DBT- BIRAC Joint Call for Proposal on 'Precision Biotherapeutics- mRNA Therapeutics' for fostering high performance Biomanufacturing under BioE3 Policy

1. Background

The **BioE3** (**Bio**technology for **E**conomy, **E**nvironment & **E**mployment) **Policy** for '*Fostering-High Performance Biomanufacturing*' has been approved by Union Cabinet in August 2024. The Policy lays down the framework for high-performance Biomanufacturing, to accelerate the development and scale up of bio-based products in the country. Biomanufacturing can fundamentally transform the global economy from today's consumptive manufacturing paradigm to the one based on regenerative principles, and will play a pivotal role promoting in '*Green Growth'* while driving country's Bioeconomy.

2. Scope of the Call

mRNA therapy can potentially transform existing therapies or target difficult-to-treat indications, including respiratory, cardiac, metabolic, and autoimmune diseases, as well as cancer. mRNA technology can be used for the following therapeutic applications:

•Replacement therapy: to compensate for a defective gene/protein, or to supply therapeutic proteins

•Vaccines: mRNA encoding specific antigen(s) to elicit protective immunity

•Cell therapy: mRNA is transfected into the cells ex vivo to alter cell phenotype or function, and these modified cells are subsequently delivered to the patient. e.g. in vitro transcribed chimeric antigen receptor mRNA (IVT CAR mRNA) T cells platform.

There are many benefits of mRNA therapies as compared to similar emerging platforms, such as modular nature with easy-to-switch sequences for specifically targeting different proteins or genes, the potential to directly affect the underlying cause of a disease, faster manufacturing times compared to antibodies or protein-based drugs, predictable pharmacokinetics, and lack of genome integration.

Recognizing the fact that mRNA therapeutics represents an emerging precision medicine field with great promise for preventing and treating human diseases, DBT and BIRAC invite proposals on 'Precision Biotherapeutics-mRNA therapeutics' under the BioE3 policy to further the indigenous development and manufacturing of this important biotherapeutic. The proposals will be invited under 2 categories:

(i) Discovery & Application-oriented Integrated Network Research
(ii) Bridging the Gap for scale up

2.1 Discovery & Application-oriented Integrated Network Research (Expected Outcomes –TRL: 3-5)

Under this category, the proposals are expected to advance cutting-edge innovative research with applied knowledge, for accelerating innovations and fostering the development of affordable solutions. The proposals may be focused on the following:

- *Optimizing mRNA Stability and Expression*: Development of new techniques to improve the stability, translation efficiency, and half-life of mRNA in vivo. This could involve mRNA sequence optimization, modified nucleotides, or co-delivery systems to protect mRNA from degradation and enhance its expression.

- *Next-generation mRNA expression vectors and platforms*: Exploration of new mRNA vaccine platforms, including Circular RNA, endless-RNA, multi-protein mRNA, and indigenous microfluidic devices for mRNA formulations.

- *mRNA for Infectious Disease Prevention and Treatment*: Expanding mRNA applications beyond COVID-19 to address other conventional and emerging viral, bacterial, and fungal infectious diseases, such as Influenza, Zika, HIV, Tuberculosis, Malaria. This includes developing multivalent vaccines or broad-spectrum therapies targeting multiple pathogens. Research could focus on optimizing antigen selection, immune modulation, and delivery mechanisms.

- *mRNA for Cancer Immunotherapy*: Development of mRNA-based therapeutic vaccines or treatments that stimulate the immune system to target and destroy cancer cells. This could involve mRNA encoding tumor-specific antigens, checkpoint inhibitors, other immune-modulatory proteins, mRNA techniques improvising intervention strategies including Chimeric-antigen receptor development, and bi- or multi-valent antigen engineering, etc.

- *Gene Editing and Gene Therapy via mRNA*: Facilitating gene editing or gene replacement therapies using mRNA. This could include strategies of CRISPR-based gene therapies, as well as mRNA approaches to correct genetic mutations, including rare genetic disorders.

- *Personalized mRNA Therapeutics*: Advancing personalized mRNA-based treatments that are tailored to individual patients, particularly in the context of rare genetic diseases, autoimmune conditions, and cancer. Research could include identifying biomarkers for patient stratification and developing individualized mRNA therapies.

- *Immunology of mRNA Vaccines and Therapies*: Investigating the immune responses elicited by mRNA vaccines and therapies, including the role of innate immunity, T cell responses, and antibody production. Research could explore strategies to modulate immune responses to enhance efficacy or reduce adverse effects.

