NIH Blueprint Neurotherapeutics Network (BPN): Funding and Resources for the Discovery of Novel Drug Candidates for the Treatment of Neurological Disorders

Shamsi Raeissi[1], Pascal Laeng[1], Mohamed Hachicha[1], Enrique Michelotti[2], Oreisa O'Neil-Mathurin[1], Mary Pelleymounter[1], , Ranga Rangarajan[1], Matthew Rice[1], Rakonda Medley[1], and Charles Cywin[1]
NIH, National Institute of (1) Neurological Disorders & Stroke (NINDS), of (2) Mental Health (NIMH), North Bethesda, MD

ABSTRACT

There remains a high unmet need for novel treatments for CNS diseases. Many academic and industry scientists are eager to undertake novel drug discovery approaches for the treatment of neurological disorders but lack some of the drug discovery infrastructure. To boost and de-risk drug discovery and development in the neuroscience field, NIH Blueprint for Neuroscience Research introduced a series of translational programs to promote neuroscience drug discovery and development efforts to mitigate the current pipeline gaps.

In this presentation, we demonstrate how NIH Blueprint Neurotherapeutics Network (BPN), by providing funding, resources (contract access to medicinal chemistry, DMPK, toxicology, drug manufacturing and formulation, as well as contract access to perform the Phase I clinical study) and expertise, have contributed to the successful translation of academic and industry discoveries in basic disease biology into novel drug candidates in clinical testing.

BLUEPRINT NEUROTHERAPEUTICS (BPN) PROGRAM VISION

"Combine Strengths of NIH and Industry Expertise for Small Molecule Neuroscience Drug Discovery & Development"

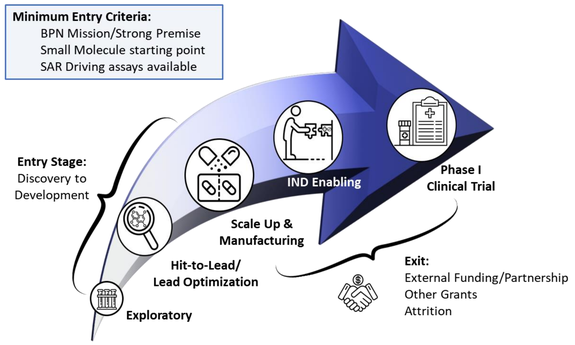
Principal Investigator Initiated Ideas
- Solid scientific premise
- Expert disease biology

Industry Experience
- Consultants with solid Pharma experience
- Industry standard via access to BPN-sponsored CROs

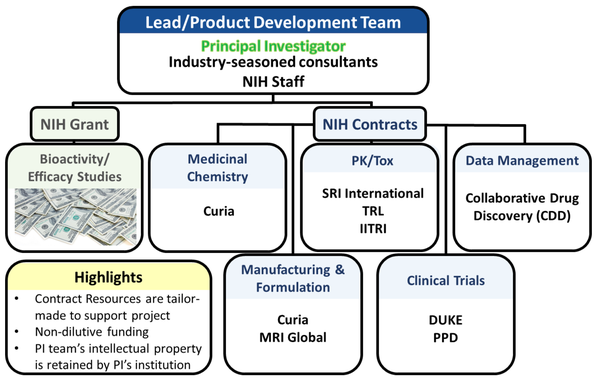
End Goals
- Decrease risks
- Advance projects to clinic and hand-off
- Maintain IP to grantee institution

BPN PROGRAM- SCOPE

Minimum Entry Criteria:
BPN Mission/Strong Premise
Small Molecule starting point
SAR Driving assays available



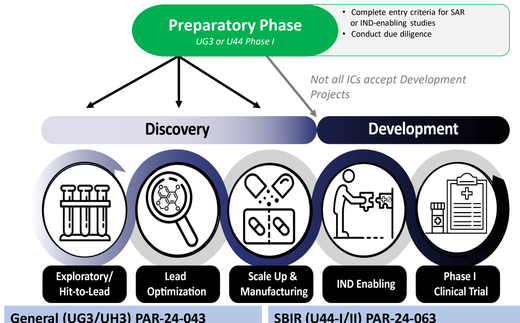
BPN PROJECT ORGANIZATION



Program progression is milestone driven

BPN – PROJECT CAN ENTER AT ANY PRE-CLINICAL STAGE

All Projects Begin with Preparatory Phase

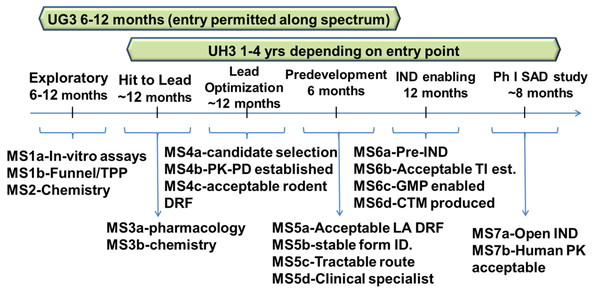


General (UG3/UH3) PAR-24-043
UG3: Up to $300K direct costs x 1 yr
UH3: Up to $1.5M/yr direct costs x 4 yrs

