply:** Contact Nora Chiang, Ph.D., [nchiang@nih.gov](mailto:nchiang@nih.gov)



# General Considerations for Applicants

# Build A Collaborative Team

- Clinicians who work with the target patient population
- Experts in the disease biology
- Experts in each aspect of drug discovery/development
- Licensing/business development advisors
- Consider partnership with biotech (STTR), pharma



# Plan with the End in Mind

- **Target population**
  - Pediatric vs. adult patients?
  - Early vs. advanced disease?
- **Dosing regimen**
  - Chronic or acute treatment?
  - Frequency?
- **Route of administration**
  - Oral? IV? Eye drops? Transdermal? etc.
- **Desired outcome**
  - Comparison to standard of care?

**Engage clinicians in developing a Target Product Profile**

# Example of Target Product Profile (TPP)

Product Properties	Minimum Acceptable Result	Ideal Result
Primary Indication	Relief of pain symptoms in diabetic neuropathy	Relief of symptoms in neuropathic pain syndromes
Patient Population	Adults with diabetes who experience neuropathic pain	Adults and children with neuropathic pain
Treatment Duration	Chronic	Chronic
Delivery Mode	Oral	Oral
Dosage Form	Tablet or capsule	Tablet or capsule
Regimen	1–2x/day	1x/day
Efficacy	A 40% decrease in pain score in 30% of patients	A 70% decrease in pain score in 50% of patients.
Risks/Side Effects	Devoid of opioid side effects Devoid of GI side effects from Non-steroidal anti-inflammatory drugs (NSAIDs) Minor or moderate CNS side effects	Devoid of opioid side effects Devoid of GI side effect from NSAIDs No CNS side effects

<http://neuroscienceblueprint.nih.gov/resources/target-product-profile.htm>



# Hit Compound $\neq$ Clinical Candidate

- Is there a sufficient therapeutic window between activity at desired and undesired targets?
  - hERG inhibition?
  - Other off-target effects?
  - Inhibitor of common CYPs?
- Is PK/PD consistent with the dosing strategy in the Target Product Profile?



**Profile your compound early on**



# Considerations

- Scientific premise

- *Explicitly discuss the quality of the data presented in prior publications in a detailed manner.*



- Rigor

- *Detail the controls being used for each type of experiment and appropriately highlight potential confounds like surgery exposure, genotype, culture-to-culture variability, and human placebo effects.*
- *Include details within the experimental design about the reduction of potential bias, including blinding, randomization, and inclusion/exclusion criteria.*
- *Describe the source of the data on which the sample size estimation (power analysis) is based **and** details about the analysis itself.*

# Some additional things to do

- Complete your required registrations at least 6-8 weeks in advance of receipt dates
- Consider submitting your application early
  - Gives you a chance to react to issues that might result in your application being withdrawn.
- Check Budget limits and permission requirements
  - For example: If you are applying to the BPN-UG3/UH3 program and **ANY** proposed budget year exceeds \$500K in direct costs then you need permission to submit. Request must be made 6-8 weeks prior to submission date.
- Talk with your tech transfer/BD group.
  - Need to plan for funding patents and licensing activities

# Training in Neurotherapeutics Discovery & Development

## *NIH Blueprint for Neuroscience Research Short Course for Academic Neuroscientists*

*March 7-10, 2018*

1. Explores various topics critical to discovery and development of neurotherapeutic agents
2. Provides individualized mentoring and assessment
3. Provides opportunities to interact with topic experts



<http://www.neurotherapeuticscourse.org>

- ✓ Over 100 people have participated to date
- ✓ Representation from 53 unique institutions/universities
- ✓ Disease area representation from 6 NIH institutes

# BPN Accepting New Applications

<https://neuroscienceblueprint.nih.gov/bpdrugs/>

**PAR-18-546** for all applicants

**PAR-18-541** for small businesses (SBIR)

Next applications due Feb 7, 2018

Special Emphasis Panel (SEP) review

[charles.cywin@nih.gov](mailto:charles.cywin@nih.gov)



# Questions

