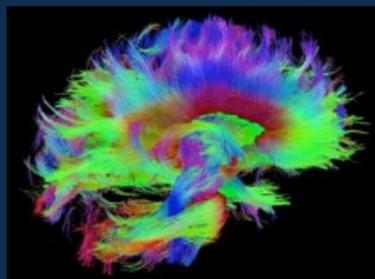
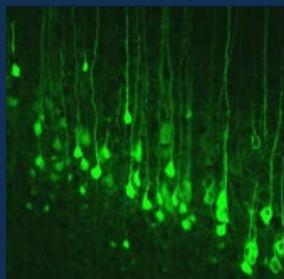


NIH **Blueprint**
for Neuroscience Research

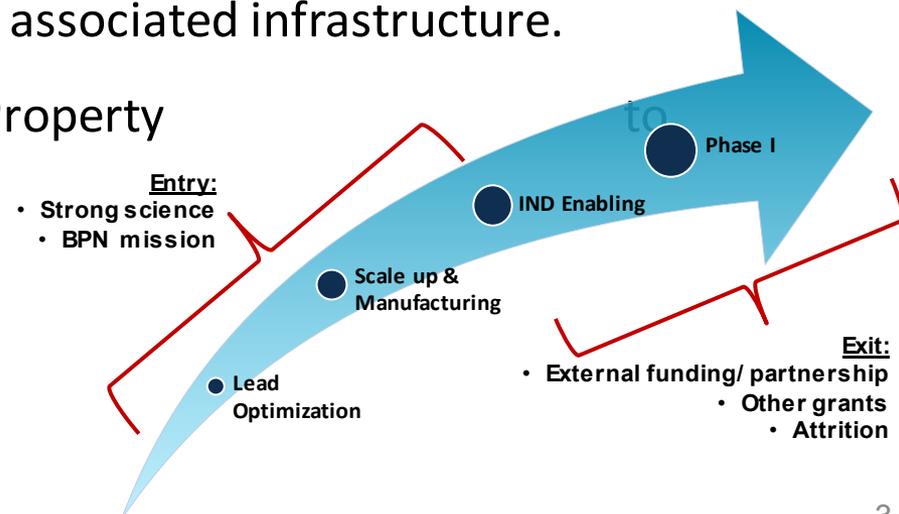
Blueprint Neurotherapeutics
Network for Biologics
(BPN-Biologics)
Q&A Webinar
May 5th, 2022



Mario Skiadopoulos, PhD
Program Director

- This webinar will be recorded.
- The recording will be made publicly available on our website.
- PDF copy of slides with embedded links will be emailed to registered attendees.
- Please use Q&A box to post all questions.
- Questions can be entered at any time and will be read during the Q&A session following the presentation (*some questions may be answered online*).
- For project-specific questions, we'll be better able to help if you send us your proposed Specific Aims and a year-to-year budget. We then can set up a call if needed.

- Program supports different biologic modalities, disease indications and entry points.
- Provide non-dilutive grant (PAR) funding and necessary resources (contracts, consultants, etc.) that are typically lacking in our research community.
- De-risk potential therapeutics to the point that industry will invest in them, allowing potential new drugs to reach patients efficiently.
- Identify the best ideas for translation in the NIH research community through this funding opportunity and associated infrastructure.
- Preserve PI/Institution's Intellectual Property facilitate licensing



- Program is for academics and small business
 - [PAR-21-163](#) (UG3/UH3) for all applicants
 - [PAR-21-233](#) (U44 Fast-track) for SBIR-eligible small businesses
- Grant funding to support biotherapeutic discovery and development projects into the clinic.
- Opportunity to get access to NIH-funded:
 - Consultants (drug discovery subject matter experts)
 - Contract research organizations (CROs)
 - Expert NIH Project Managers and Science Officers
- Multi-disciplinary Special Emphasis Panel (SEP) review



Next receipt date: August 9, 2022

Participating Institutes and Centers:



National Center for
Complementary and
Integrative Health

Hye-Sook Kim, PhD

hye-sook.kim@nih.gov



National Eye
Institute

Tom Greenwell, PhD

greenwellt@mail.nih.gov



National Institute
on Aging

Lorenzo Refolo, PhD

refolol@mail.nih.gov



National Institute
on Alcohol Abuse
and Alcoholism

Qi-Ying Liu, MD, MSci

liuqiy@mail.nih.gov



Eunice Kennedy Shriver National
Institute of Child Health and
Human Development

Zhaoxia Ren, PhD

zren@mail.nih.gov



National Institute
of Drug Abuse

Jason Sousa, PhD

jason.sousa@nih.gov



National Institute of
Dental and Craniofacial
Research

Melissa Ghim, PhD

melissa.ghim@nih.gov



National Institute
of Mental Health

Enrique Michelotti, PhD

michelottiel@mail.nih.gov



National Institute of
Neurological Disorders
and Stroke

Mario Skiadopoulos, PhD

Mario.skiadopoulos@nih.gov

Applications should focus on a single indication that falls within the mission of one of the participating ICs:

