Inviting Expression of Interest (EoI) to develop indigenised therapeutics for priority rare genetic disorders in India

Background

Rare disease is a condition of low prevalence affecting a small population compared with other prevalent diseases. Rare diseases may be individually rare, but collectively, is a major healthcare issue.

In this context, the aim of this EoI is to encourage research, development, commercialization and indigenization oftherapies including small molecules, enzyme replacement therapy (ERT), substrate reduction therapy (SRT), biosimilars and other newer therapeutics in the country for the following priority rare genetic disorders-

- Duchenne Muscular Dystrophy (DMD)
- Spinal Muscular Atrophy (SMA)
- Lysosomal Storage Disorders: Gaucher Disease, Pompe Disease, Fabry's Disease, Mucopolysaccharidosis (MPS),Niemann Pick Disease
- Tyrosinemia
- Neurofibromatosis
- Familial Hypercholesteromia

DMD is an X-linked recessive muscular dystrophy caused by the mutation of the dystrophin gene and affects nearly 1 in 3500 live male births. Majority of patients have progressive muscle weakness and leads to respiratory, cardiac and orthopedic complications. Currently, there is no known cure for DMD. However, FDA approved treatments include Deflazacort, Ataluren, Elevidys (delandistrogenemoxeparvovec-rokl), Exondys 51 (eteplirsen), Vyondys 53 (golodirsen), and Amondys 45 (casimersen)and many drugs are in pipeline.

SMA is an autosomal recessive disorder caused due to mutation in Survival Motor Neuron-1 (SMN1) gene and affects nearly 1 in 10,000 live births in India. It causes progressive anterior horn cell degeneration in spinal cord, leading to muscular atrophy and paralytic weakness. Nusinersen was the first approved drug for its treatment which comes with a life-time expense of several lakhs. Risdiplam is approved for children >2 months of age and has been approved for marketing in India.

India has prevalence in Gaucher, Pompe, Fabry diseases, mucopolysaccharidosis (MPS)andNeimann Pick disease (NPD) among other lysosomal storage disorders (LSDs). The prevalence is1 in 2500-5000 for Gaucher, 1 in 40,000-300,000 for Pompe, 1 in 40,000-70,000 for Fabry, 1 in 25,000 for MPS and 1 in 250,000for NPD. LSDsis one of the rare genetic diseases and a heterogeneous group of inborn errors of metabolism caused due to the defects in lysosomal enzyme, transport or membrane proteins. This results in the accumulation of the substrates/intermediates which leads to clinical phenotype. Many of these diseases are treated with enzyme replacement therapy (ERT) or substrate reduction therapy (SRT).

The cost of ERTs is exorbitant, and is beyond reach of most patients. Some of the drug companies are providing ERT to limited number of patients under their humanitarian access programs. Currently approved drugs are Fabrazyme (agalsidase beta) for Fabry, Cerezyme (imiglucerase), and Cerdelga (eliglustat) for Gaucher, Nexviadyme (Avalglucosidase alfa powder), and Myozyme (alglucoside alfa) for Pompe and ALDURAZYME® (laronidase), VIMIZIM®(elosulfase alfa), NAGLAZYME®(galsulfase) and ALDURAZYME (laronidase)

for MPS, and Xenpozyme (Olipudase alfa powder) for NPD.Miglustat, Eliglustat and Venglustat are competitive inhibitors of the glucosylceramide synthetase developed as SRT to treat Gaucher disease. Several others are under development for Fabry and Gaucher disease.

Tyrosinemia is a rare autosomal recessive genetic metabolic disorder, caused due to lack of the enzyme fumarylacetoacetate hydrolase required for final breakdown of tyrosine. Moreover, tyrosine accumulation in liver, kidney and central nervous system causes hepatomegaly, jaundice and progress to cirrhosis, hepatocarcinoma and severe liver diseases. Its incidence and prevalence in India is unknown due to lack of reports. FDA approved Orfadin (Nitisinone) capsule and oral suspension formulation is available but is not affordable by Indian patients.

Neurofibromatosis is a group of disorders that cause tumor development in the nervous system, affecting 1 in 3000 individuals. This could result in hearing loss, learning impairment, vision loss, severe pain and cardiovascular problems. An FDA approved drug, selumetinib (Koselugo) is available for treatment of children >2 years of age.

Familial Hypercholesteromia is an autosomal dominant disorder that causes high low-density lipoprotein (LDL) level leading to early age heart attacks and affects nearly 1 in 350 children.Evolocumab is an approved monoclonal antibody inhibitor in India for children >12 years of age.

Priority Research Question

To develop the indigenizedtherapies including small molecules, enzyme replacement therapy (ERT), substrate reduction therapy (SRT), biosimilars and other newer therapeutics in the country for the above-mentioned raregenetic disorders.

Objectives

- To develop/ indigenize newer/ existing therapies in the country
- To foster collaboration and partnerships between government agencies, non-governmental organizations, health and other related systems, and community-based organizations to accelerate the development of technology.

Format of EoI to be submitted

Interested companies may submit the EoI with the following components:

1. Rationale of proposed work
   The proposal should clearly state the aim and objectives of the proposed study.

2. Background:
   Theproposal should provide evidence from previous research on the proposed area(in the country or elsewhere); any challenges and opportunities envisaged in the proposed area of work.

3. Study implementation plan
   Provide a clear and brief description of implementation plan pertaining to the study including definite timelines

4. Address feasibility and scalability
   Address the feasibility and scalability of the technology, including the resources needed for development, the intellectual property right, and the immediate potential for wider adoption and scale-up in India.

5. Project team
   Summarize the composition of the working team based on the expertise of the individual team members in designing and implementing the project.

6. Extent of collaboration sought from ICMR
   ICMR can collaborate and assist in preclinical, clinical research and regulatory approvals.

Additional documents

Please provide the following:

- One-page company profile mentioning the experience in developing therapeutic products
- Patents granted

Who can submit the EoI?

The EoI can be submitted through ONLINE MODE ONLY by pharmaceutical/biotechnology companies which are already involvedor are ready to work in the area of therapeutics in rare genetic diseases in collaboration with ICMR(documentary evidence of their recognition, including a DSIR certificate should be available).

Points to be kept in mind while submitting the EoI

- The EoI must address the specific need in the above-mentioned area.
- The EoI should include development of an indigenized translational therapy.
- A concept note in the above-mentioned format should be mailed as a PDF to consortiumrarediseases@gmail.com

Last date of Submission: 29th Febraury 2024, 23:59 hrs, IST

For any queries related to the call, please contact:

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