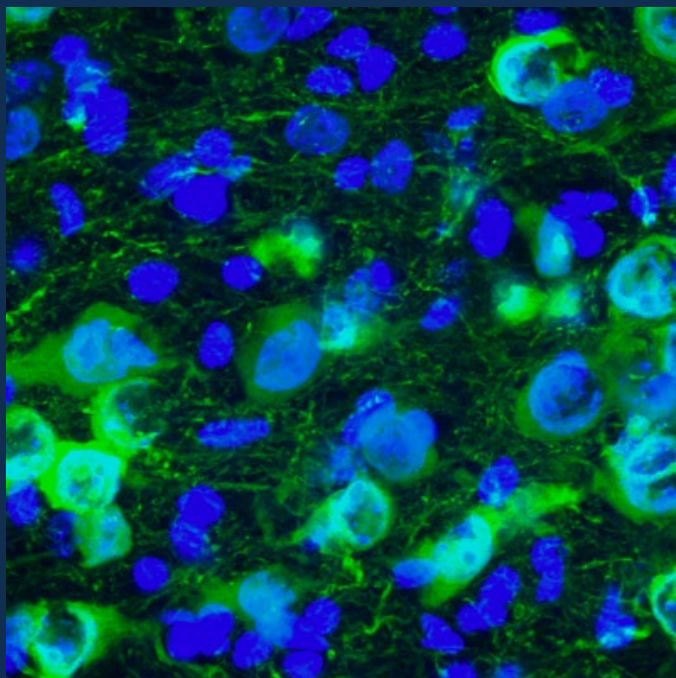


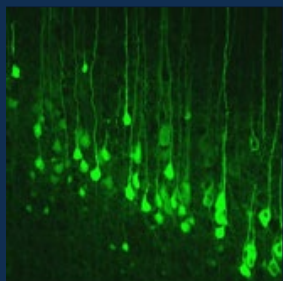


NIH **Blueprint**
for Neuroscience Research

Blueprint Neurotherapeutics Network for Biologics (BPN-Biologics)

Q&A Webinar

June 7th 2021



Ann-Marie Broome, PhD, MBA
Program Director, Biologics

- 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 by a presenter 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 an aims page and we can set up a call.

***“Combine Strengths of NIH and Industry Expertise
for Neuroscience Drug Discovery”***

NIH investigator-initiated ideas

- Solid scientific premise
- Expert disease biology - assays and models

Industry expertise

- Consultants with extensive pharma experience across all R&D disciplines
- Pre-established industry-standard contract services

End Goals

- Maintain IP
- Decreased risk as projects advance
- Advance projects to clinic and hand-off

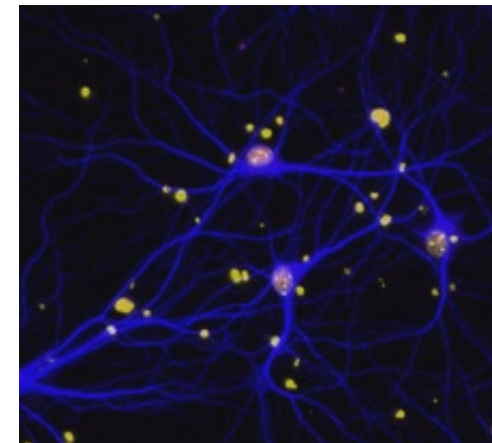
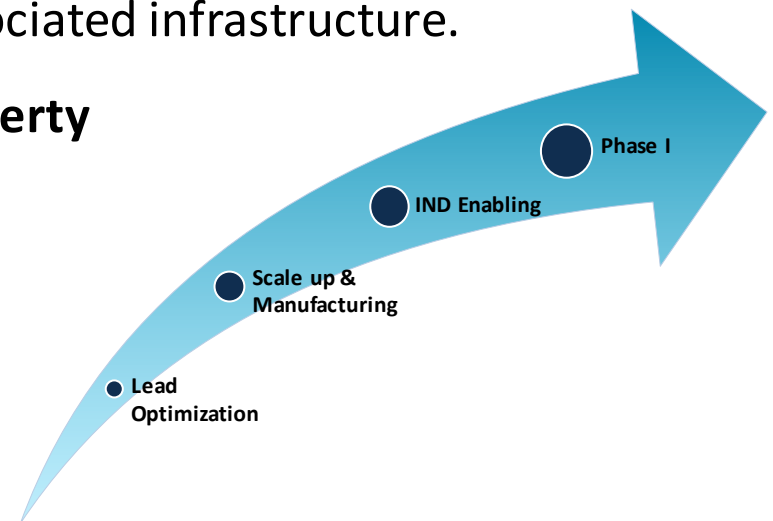