- Alzheimer's, mild cognitive impairment and other age-related dementias (**NIA**)
- Alcohol abuse and alcoholism (**NIAAA**)
- Diseases and disorders of the visual system, especially cataracts, glaucoma, age-related macular degeneration, retinitis pigmentosa and other conditions (**NEI**).
- Temporomandibular joint disorder, trigeminal neuropathies, burning mouth syndrome, and other painful disorders of the orofacial region (**NIDCR**).
- Developmental disorders, diseases and conditions in pediatric population (**NICHD**)
- Mental disorders, especially treatment-resistant depression, bipolar disorder, schizophrenia, PTSD, and autism spectrum disorder (**NIMH**)
- Neurological disorders and stroke (**NINDS**)
- Natural products and microbial therapies to modulate NS-based symptoms including pain, sleep disorders, anxiety disorders, mild depression and stress, etc. (**NCCIH**)
- Drug addiction and substance use disorders (**NIDA**)

A Customized Combination of Infrastructure, Expertise, and Funding

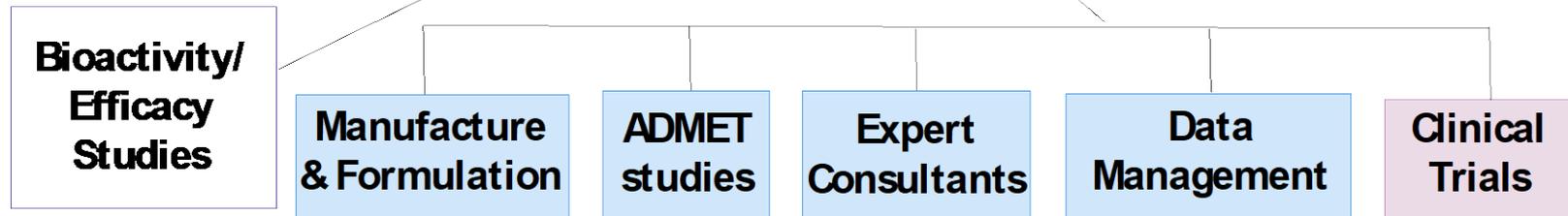
External Oversight Committee (EOC), 5-7 members

Lead Development Team:

- ✓ Principal Investigator
- ✓ Investigator's Team
- ✓ Industry-seasoned consultants
- ✓ NIH staff

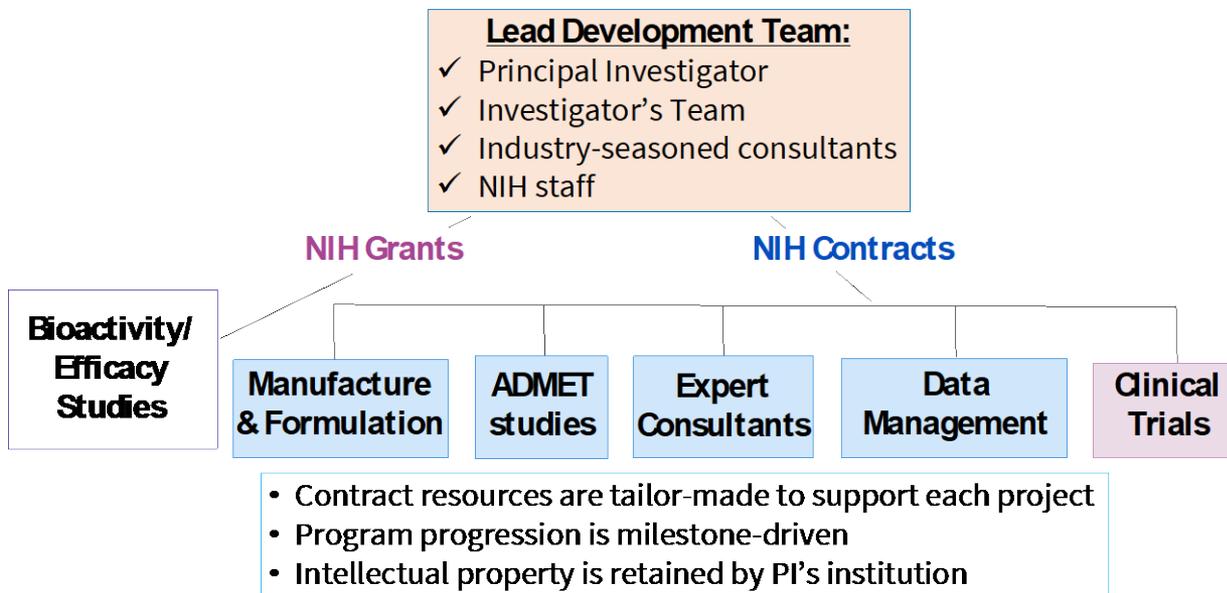
NIH Grants

NIH Contracts



- Contract resources are tailor-made to support each project
- Program progression is milestone-driven
- Intellectual property is retained by PI's institution

