Call Details for RFA on Drug Development

India is a leader in global generic pharmaceuticals manufacturing. However, many generics manufactured in India are at the end of their respective product life cycle, with limited new research and development taking place on new drugs. Furthermore, our country has a high burden of both communicable and non-communicable diseases and is vulnerable to epidemics. In order to keep pace with global innovation and to improve health outcomes, there is a need to foster R&D for new and cost-effective therapies. With the aim to take India at global map in terms of R&D innovations in the area of drug development in our country, the Department has initiated a **new program on "Drug Development"** with a vision to develop indigenous and cost-effective new drugs against the following diseases:

I. Communicable Diseases

- Tuberculosis

II. Non-Communicable Diseases

- Cardio-Vascular Diseases (CVD),
- Chronic Obstructive Pulmonary Diseases (COPD) and
- Cancer (oral, head and neck, cervical and breast cancer)

The **Department of Biotechnology (DBT)** in collaboration with its Public Sector Undertaking, **Biotechnology Industry Research Assistance Council (BIRAC)** invites proposals in the area of "**Development of Drugs from existing leads with established proof of concept**".

Purpose of the Call:

The goal of this Call is to support **milestone-driven proposals focused on lead optimization and preclinical testing of candidate therapeutics for the given four diseases**. All proposed studies must be directed to regulatory submission in India and therefore this Call excludes basic research, studies of disease mechanisms or epidemiological studies. Applications are expected to have defined Milestones and Timelines detailing how the project will move forward with identified key Go / No Go decision points.

Of the Drug Development stages as defined below, this Call is intended for research and development activities focused *ONLY* on **Lead optimization and preclinical development and Clinical therapeutic validation** to a point where there is sufficient scientific evidence to justify filing for regulatory approval:

I. **Lead optimization and preclinical development:** These activities are expected to be carried out under requirements of the New Drugs and Clinical Trial Rules, 2019. Processes by which additional alterations to an identified therapeutic lead may be made in conjunction with preclinical assessments of its *in vivo* pharmacokinetics, efficacy, and safety. The goal is to generate a lead clinical candidate, establish industrially feasible synthesis, generate chemical and pharmaceutical information on the proposed drug substance and drug product, and associated data package that supports regulatory approval for the initiation of clinical validation. Lead optimization and preclinical development studies include proof of efficacy in more animal models of disease, establishment of pharmacokinetics of the therapeutic as well as *in vivo* studies exploring its safety/toxicity.

II. Clinical therapeutic validation: Studies conducted in human patient populations to fully understand the efficacy and safety profiles of a compound and its associated target.

Scope of this Call:

This Call is aimed to support **collaborative proposals that combine complementary and synergistic research strengths in proposed lead candidate(s)/preclinical therapeutic lead(s)**. Proposals must have one or more identified preclinical therapeutic leads with supporting efficacy data (in animal models; supported by *ex vivo* human cells/tissues, iPSC-derived organoids, and well justified *in vitro* target/pathway engagement) for the above mentioned four diseases. The proposals with any one of following criteria would be encouraged for support:

1. An unmet medical need/gap should be addressed.
2. The therapeutic leads should preferably be patentable entities.
3. Mode of action of the lead molecule & drugability of the identified lead, IP space must be specified during proposal submission.
4. Funding may be sought for clinical studies or interventional clinical trials.
5. Superiority/non-inferiority to the standard of care should be demonstrated.
6. Repurposing of existing leads may also be considered.

Applications not appropriate under this Call:

This Call is not intended to support earlier stages of work to generate assays, conduct screens for small molecules or biologic agents, or those primarily focused on early-stage validation of targets. The program scope excludes basic research and studies of disease mechanism. Applications for which the primary outcome is the development of a diagnostic or biomarker are also not appropriate. The following are types of applications that are not appropriate under this Call:

1. Applications for which therapeutic lead molecules or biologics have not yet been identified (e.g. assay development projects, screening of compound libraries, fractionation of natural products, target identification efforts).
2. The development of novel tools, models, or technologies without an integrated plan for their use in lead optimization or preclinical development.
3. Research focused primarily on understanding normal biology or disease processes.
4. Formulation of leads to enhance efficacy or reduce toxicity

Expectation from the Applicants:

- Collaborative proposals with clinicians would only be considered for funding.
- The primary applicant for this call can either be academia or industry. He/She may submit the proposal in a consortia mode where academia, industry and clinicians are involved. Academia will be supported by DBT however, industry through BIRAC.
- Primary applicant and all the collaborators should have prior experience in the relevant disease, technology or other respective areas demonstrated through prior publications and data published from their respective labs/ institutes.
- A PI/Co-PI within the consortia should be the coordinator of the consortia. The role of coordinator would be:

- Planning, development, implementation and management of the consortia. Coordinator will coordinate with all the other partners ensuring effective implementation and management of the overall consortium's scientific activities.
- Ensuring that the expenses presented by unit partners correspond with the activities agreed by the unit partners
- Submit regular reports and other documentation on behalf of the Consortium

Collaborations:

1. Academia with academia
2. Academia with industry
3. Industry with academia
4. Industry with industry

Please note that even for collaborators, the basic eligibility criteria as below need to be met.

