Technology Development/Transfer Opportunities:
Working with Federal Laboratories

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Marymount University Ballston Campus
Working with Federal Laboratories

- Mechanisms
- Examples
- Test Three Common Assumptions
- New Translational Paradigms at NIH
Variety of Mechanisms and Programs Offered by Each Federal Laboratory

- License inventions made by federal laboratories
- Collaborate with scientists working in federal laboratories
- SBIR-Technology Transfer (NIST, NIH)
- Gain access to unique equipment or facilities
- Obtain samples of research materials or tissues
- Gain access to drug development expertise and resources
Examples from NIH

- **License & CRADA:**
  - A small business licenses an NCTT invention, and collaborates with the NCTT inventors under a CRADA. The invention is developed into a commercial product marketed by the small business.

- **Drug Development Resources:**
  - A university start-up or small business receives resources through NCTT Bridging Interventional Development Gaps (BrIDGs). BrIDGs is intended to advance promising therapies into the clinic by providing in-kind services to overcome late stage preclinical therapy development obstacles.

- **Unique Testing Facilities:**
  - Tox21 Initiative uses quantitative high throughput screening (qHTS) approach to profile a collection of 10,000 compounds composed of environmental chemicals and drugs approved for human and animal use against a battery of cellular and biochemical assays for their potential to perturb biological pathways that may result in toxicity.
Test Three Common Assumptions about Collaborating with Federal Laboratories
Assumption #1

Would the federal government take control of the business?

• Reality
  • Company retains ownership of inventions made by its employees made under a government grant or contract
  • Company retains ownership of inventions made by its employees under a Cooperative Research and Development Agreement (CRADA)
  • Government retains a non-exclusive royalty-free license to practice

• Lessons/Opportunities
  • Consider how a company may advance a project using resources from a federal laboratory
Assumption #2

Are agreement terms with Federal Laboratories rigid? Do they take a long time to establish?

- Reality
  - Some terms are in the agreement because the terms are required by statute, regulation, or essential policies of the federal laboratory
  - Other terms may be fully negotiable
  - Timelines vary -- from months to days
- Lessons/Opportunities:
  - Talk with the negotiator from the federal laboratory to gain a realistic perspective (project and mechanism specific)
  - Talk with the negotiator from the federal laboratory before undertaking a major mark-up of a federal template
  - When selecting outside counsel, consider their depth of experience with federal agreements/contracts
Assumption #3

Is it hard to fine information about resources and programs?

- Reality
  - Federal laboratories are required by law and policy to be transparent. Federal laboratories post information on opportunities.
  - Decentralized. Location and timing of announcements varies by agency, program and by mechanism.

- Opportunity:
  - Sign up to receive announcements from federal laboratories of interest
  - FLC-Mid Atlantic is compiling a list of available resources at Federal Labs in the Mid-Atlantic Region.
The Changing Landscape of Translational Therapeutics Discovery

NIH Center for Translational Therapeutics
National Institutes of Health
NIH Center for Translational Therapeutics: An Integrated Pipeline

Project Entry Point

- Unvalidated target
- Validated target
- Target assay
- Lead compound
- Preclinical development candidate
- Clinical development candidate

Target Validation

- RNAi
- Probe Development
- Preclinical Development/TRAAD

Assay Dev

- NIH-RAID
- Clinical Trials
- FDA approval

Probe/Lead Development

- Systems Toxicology
- Repurposing
- Paradigm/Technology Development

Preclinical Optimization

- Leads for therapeutic development
- Approved drugs effective for new indications
- Drugs suitable for adoption for further development
- Novel clinical trial designs

Preclinical Development

- Small molecule and siRNA research probes
- Predictive in vitro toxicology profiles
- More efficient/faster/cheaper translation and therapeutic development

Clinical Trials

- Approved drugs effective for new indications
- Drugs suitable for adoption for further development
- Novel clinical trial designs