External Oversight Committee (EOC), 5-7 members



- FOA is written broadly to account for different modalities, disease indications and entry points
- Based on the modality and level of associated risk, there may be different trajectories and different expectations on what's really needed to be ready for the program – and to be successful within the program
- Proposals need to be very streamlined to get everything done within the desired time frame



Preclinical Services

Manufacturing
AAVs, ASOs, Peptides, Mabs,
Cell-based therapeutics, etc
Formulation
Fill-finish

Preclinical Studies
Bioassays Validation, PK/PD,
ADME, Toxicology,
Serological testing

Consultant SMEs



CMC

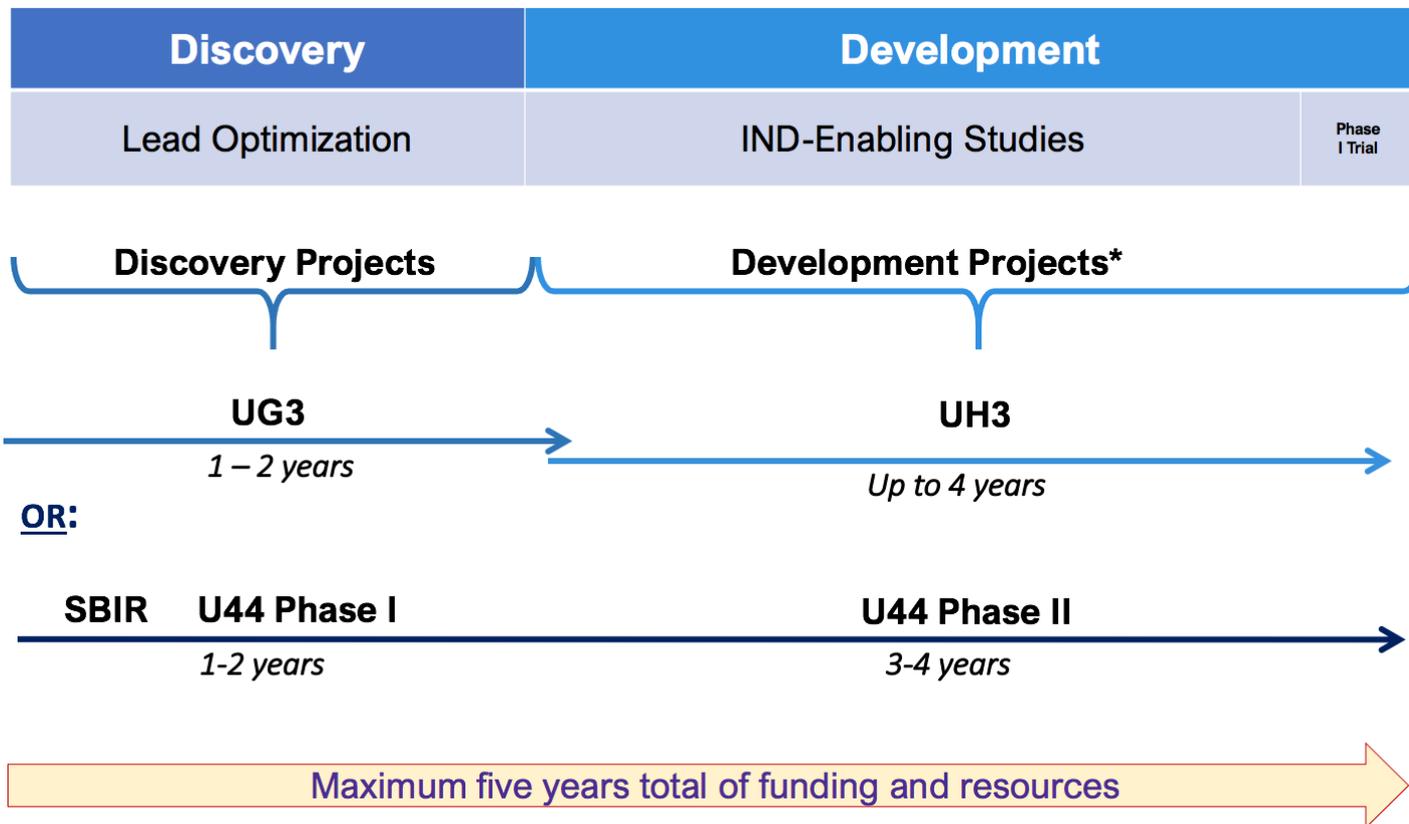
Regulatory

PK/Tox

Medical Writing

Quality

Biostatistics



Projects can enter at either the:

- Discovery stage: for lead characterization and optimization to improve the potency and/or suitability for clinical testing
- Development stage: to advance a development candidate through IND-enabling toxicology studies and Phase I clinical testing
- All Projects begin with a Preparatory Phase
- ***All projects should reach the clinical trial stage (regardless of entry point) within a maximum of 5 years***

* Not all ICs accept Development Projects

Mechanism	Mechanism Name	Length	Budget
UG3/UH3	Research Project, Cooperative Agreements	Up to 5 years (UG3 – up to 2 years)	Not limited, but must reflect the actual needs of the proposed project
U44	Small Business Innovation (SBIR) Cooperative Agreements <i>*Fast-track</i>	Phase I: Up to 2 years Phase II: Up to 3 years	Phase I: Up to \$500,000 per year*; Phase II: Up to \$1,500,000 per year. Must be reasonable and appropriate.

*NINDS rules check specific IC rules

Mechanism	Mechanism Name	Length	Budget
UG3/UH3	Research Project, Cooperative Agreements	Up to 5 years (UG3 – up to 2 years)	Not limited, but must reflect the actual needs of the proposed project
U44	Small Business Innovation (SBIR) Cooperative Agreements <i>*Fast-track</i>	Phase I: Up to 2 years Phase II: Up to 3 years	Phase I: Up to \$500,000 per year*; Phase II: Up to \$1,500,000 per year. Must be reasonable and appropriate.

*NINDS rules check specific IC rules

Applications from Foreign Organizations: Reviewers will assess whether the project presents special opportunities for furthering research programs through the use of unusual talent, resources, populations, or environmental conditions that exist in other countries and either are not readily available in the United States or augment existing U.S. resources.