Eligibility criteria:

1. **Eligible Organizations**
   a. Central/State Govt. Institutions of Higher Education and research
   b. Private Institutions of Higher Education and research
   c. Research institutes, universities, medical schools, IIT's and other engineering institutions, other recognized research laboratories in the public sector and not-for-profit institutions.
   d. The institution must be recognized by DSIR as a Scientific and Industrial Research Organization (SIRO), if outside public sector.
2. **Required Registrations**
   Private institutions/Hospitals/ NGOs should be registered in Darpan Portal, Niti Aayog website.
3. **Eligible Individuals-Principal Investigator(s)**
   Scientists working in Universities/Academic Institutions/National Laboratories/Industries [Department of Scientific & Industrial Research (DSIR)-Recognized R&D Centre] & Non-Profit Organizations with necessary facilities and strong scientific background in the proposed area as the Principal Investigator(s) are invited to develop an application for support.
4. **Eligible Industry (Companies)**
   An Indian company is defined as one which is registered under the Indian Companies Act, 2013 and minimum 51% of shares of the Company should be held by Indian citizens holding Indian passport. (Indian Citizens do not include Persons of Indian Origin (PIO) or Overseas Citizen of India (OCI) holders).

Proposal contents:

A proposal should be well written with clearly defined specific objectives, work plan, expected outcomes in terms of quantifiable targets, tentative budget estimates and biodata of the investigator/s giving details regarding the expertise along-with the list of relevant research papers in the proposed research area. The following information should be included in the scientific hypothesis:

i. Justification of selected Target for any one of the identified disease and Therapeutic/s. Applications must include a strong justification for the selection of both the target and therapeutic (e.g., small molecule chemical scaffold or biologic) as well as a discussion of the relevant prior art, intellectual property, and competitive landscape.

ii. Technical Prerequisites for proposals:

a. Therapeutic lead candidate(s):

- Applications must include details on the lead
  - Applications which propose to conduct lead optimization should discuss optimization approaches.
  - Applications must include an in-depth description and efficacy of their initial candidate agent in a suitable animal model as well as a detailed plan for the generation and/or synthesis of refined derivatives.
  - The submission of applications with back-up agents is encouraged to increase the overall likelihood for a successful project.

b. Assays.

- The application should provide a sound rationale for the choice of established *in-vitro* and / or *in vivo* assays that will be used to further support the lead candidate optimization and / or preclinical development.
- Assays should be presented within the context of a testing flow diagram for testing newly derived agents and should be of sufficient throughput to support testing based on their position in the flow diagram.

c. Milestones and Timeline.

Applications lacking the Milestones and Timeline section will be deemed incomplete.

Application must include the following

- Project performance and timelines for the proposed objectives. (A detailed schedule or timeline for the anticipated attainment of each milestone and the objective of extending both target and therapeutic validation)
- This section should also include:
  a. A clear description of all interim objectives to be achieved during the course of the project and how they relate to the overall goal of advancing the preclinical agent toward clinical trials;

  b. Clearly delineated Go / No-Go decision points;
  c. Succinct plans for the future development of the resulting therapeutic as it pertains to regulatory approval processes.

<u>Evaluation criteria</u>:

1. Scientific merit
2. Clarity of hypothesis
3. Relevance and ability to implement approaches
4. Background of the investigator
5. Feasibility of conducting the research in the present settings

Mode of Selection:

Proposals received will be screened and short-listed by an expert committee constituted by the Department. The short-listed proposals would be further considered for funding as per DBT norms.

Mode of Submission:

Proposals may be submitted online in the DBT R&D format through DBT- eProMIS (http://dbtepromis.nic.in/Login.aspx) under Category of Area-'**Drug Development**', clearly stating '**Proposal against Call for Proposal**'. Subsequently, two hard copies should also be sent to: Dr. Vinita N. Chaudhary, Scientist 'E', Department of Biotechnology, Block- 2, Room No.705, 7thfloor, CGO Complex, Lodhi Road, New Delhi – 110003.

For any queries please contact:

Dr. Vinita Chaudhary, Joint Director, DBT:**vinita.chaudhary@nic.in**
Dr. Aparna Sharma, Manager-Technical, BIRAC **tech01.birac@nic.in**

Timeline:

Call for Proposal opens: 01.01.2020

Call for Proposal closes: 29.02.2020