Image Credit: Lennart Mucke,
University of California, San Francisco

- Program broadly accounts for 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 to 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



Upcoming receipt dates: August 10, 2021, and February 9, 2022



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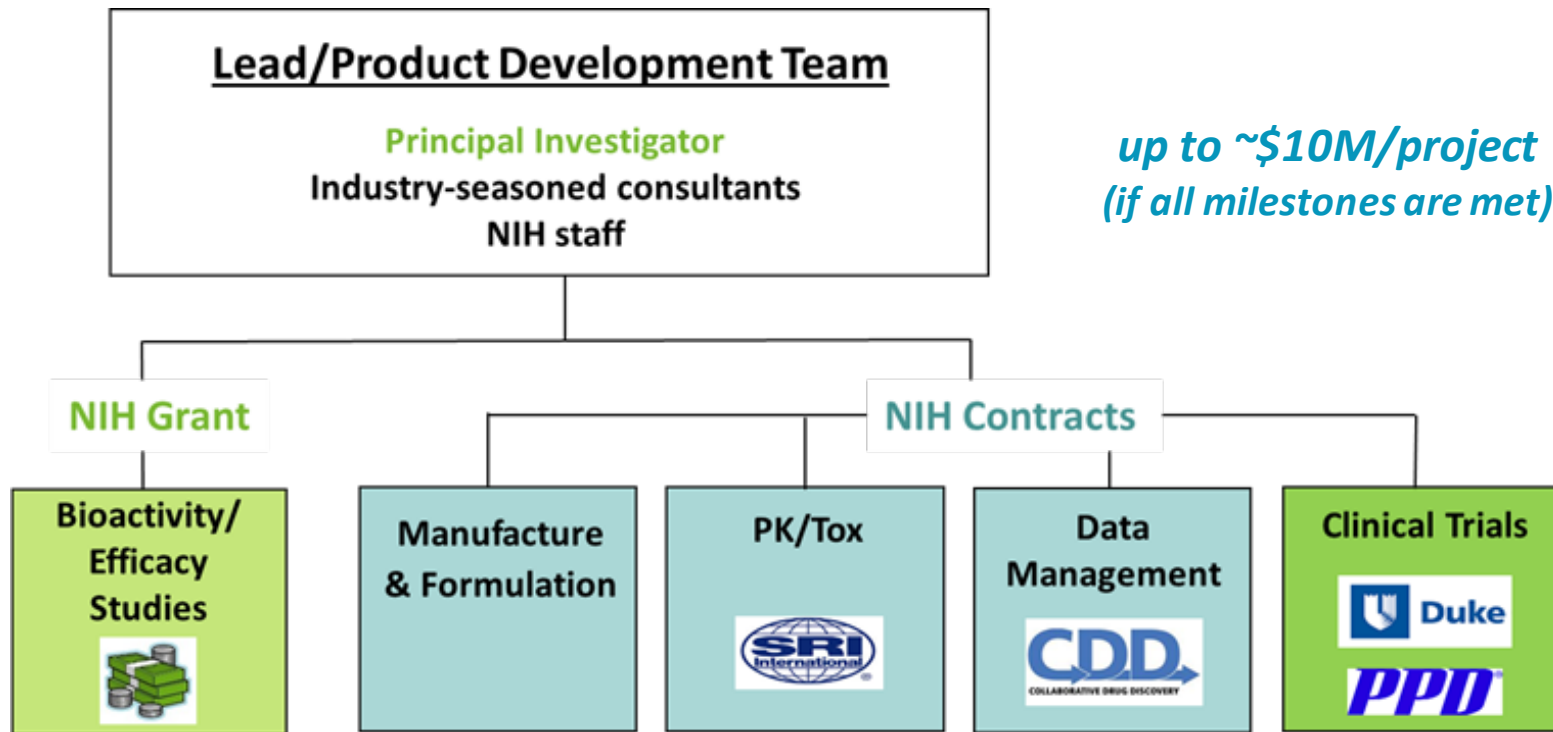


Zhaoxia Ren, PhD
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Applications should focus on a single indication that falls within the mission of one of the participating ICs:

- 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 Funds



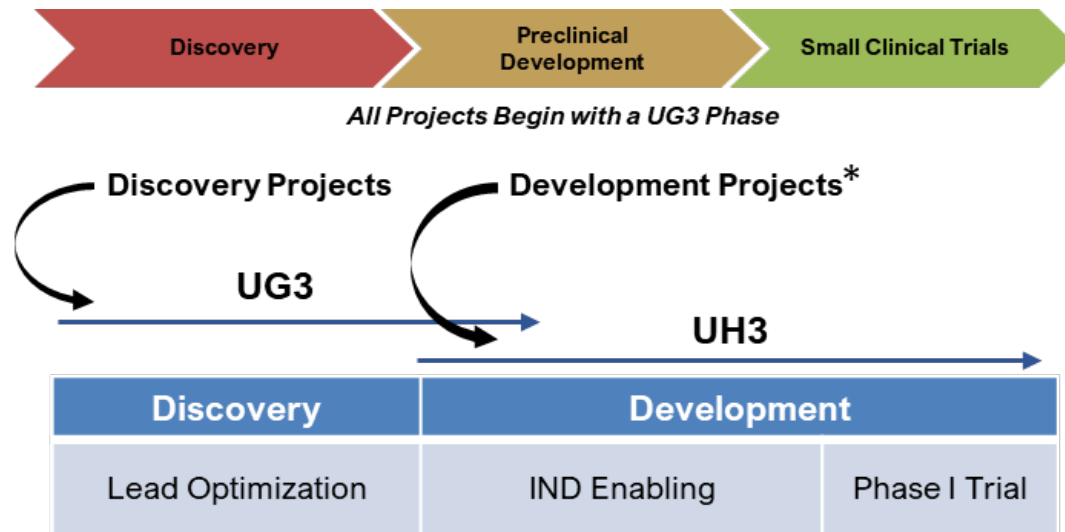
- Contract resources are tailor-made to support each project
- Flexibility in the mix of contract access and grant support
- PI team's Intellectual Property retained by PI's Institution

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



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



*Not all ICs accept Development Projects

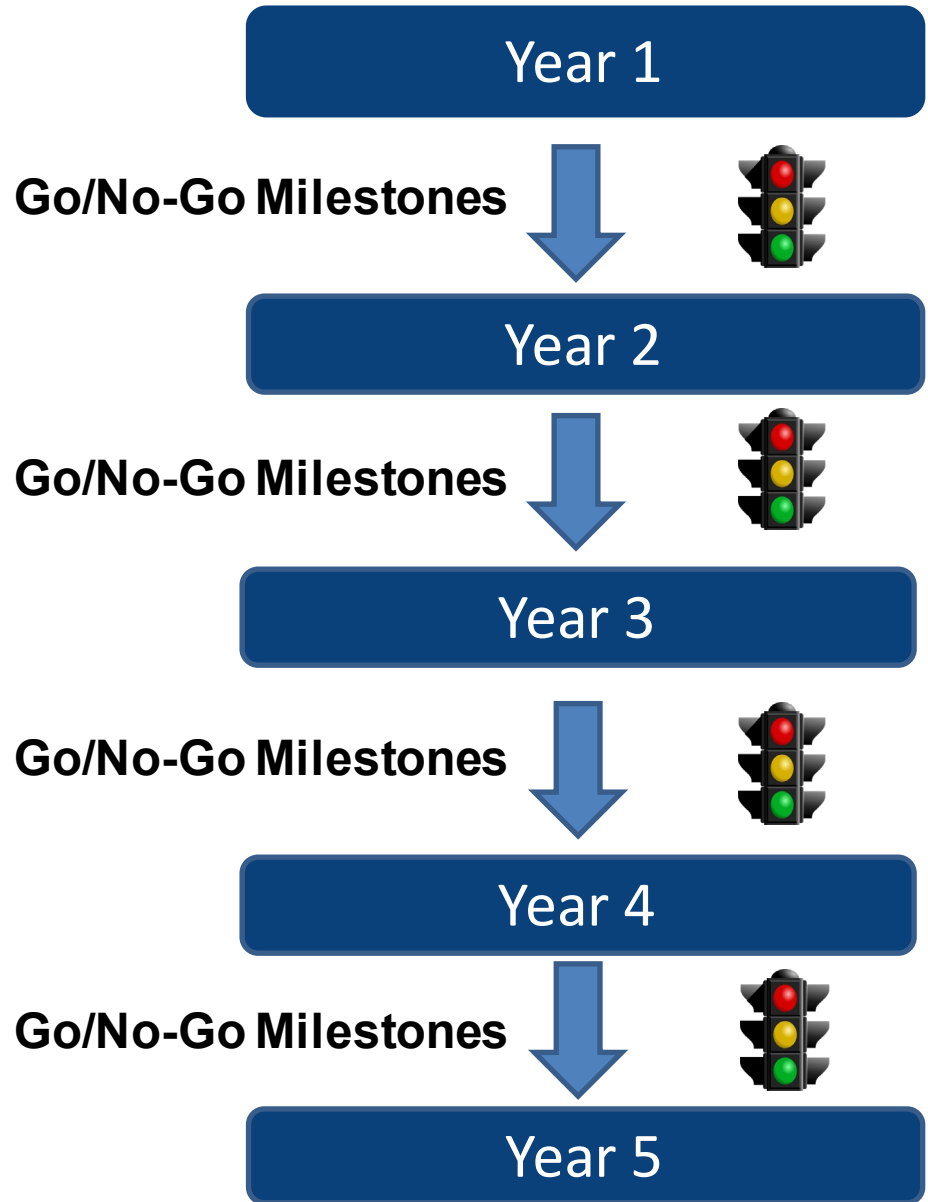
All projects should reach the clinical trial stage (regardless of entry point) within a maximum of 5 years