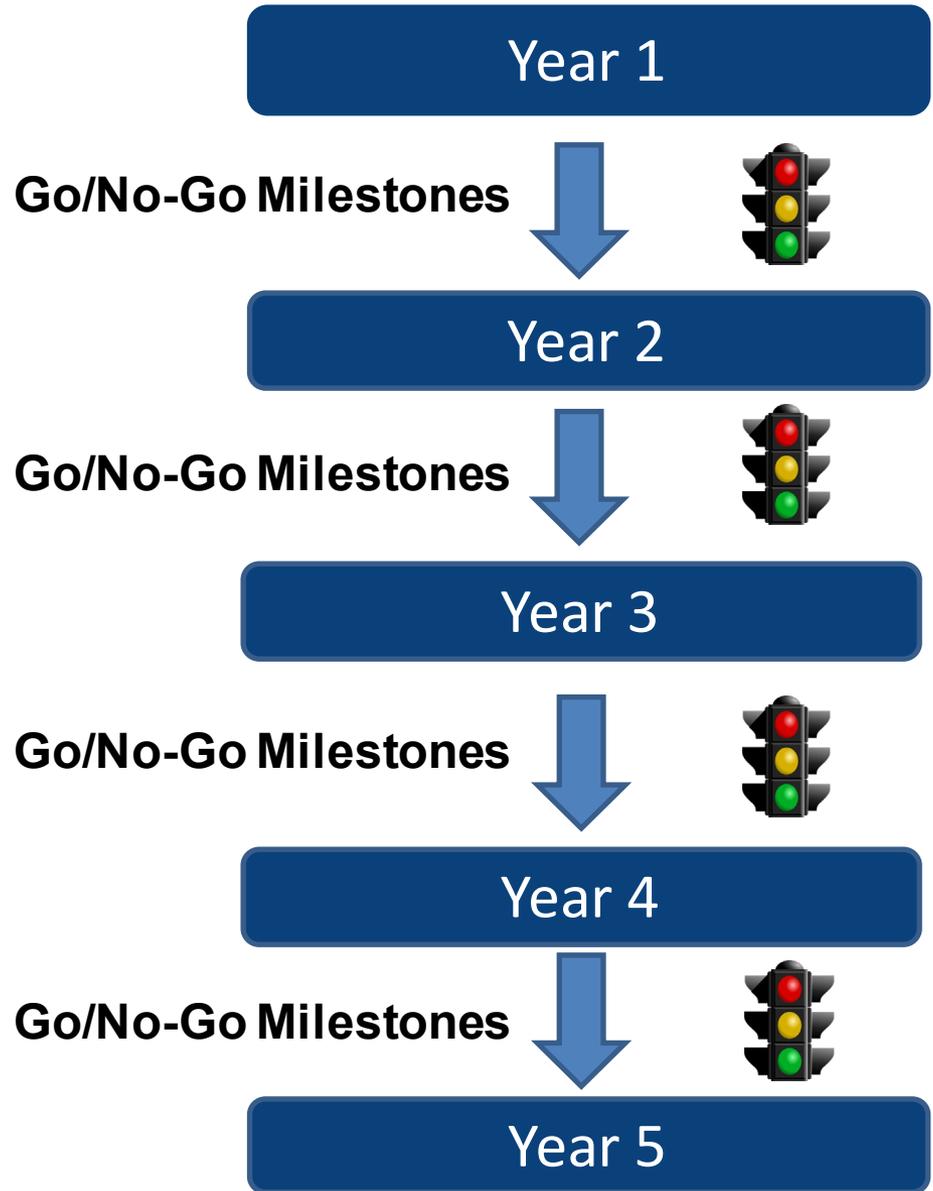


- Inventorship determined per US patent law
- NIH Blueprint has no stake in the IP
- Prior to grant award, PI's institution must have up-front IP agreements in place with all potential inventors. These agreements must address:
 - Who will hold title to IP on new biochemical matter/use
 - Royalty arrangements
- IP agreements should aim for unencumbered IP, consistent with the Blueprint program goal to create a licensable product

*Clear, Quantitative and
Definitive Milestones are
Essential*

*Annual Go/No-Go point
at the end of each year*

*Transition occurs via
Administrative Review*



Entry Criteria for Discovery Stage Projects:

- Identified one or more lead biologic agent(s) sufficiently profiled so that the parameters still to be optimized can be quantitatively specified.
- Established preliminary *in vivo* efficacy* and target engagement data using agent(s) in relevant animal model(s).
- Key *in vitro* and *in vivo* assays are suitable to drive characterization and optimization of the biologic agent(s)
- No obvious legal/IP constraints



End Goals:

- A clinical candidate with appropriate bioactivity, stability, manufacturability, and bioavailability by the intended ROA for development.
- Target engagement with defined minimal and optimal doses by the intended ROA and *in vivo* efficacy when applicable.

Example activities supported during the Discovery UG3 phase:

- Characterization of identity and properties
- Lead optimization to improve effectiveness, diminish toxicity, and improve ADME
- Optimization and/or qualification of appropriate assays for PK, target engagement, biodistribution, or other assays to monitor safety available to be used in the UH
- Determination of optimal route of administration (ROA)
- Demonstration of adequate/stage-appropriate preliminary safety, such as safety pharmacology and/or dose-range finding toxicology

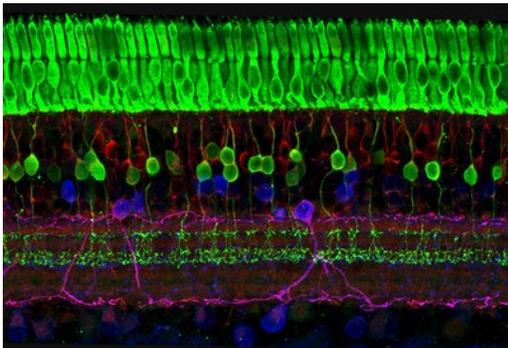


Image Credit: Wei Li, NEI

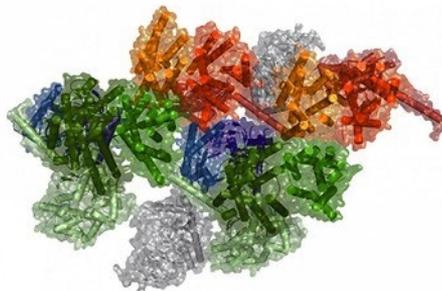


Image credit: Sergi Ferre, NIDA



All applications proposing to enter at the Development stage will begin with a UG3-funded phase (up to two years).

Entry Criteria for the Development Stage:

- A strong body of data linking the putative therapeutic target to the proposed disease indication
- Rationally laid out biological activity by the planned ROA with exposure levels for activity being achievable based on ADME properties appropriate for the intended clinical use.
- Demonstration of the PD/PI's institution ability to develop or commercialize the proposed biologic

End Goals:

- Submission of IND package
- Phase I Clinical Trial



Development stage activities in preparation for IND-enabling studies:

- Non-GLP toxicology studies (i.e., dose-range finding toxicology)
- Formulation
- Scale up manufacture and stability studies
- Repeat of *in vivo* studies in the same or a different animal model
- A pre-IND meeting with FDA, if not already conducted

Development Activities include the following:

- cGMP manufacturing of material for IND-enabling and/or Phase I clinical testing
- IND-enabling safety and tox studies to determine a basis for clinical dose extrapolation using a relevant animal model
- Preparation and filing of the IND document
- Phase I clinical trial

Clinical Trial Design:

- Single dose or SAD which may be placebo-controlled or open-label studies
- MAD may be requested only if agent has a short half-life
- CT outcomes may include safety, tolerability, PK/PD, target engagement and target modulation endpoints
- BPN-Biologics contractors can conduct Phase I CTs for investigational agents that may include large biomacromolecules in healthy volunteers or demographic subsets of healthy volunteers.
- If only diseased patients are expected to be enrolled, the applicants' own clinical site(s) must be proposed.
- Applicants are **strongly advised** to discuss plans with NIH program staff prior to submitting their application to determine whether a CT is feasible within the proposed timeframe and/or available BPN-Biologics contract resources.

- Read the entire Funding Opportunity Announcement carefully
- Discuss your proposal with NIH BPN-Biologics Program Director (PD) home Institute's PD for disease interest
- Contact SBIR PD for SBIR specific issues
- Put forth solid scientific preliminary data to support your proposal and address the rigor of that data in your research strategy section
- Clearly indicate what will be done as part of the grant and what is expected to be done by NIH BPN-Biologics contractors
- Include all activities required to submit an IND package to the FDA
- Include budget pages for all years of the grant

Address Rigor

Preliminary and supporting data

- Explicitly discuss the quality of the data presented in prior publications in a detailed manner. *Were they done in a rigorous manner, utilizing randomization, blinding, inclusion/exclusion criteria and the appropriate power analysis?*

Approach

- Provide details for the controls being used for each type of experiment and appropriately highlight potential confounds like surgery exposure, genotype, 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

DISCOVERY STAGE (UG3 or U44 Phase I)

Lead Optimization Specific Aims (Milestones):

1. Lead Candidate(s) Optimization activities to optimize/down select final lead candidate
2. Small scale manufacture (as needed)
3. *In vitro* characterization studies (as needed)
4. *In vivo* characterization (as needed)
5. Delivery routes optimization
6. Dose range determination
7. Pre clinical and clinical bioassays validation
8. Preliminary PK/PD, toxicology studies
9. Final clinical lead candidate down selection
10. FDA meeting (e.g., INTERACT, pre IND)

DEVELOPMENT STAGE (UH3 or U44 Phase II)

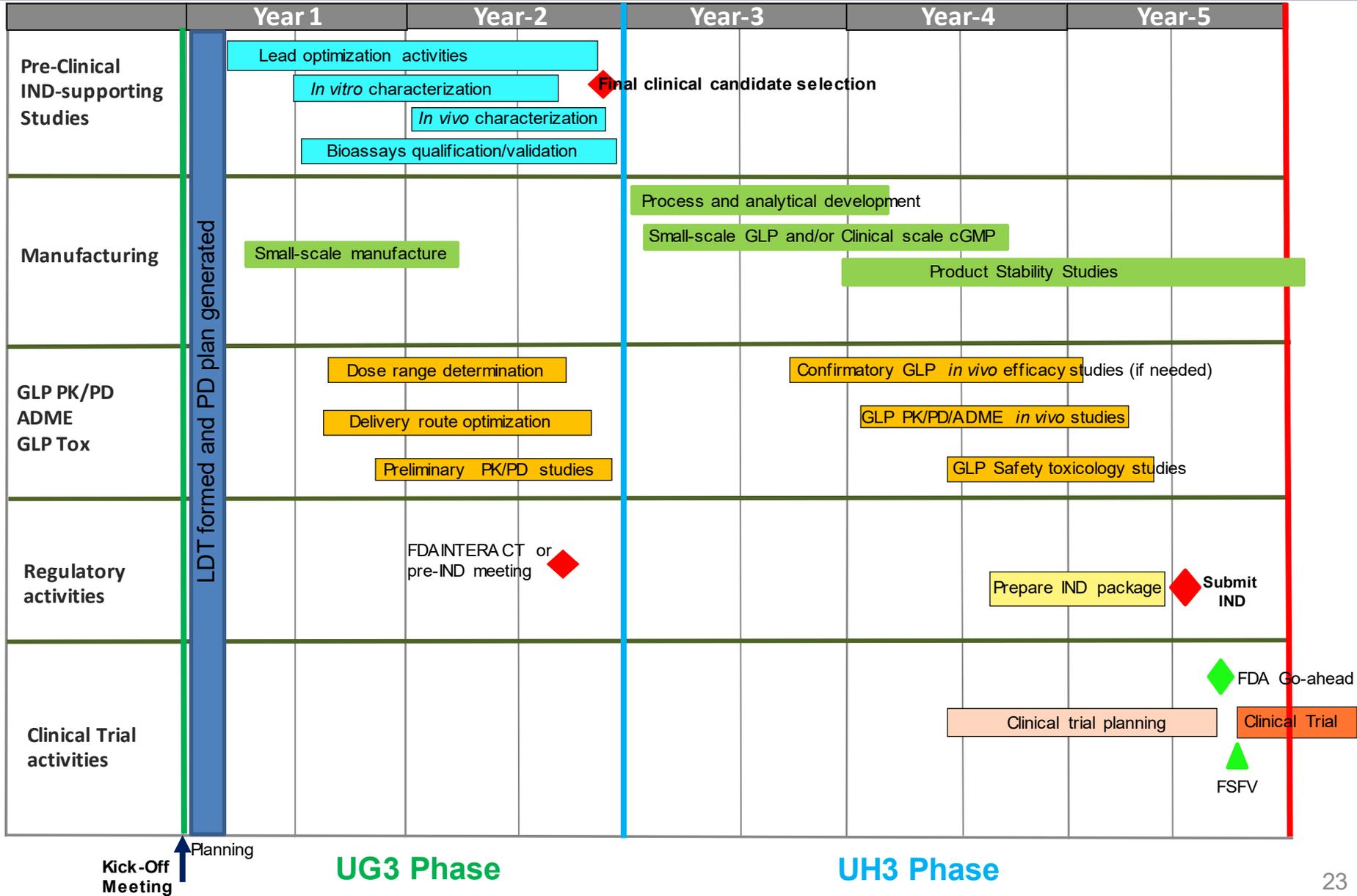
cGMP Manufacturing Specific Aims (Milestones):