SBIR (U44-I/II) PAR-24-063
Phase I: Up to $500K/yr*($700K total across ≤2 yrs)
Phase II: Up to $1.5M/yr ($3M total across ≤3 yrs)

*NINDS rules check specific IC rules If no vertebrate animal work $225K/yr

MILESTONE PROGRESSION BY STAGE



ENTRY CRITERIA

Discovery

Disease Biology
- Novel target for the disease
- Strong biological validation
- Feasible path to the clinic

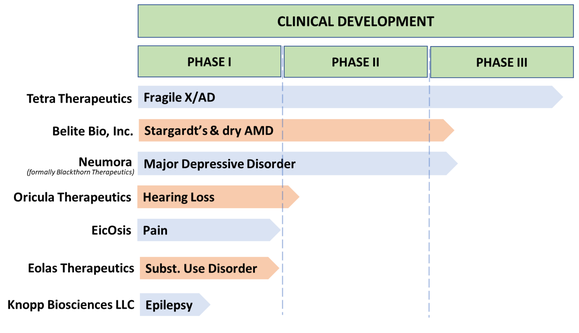
Assays
- Robust in-vitro assay for optimization
- Strong confirmatory assays

Compounds
- Project must require medicinal chemistry
- Amenable to chemistry
- IP free of obvious roadblocks

Development

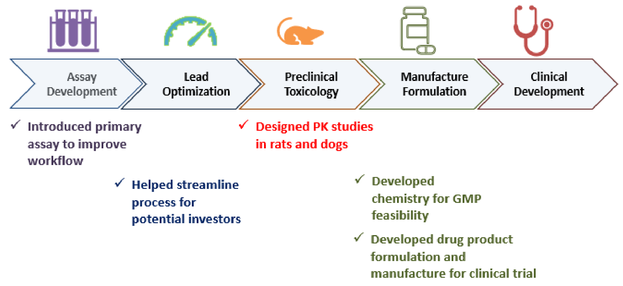
Fully Optimized Compound
- Strong data linking target to disease
- Biological & ADMET activity appropriate for intended clinical use
  - Efficacy/PD when delivered by clinically intended route
  - Fully profiled, defensible ADMET results
- Feasible path to the clinic
- IP free of obvious roadblocks

BPN PROJECTS SUCCESSFUL POST-PROGRAM PROGRESSION



10 projects have announced additional industry funding since utilizing the BPN

KNOW HOW AND EXPERTISE PROVIDED



A CROSS-NIH INSTITUTES EFFORT

NIH National Institute of Neurological Disorders and Stroke — Charles Cywin, PhD, charles.cywin@nih.gov
NIH National Institute on Aging — Lorenzo Refolo, PhD, refolol@mail.nih.gov
NIH National Institute on Alcohol Abuse and Alcoholism — Qi-Ying Liu, MD, MSci, liuqiy@mail.nih.gov
NIH National Center for Complementary and Integrative Health — Yisong Wang, PhD, yisong.wang@nih.gov; Patrick C. Still, PhD, patrick.still@nih.gov; Emrin Horgusluoglu, Ph.D., emrin.horgusluoglu-moloch@nih.gov
NIH National Institute on Drug Abuse — Elena Koustova, PhD, MBA, koustovae@mail.nih.gov; Tanya (Tatiana) Ramey, MD PhD, tanya.ramey@nih.gov
NIH National Institute of Mental Health — Enrique Michelotti, PhD, michelottiel@mail.nih.gov
NIH Eunice Kennedy Shriver National Institute of Child Health and Human Development — Zhaoxia Ren, PhD, zren@mail.nih.gov
NIH National Institute of Dental and Craniofacial Research — Melissa Ghim, PhD, melissa.ghim@nih.gov; Yolanda F. Vallejo-Estrada, Ph.D., Yolanda.Vallejo-Estrada@nih.gov
NIH National Eye Institute — Tom Greenwell, PhD, greenwellt@mail.nih.gov; Neeraj Agarwal, Ph.D., agarwalnee@nei.nih.gov

CONTACT INFORMATION

Dr. Charles Cywin
Director, Small Molecule Neurotherapeutic Development
charles.cywin@nih.gov

Visit the BPN Webpage