Genome-wide RNAi systems biology data

Chemical genomics systems biology data

Leads for therapeutic development

Approved drugs effective for new indications

New drugs for untreatable diseases

Deliverables

NCTT
The Problem of Rare and Neglected Diseases

• ~7,000 diseases affect humankind – but only a small fraction support commercial development of therapeutic agents

• Two types of neglected diseases:
  – Low prevalence, i.e., “rare” (<200,000 prevalence in U.S.)
    • There are >6000 rare (orphan) diseases
    • Cumulative prevalence in U.S. ~ 25 – 30 million
    • Most are single gene diseases
    • <200 have any pharmacotherapy available
  – High prevalence but “neglected”
    • Occur chiefly among impoverished and marginalized populations in developing nations (treatment costs prohibitive)
    • Most are infectious
Economics and risks of drug development

Probability of success

Cumulative Cost

Dedicated Chem-Biol Project Team formed

Compound accepted into Clinical Development

Target identification

Assay development

Screening (HTS or otherwise)

Hit-to-Probe

~ 3 yrs

1 yr

1 yr

1 yr

Indefinite

1 yr

2 yrs

~3 yrs

Ph I

Ph II

Ph III

Clinical Trials

1.5 yrs

Regulatory review

Ph IV-V (Additional indications, Safety monitoring)

Indefinite

~3 yrs
Conventional roles of public and private sectors in drug development

**Probability of success**

**Cumulative Cost**

**NIH-Funded Basic Science**

**Pharma and Biotech**

**FDA**

- **Ph II**
  - Compound accepted into Clinical Development
  - Lead Development, Optimization
  - Clinical Trials
  - Probability of success (HTS or otherwise)

- **Ph I**
  - Assay development
  - Lead Development, Optimization
  - Clinical Trials

- **Ph III**
  - Hit-to-Probe
  - Clinical Trials

- **Ph IV-V**
  - Regulatory review

**Dedicated Chem-Biol Project Team formed**

- Dedicated Chem-Biol Project Team formed
- Compound accepted into Clinical Development

**Timeline**

- Indefinite
- 1 yr
- 1 yr
- 1 yr
- ~3 yrs
- 1 yr
- 2 yrs
- ~3 yrs
- 1.5 yrs
- Indefinite
- Ph IV-V (Additional indications, Safety monitoring)
Molecular Libraries and Imaging

OVERVIEW

Small molecules, often with molecular weights of 500 or below, have proven to be extremely important to researchers to explore function at the molecular, cellular, and in vivo level. Such molecules have also been proven to be valuable for treating diseases, and most medicines marketed today are from this class.

"...To empower the research community to use small molecule compounds in their research, whether as tools to perturb genes and pathways, or as starting points to the development of new therapeutics for human disease."
Molecular Libraries program takes first steps in drug development

Public Sector Science with MLI

- Dedicated Chem-Biol Project Team formed
- Compound accepted into Clinical Development

- Target identification
- Assay development
- Screening (HTS or otherwise)
- Hit-to-Probe
- Lead Development, Optimization
- Ph I (Safety)
- Ph II (Dose finding, initial efficacy in patient pop.)
- Ph III (Efficacy and safety in large populations)
- Ph IV-V (Additional indications, Safety monitoring)

Cumulative Cost

Probability of success
The long pathway to drug development

**Basic Research**

- **NCGC, Molecular Libraries Initiative**
  - Indefinite
  - Identify Target
  - 3 yrs
  - Identify chemical starting point for drug

**“Valley of Death”**

- NIH RAID
  - 4 yrs
  - Make many chemical modifications to give drug beneficial effect without side effects

**Pharmas, Biotechs NIH Clinical Center, Academic Clinical Centers**

- Ph I
  - 1 yr
- Ph II
  - 2 yrs
- Ph III
  - ~3 yrs
- Review
  - FDA
  - 1 yr

**Patient Use**

1 yr
The long pathway to drug development

Basic Research

NCGC, Molecular Libraries Initiative

3 yrs

Indefinite

Identify Target

Identify chemical starting point for drug

4 yrs

Make many chemical modifications to give drug beneficial effect without side effects