11. Process and analytical development
 12. Small-scale GLP and/or clinical scale cGMP manufacturing
 13. Fill-Finish, release testing, and product stability studies
- Pre-clinical IND enabling studies:**
14. Confirmatory *in vivo* efficacy study using cGMP material (if required)
 15. GLP PK/PD study using cGMP material in appropriate animal model(s)
 16. Safety toxicology studies using cGMP material in appropriate animal model(s)
 17. IND package preparation and submission (required)
 18. Phase 1 clinical trial preparation (optional)
 19. Phase 1 clinical trial initiation (optional)

Please note: *Specific Aims will vary by project; the order of the listed activities may also vary according to the needs of the project. The activities listed above are general examples, not all of them may need to be included, and there may be some activities, not listed here, that will be required for a specific project.*



Example of product development swimlane diagram



- Complete your required registrations at least 6-8 weeks in advance of receipt dates.
- If you are applying to the UG3/UH3 FOA and **ANY** proposed budget year exceeds \$500K in direct costs (excluding F&A) then you need permission to submit. Requests **must** be made at least 6-8 weeks prior to submission date.
- Talk with your tech transfer/BD group.
 - Need to plan for funding patents and licensing activities

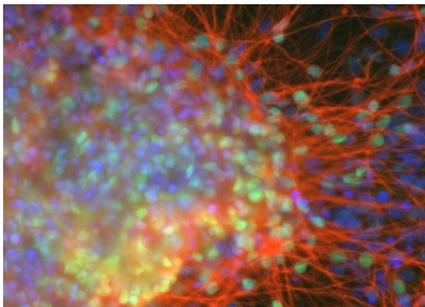


Image credit: NCATS

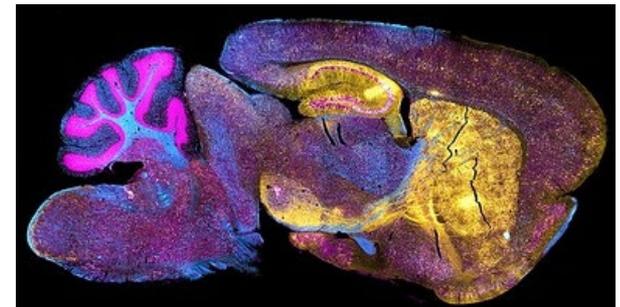


Image credit: I. Williams, NICHD



Things NOT to do

- Please do not plan for this to be sole funding for your lab
 - Milestone driven program can end abruptly.
- Please do not under-resource your budget to avoid limits
- Please do not plan for BPN contracts for disease biology or one-off in vitro ADMET experiments.
- Please do not code your application as Clinical Trial if your plan is to use the BPN contractors.
 - If you do plan to run your own trial it will be a delayed onset

<https://neuroscienceblueprint.nih.gov/neurotherapeutics/bpn-biologics>

Neurotherapeutics

Blueprint Neurotherapeutics Network (BPN) for Small Molecules

Blueprint Neurotherapeutics Network for Biologics (BPN-Biologics)