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 \$700,000 per year; Phase II: Up to \$1,500,000 per year. Must be reasonable and appropriate.

*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

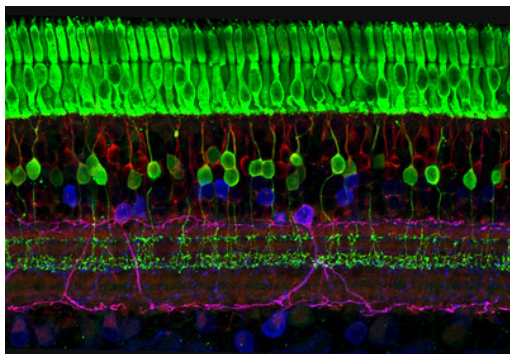


Image Credit: Wei Li, NEI

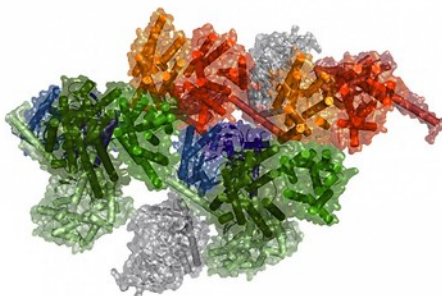


Image credit: Sergi Ferre, NIDA



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 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
- Address obvious criticisms of the biology
- Clearly indicate what will be done as part of the grant and what is expected to be done by BPN-Biologics contractors
- Include budget pages for all years of the grant

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

- 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 6-8 weeks prior to submission date.
- Talk with your tech transfer/BD group.
 - Need to plan for funding patents and licensing activities

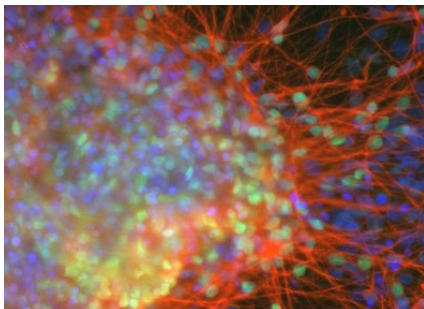


Image credit: NCATS

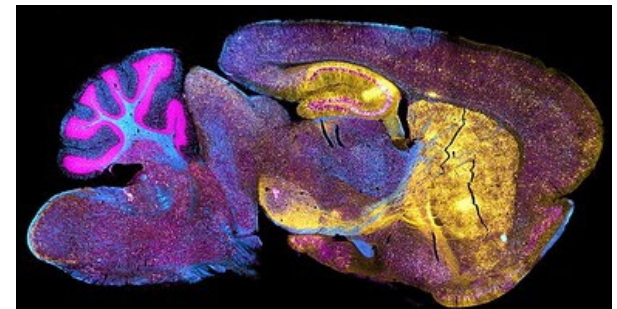


Image credit: I. Williams, NICHD

- Do not plan for this to be the sole funding for your lab.
 - Milestone driven program can end abruptly.
- Do not under-resource your budget to avoid limits.
- Do not plan for BPN-Biologics contracts for disease biology or one-off *in vitro* ADMET experiments.
- Do not code your application as clinical trial if your plan is to use the BPN-Biologics 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

Other NIH Programs for
Translational Neuroscience
that Support Biologics

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 all the Blueprint Neurotherapeutics funding opportunities.](#)

Questions after the webinar is completed?

Additional information can be found on our [BPN-Biologics website](#)

For project-specific questions, please contact us by email.

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Coronavirus Disease 2019 (COVID-19):
[Information for NIH Applicants and Recipients of NIH Funding](#)