1 yr

Ph I

Ph II

Ph III

~3 yrs

IND

Pharma, Biotechs
NIH Clinical Center, Academic Clinical Centers

NIH RAID

TRND

FDA

1 yr

Patient Use

Review
NIH Therapeutics for Rare and Neglected Diseases (TRND) Program

Creating a Drug Development Pipeline at NIH

• Congressionally-mandated effort to speed development of new drugs for rare and neglected diseases
• Administration and governance at NIH
  – Governance/oversight by Office of Rare Diseases Research
  – Administered by NHGRI
• Operations: collaboration between intramural and extramural labs with appropriate expertise
• Projects will:
  – Enter TRND at a variety of stages of development
  – Be taken to phase needed for external organization to adopt for clinical development
TRND Science

- In-house laboratories with expertise in preclinical drug development will collaborate with external laboratories with expertise in disease/target.

- Distinguishing features
  - Disease agnostic, take advantage of cross-cutting mechanisms
    - “Diseaseome” approach
  - *Science* of preclinical drug development
    - Reasons for successes and failures will be investigated and published
  - Technology/paradigm development
    - 20% of effort, toward improving success rates
  - Large-scale systematic repurposing

- Project-specific activities
  - Medicinal chemistry
  - Efficacy, pharmacology, ADME, toxicology, PK/PD
  - Compound scale-up, formulation
  - First in human clinical trials as needed for project
### TRND Pilot Projects

Chosen to establish processes in advance of solicitation, with diversity of project stage, type of disease and collaborators.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Type</th>
<th>Pathology</th>
<th>Collaborators</th>
<th>Compound type</th>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schistosomiasis, Hookworm</td>
<td>Neglected</td>
<td>Infectious parasite</td>
<td>Extramural</td>
<td>NME</td>
<td>Early (lead optimization)</td>
</tr>
<tr>
<td>Niemann Pick C</td>
<td>Rare</td>
<td>CNS, liver/spleen</td>
<td>Disease Fnd, Extramural, Intramural</td>
<td>Repurposed approved drug</td>
<td>Mid-stage</td>
</tr>
<tr>
<td>HIBM</td>
<td>Rare</td>
<td>Muscle</td>
<td>Biotech, Intramural</td>
<td>Intermediate replacement</td>
<td>Pre-IND</td>
</tr>
<tr>
<td>Sickle Cell Disease</td>
<td>Rare</td>
<td>Blood</td>
<td>Nonprofit, Intramural, Extramural</td>
<td>NME</td>
<td>Mid-stage</td>
</tr>
<tr>
<td>Chronic Lymphocytic Leukemia</td>
<td>Rare</td>
<td>Cancer</td>
<td>Disease Fnd, Extramural</td>
<td>Repurposed approved drug</td>
<td>Pre-IND</td>
</tr>
</tbody>
</table>
TRND Program Timeline

- **FY09**: infrastructure (May 2009)
- **FY10**: infrastructure and pilot projects (June 2010)
  - Budget $24M
  - Focus: governance, hiring, research community outreach, pilot projects
- **FY11**: infrastructure and project solicitation
  - President’s budget recommends $50M
  - Solicitation of projects in Sept 2010; project work to begin in May 2011; 3-5 projects
  - Second solicitation to close April 2011; project work to begin in November on an additional 3-5 projects
- **FY12**: Maturing program
  - 40,000 sq ft laboratories completed Q1 2012
  - Intramural staff hiring continues until fully staffed
  - Projects will be reviewed regularly to assess progress
TRND is Different

Usual NIH mechanism

Funding announcement $  Apply  Review  Funding decision

TRND

Solicitation at Proposal
CENTRAL  Apply  Review  Select
Collaborators & Form
Project Teams  Receive in-
Kind Research & Collaborate
with NIH Intramural Scientists
http://trnd.nih.gov

THERAPEUTICS FOR RARE & NEGLECTED DISEASES
Bridging the Gaps in Discovery and Development of Therapeutics for Rare and Neglected Diseases

Home

The TRND program is currently accepting applications for a TRND drug development project at ProposalCentral.