BPN Funding Opportunities

How BPN-Biologics Works: The Virtual Pharma Model

BPN-Biologics Resources

BPN-Biologics Frequently Asked Questions

BPN-Biologics Participating Institutes and Contacts

External Oversight Committee (EOC)

Other NIH Programs for Translational Neuroscience that Support Biologics

Blueprint MedTech

Blueprint Neurotherapeutics Network for Biologics (BPN-Biologics)

Recent advances in biology offer unprecedented opportunities to discover new treatments for nervous system disorders. Biotherapeutic development, however, has inherent complexities with regards to characterization, manufacturing, delivery, and administration. Many academic laboratories and small business enterprises don't have the full scope of expertise and resources needed to translate and guide their therapeutics into the clinic. For instance, all therapeutic candidates including biologics, must obtain the requisite toxicology and safety pharmacology data package and undergo regulatory review by the Food and Drug Administration (FDA). If the researchers cannot successfully navigate or overcome these hurdles, they may ultimately have difficulty attracting venture capital investment or pharmaceutical industry interest.

Building upon the success of BPN for small molecules, the NIH Blueprint for Neuroscience Research established the **Blueprint Neurotherapeutics Network for Biologics (BPN-Biologics)**, which includes the spectrum of biologics:

- biotechnology products and biologics-based therapies (e.g., peptides, proteins)
- gene-based therapies (e.g., oligonucleotide and viral based)
- cell therapies, and
- other novel emerging therapies (e.g., microbial and microbiome therapies)

BPN-Biologics provides non-dilutive funding and resources for biotherapeutic drug discovery and development, from lead optimization through phase I clinical testing. We offer grant funding for work that you intend to do yourself and in-kind access to NIH-funded contract research organizations (CROs) for activities that you prefer to outsource and consultants with expertise in various aspects of drug discovery and development. You decide which combination of funding, CROs, and consultants will best fit your drug development needs. In addition, your institution is assigned the intellectual property rights to therapeutic agents discovered and developed within the program.

[View the June 7, 2021 BPN-Biologics Q&A Webinar](#)

[View the October 20, 2021 BPN-Biologics Q&A Webinar](#)

Current BPN-Biologics funding opportunities:

[PAR-21-163](#) Blueprint Neurotherapeutics Network (BPN): Biologic-based Drug Discovery and Development for Disorders of the Nervous System (UG3/UH3 [Clinical Trial](#) Optional)

[PAR-21-233](#) Blueprint Neurotherapeutics Network (BPN): Biologic-based Drug Discovery and Development for Disorders of the Nervous System (U44 [Clinical Trial](#) Optional)

Please email your inquiries to: bpn-biologics.questions@nih.gov

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.

Program Director

Charles Cywin, PhD
charles.cywin@nih.gov

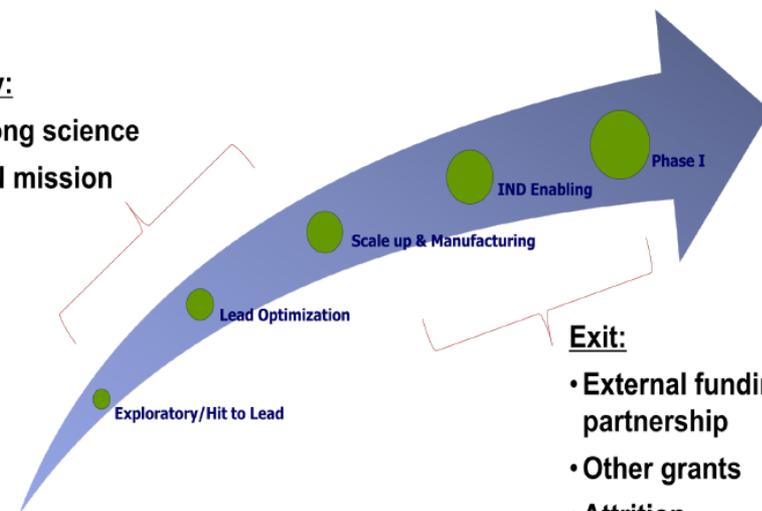


<https://neuroscienceblueprint.nih.gov/bpdrugs/>



Entry:

- Strong science
- BPN mission



Exit:

- External funding/
partnership
- Other grants
- Attrition

**Next Application Receipt Date:
August 9th 2022**





Additional information can be found at:

Our website



BPN-Biologics FAQs



For your project-specific questions, please email inquiries to:

bpn-biologics.questions@nih.gov

BPN-Biologics Staff:

Program Director: Mario Skiadopoulos, PhD

Health Program Specialist: Elena Barnaeva, MS

Health Program Specialist: Shruthi Thomas, MS

mario.skiadopoulos@nih.gov

elena.barnaeva@nih.gov

shruthi.thomas@nih.gov