- *mRNA Delivery Technologies*: Innovation in methods to enhance the delivery of mRNA to target cells, tissues, and organs, using lipid nanoparticles (LNPs), viral vectors, exosomes, or other nanomaterials. Research should focus on improving delivery efficiency, targeting specificity, and overcoming challenges related to stability and immune response.

- *Scalability and Manufacturing of mRNA Products*: Improving the production and scalability of mRNA vaccines and therapeutics, with a focus on cost reduction, efficiency, and manufacturing for global access. This could involve innovations in RNA synthesis, purification, and quality control.

2.2. Bridging the Gap for Scale-up (Expected Outcomes –TRL: 5-8)

Under this category, proposals should focus on:

- *Advancing existing POCs (with available animal data) to pre-clinical formulations and pre-clinical formulations to clinical trial phase I/II*

3. Key requirements for the proposed projects

a. Developed technology (if applicable) should be sustainable from an economic and environmental point of view and the technology should be scalable.

b. Gap in the technology to be addressed and strategies proposed to address the gap should be outlined clearly.

c. Proposals must mention the present TRL level of the technology and the TRL proposed to be attained at the end of project duration

d. The proposal should strictly adhere to the prescribed proforma.

e. The proposals with clear focus and likely execution of deliverables within timelines will be preferred.

f. All proposals must adhere to statutory regulatory requirements.

4. Mode of Submission

Proposals maybe submitted by both Academia and Industry applicants, either independently or as a collaborative project.

a. For proposals from Academia/Research Institutions: Interested applicants should submit the proposals in the prescribed format duly forwarded by the executive head of the institution through the Department's e-ProMIS portal (www.dbtepromis.nic.in).

b. For proposals from Industry and Industry-Academia collaboration: Interested applicants should submit the proposals in the requisite format duly forwarded by the executive head of the Company/LLP/Institution by logging to the BIRAC website (www.birac.nic.in).

5. Eligible Organizations

5.1 Academic Organisations

a. Proposals may be submitted by interested applicants engaged in research activities at various Institutions/Universities/Societies/Trusts/NGOs/ Foundations/Voluntary Organizations, recognized as a Scientific and Industrial Research Organization (SIRO).
b. The Principal investigator must have at least four years of the employment remaining in the institution at the time of proposal submission.

5.2 Industry

a. Eligibility criteria for the Industries will be as per "Implementation Plan for the Biomanufacturing and Biofoundry Initiative" attached at ANNEXURE I.
b. Pre-requisite documents required to be submitted by the Industry as per the BIRAC norms are as follows:

5.2.1 Companies/Startups

a. Incorporation certificate.
b. CA/CS certified shareholding pattern as per BIRAC format (Companies having a minimum of 51% Indian shareholding / individuals holding Indian passports are only eligible) mentioning UDIN number.
c. Details regarding in-house R&D facility, if any; or Incubation Agreement with recognized Incubator.
d. Audited financial details of latest last three financial years,
e. Copy of passports of the shareholders if required (in support of 51% eligibility criteria).

5.2.2 Limited Liability Partnership

a. Incorporation/Registration Certificate.
b. Partnership deed; CA/CS certified certificate which states that minimum half of the partners are Indian citizens mentioning UDIN number.
c. Copy of passports of Indian partners/subscribers
d. Research mandate/ details regarding in-house R&D facility, if any/Incubation agreement
e. Audited financial details of the last three financial years;
   Companies/LLP if recommended have to provide a declaration stating that Company/LLP is not in default of BIRAC OR any other organization. Further there are no Legal Proceedings going against the applicant.

6. Evaluation Criteria

The proposals will be evaluated as per existing norms of DBT and BIRAC.

7. Funding Modalities

a. Projects having academic partners only will be funded by DBT. Projects involving Academia and Industry or only Industry will be supported by BIRAC.

b. Extent of funding will depend on the proposed activities and will be in alignment with the "Implementation Plan for the Biomanufacturing and Biofoundry Initiative" attached at ANNEXURE-1.

c. Project duration will be upto 2 years, extendable upto 5 years based on performance.

8. Scope of Intellectual Property Generated During the Duration of the Project

The Intellectual Property (IP) generated during the duration of the project will be in accordance with the IP Policy of DBT and BIRAC.

9. Discretion

DBT/ BIRAC shall reserve the discretion on determination of sanction of funding and processes as per its standard norms and such determination shall be final. The selection process is not open to review.

10. Contact Information

Any queries may be addressed to Dr. Varshneya Singh, Sc-'D', DBT @ BioE3-mRNA@dbt.nic.in (for academia applicants only) and Dr. Dhiraj Kumar, Chief Manager, BIRAC @ dkumar.birac@nic.in (for industry applicants only).

Last date for submission of proposals is 15th May 2025.

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