The National Institutes of Health (NIH) TRND program is part of a congressionally directed initiative to accelerate the development of new drugs for rare and neglected diseases. TRND is a partnership with the pharmaceutical industry, academia, and biotechnology companies to work on rare and neglected diseases.

The TRND program will lead to a well-organized project at a single company that requires the development of a new product for rare or neglected diseases. The project must be at least at the stage of a validated lead series in order to be considered for TRND. Special consideration will be given to projects with the potential to address more than one rare or neglected disease by virtue of shared pathophysiology, and projects with a well-developed strategy to exit TRND and complete clinical development, registration, and marketing.

General Instructions

At this time, TRND is considering only small molecule or biologic therapeutic development projects for collaboration. Gene therapy, devices, diagnostics, and medical procedures are not responsive at this time.

Proposed projects must target an untreated or poorly treated rare or neglected disease, as defined here:

http://rarediseases.info.nih.gov/files/Rare_Diseases_FAQs.pdf

Special consideration will be given to projects with the potential to address more than one rare or neglected disease by virtue of shared pathophysiology, and projects with a well-developed strategy to exit TRND and complete clinical development, registration, and marketing.

Projects must be at least at the stage of a validated lead series in order to be considered for TRND. Projects requiring earlier-stage resources, including assay development, high-throughput screening, and initial medicinal chemistry optimization of screening hits, are not appropriate for TRND; researchers interested in these resources are directed to other NIH resources including the Molecular Libraries Program.

Required Documents for Therapeutics for Rare and Neglected Diseases Program Applications

A. TRND Concept Application

The concept application document should not exceed 5 pages (rial 11pt, single space, 1" margins, not including the pages that contain tables provided to collect data on lead compounds). Graphs, pictures and tables should be included in the text. The application should succinctly define the scientific nature and rationale of the proposed project and the current stage of its development, and should include the following:

1. Background: Provide a brief summary of the disease to be treated and the rationale for the type of small molecule compound or biologic therapeutic in order to provide the reviewers an understanding of the opportunity. Include data on rare or neglected disease status, the current standards of care for the disease, and why new therapies are needed. Very briefly describe the competitive landscape and efficacy data on comparator compounds, if any.
Application Process

THERAPEUTICS FOR RARE & NEGLECTED DISEASES
Bridging the Gaps in Discovery and Development of Therapeutics for Rare and Neglected Diseases

Required Documents for Therapeutics for Rare and Neglected Diseases
Program Applications

A. TRND Concept Application
The concept application document should not exceed two pages and should be included in the text. The application should include a brief summary of the project and the current stage of its development, and should address the following:

1. Background or biological basis for the neglected disease
   - Provide a clear description of the neglected disease
   - Describe the unmet medical need

2. Therapeutics for FDA approved drugs
   - Summarize the current state of the neglected disease
   - Describe the disease's burden
   - List all previously approved drugs for the neglected disease
   - Summarize the clinical trials for approved drugs

3. Current status of research and development
   - Briefly describe the current status of research and development efforts
   - Summarize the resources available for the project
   - Describe the availability of existing research tools and databases

The purpose of this solicitation is to identify collaborative development, and all rare disease research collaborations with biotechnology companies working on rare and neglected diseases.

The TRND program provides an opportunity to participate in the rare disease drug development capability with neglected disease drug development capabilities and resources in a collaborative environment with the goal of advancing human clinical trials. TRND uses a solicitation applications to develop collaborations. If the drug originator applicant is selected, a partnership will be mutually agreed on a joint program development program. The applicant investigators and oncology biomedical/disease expertise throughout

B. Appendices

- **Appendix 2**: References are provided to applicants for in vitro ADME assays and in vivo pharmacokinetics assays. This portion of the template need not be included in uploaded proposal.

- **B. Appendices**
  - **References**: Please provide no more than 15 references that relate directly to the project. Upload at least 5 key reference papers as PDF files to accompany the proposal.
  - **Public Abstract**: The selected drug development projects that put collaborative agreements into place with TRND will have a public abstract and timeline posted on the TRND website. Please provide a non-confidential abstract that describes the disease, the projects, the medical treatment goals, and the timeline.
  - **Intellectual Property (IP) Information**: The applicant should include a list of any patents issued or pending, with respect to either the agent or to any non-commercially available technology/material required for the development of the agent. In the event that an application requires the use of non-commercially available technology/equipment that is patented by a third party, the applicant must provide documentation that the patent holder does not object to the applicant's use of the proposed project.

Each TRND application must include the information described below signed by an authorized staff member overseeing IP in the technology transfer at the applicant's institution or company. This verifies that he/she has reviewed the TRND request and that the technology is eligible for consideration by the TRND program. If the technology is found not to be eligible for use as outlined in the TRND application, and it is central to the investigator's proposal, submission to the TRND program is not encouraged.

If available, the following information is requested:

- **Details of all the following rights that are owned by your institution and will be used in the project (the “institution’s IP”):**
  - Patents and patent applications
  - Significant know-how
  - Registered trademarks, applications for registered trademarks, and other marks
  - Registered designs, applications for registered designs, and significant other designs
  - Significant copyright works and other IP rights

- **Details of all employees, consultants, and other parties involved in the development of the institution’s IP related to the TRND project submission. (Are there contributors outside the institution, and if so, what was their role in development?)**

- **A complete list and brief description of all agreements with third parties related to the TRND project submission:**
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Grant Opportunities - Deadlines displayed in U.S. Eastern Time

NIH - Therapeutics for Rare and Neglected Diseases

If you would like to check for a specific grant making organization, you may utilize the drop-down list above. To see all available opportunities, select "Show All"

Grant Maker | Programs (Click for Guidelines) | LOI Deadline | Proposal Deadline | Contact Information | FAQ
--- | --- | --- | --- | --- | ---
NIH - Therapeutics for Rare and Neglected Diseases | NIH - Therapeutics for Rare and Neglected Diseases | 12/16/2010 5:00:00 PM | - | - | -

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https://proposalcentral.altum.com/default.asp?GMID=80
NCTT Staff

Scientific and Admin Management, 6
Lab Operations, 2
Automation and Cmd Mgt, 6
Chemistry, 15
Informatics, 7
Assay Development and Biology, 18
TRND Program Evaluation Criteria
(criteria and weight of criteria):

• Target and therapeutic validation (30%)
• Strength of current data package (30%)
• Feasibility to reach First in Human (20%)
• Medical impact relative to current Standard of Care (10%)
• Likelihood of external adoption (10%)
Criteria: Strength of Data Package

- Medicinal Chemistry
- ADME
- PK/PD
- Toxicology
- In vivo models
- Secondary and tertiary assays
- Formulation
- Chemical Manufacturing and Controls (CMC) – small molecules
- Expression/Purification – Biologics
TRND Proposals Round 1

Treatment Modality

- Biol: 27%
- Sm Mol: 73%

Disease Areas

- CNS: 20%
- Cancer: 13%
- Infectious Diseases: 15%
- Others: 16%
- Cardio-pulmonary: 5%
- Muscular: 5%
- Metabolic Diseases: 5%
- Renal: 2%
- Addictive Disorder: 2%
- Blood Disorder: 13%
- Skin Disorder: 4%
- Other: 16%