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Foreword

The rare genetic disease research landscape in India

I am delighted to see this special issue on 'The Rare Genetic Disease Research Landscape in India" by the *Journal of Biosciences*, published by the Indian Academy of Sciences in collaboration with Springer Nature. It is the first time that a mainstream biology journal has decided to publish a whole issue on rare genetic disorders. I congratulate the editorial board of the *Journal of Biosciences* for their timely support to encourage research in this area. I also believe that this issue will increase awareness about rare genetic diseases research and encourage many in India to enter the field.

The number of patients with these diseases is significantly high in India due to its vast population with many different ethnic groups practicing consanguineous marriages as compared with the number that have been diagnosed. In recent years, there has been considerable expansion of facilities for diagnosis of rare genetic disorders due to governmental support and emergence of many DNA sequencing-based technologies. However, we need to further expand our ability to train clinicians for diagnosis and management of the patients as there are not enough trained clinicians and genetic counsellors to manage these patients across India, particularly in remote and rural areas.

Making approved orphan drugs available to our citizens at an affordable cost has been a major bottle-neck for many years, although a few of our companies manufactured the active pharmaceutical ingredients (APIs) for the foreign markets. Until recently, the nation did not enjoy the benefit of having the finished formulations, and these had to be imported with resultant huge prohibitive costs to patients.

Realizing this urgent need to indigenously manufacture internationally approved drugs for rare diseases in affordable formulations/dosage forms, the government undertook steps to prioritize these diseases and catalyze the production of required drugs by engaging with academia, drug manufacturers, and regulators. Following these initiatives, four orphan drugs (Cap Nitisinone, Cap Eliglustat, Cap Trientine, and Cannabidiol Oral Solution) for the treatment of rare diseases (tyrosinemia type 1, Gaucher's disease, Wilson's disease, and Dravet/Lennox–Gastaut syndrome-related seizures) have now been made available in the Indian market at 1/60th to 1/100th the annual cost reduction per patient, vis-à-vis the same were they imported. In addition, as of this writing, four more small-molecule drugs (sapropterin, miglustat, sodium phenyl butyrate, and carglumic acid for treatment of phenylketonuria, Gaucher's disease, and hyperammonaemia, respectively) are in the pipeline for required regulatory clearance and market launch. While these are only initial steps, the government is also keen to make available other approved modalities of treatment for rare diseases, inclusive of genetic therapy and enzyme replacement therapy, in the immediate future.

The rare disease research landscape in India is still developing, and one of the main reasons is the lack of understanding about these diseases even among clinicians and scientists. As a result, there are not enough investigators working in this area and the pace of development is slow. Rare disease drug discovery cannot happen unless there is collaboration among researchers, clinicians, regulatory authorities, and the industry. India has shown during the COVID pandemic that when all stakeholders come together, solutions are delivered even for complex issues. The same urgency and motivation are required to develop rare disease treatments as it has become an emergency situation for our society and patients.

This special issue of the *Journal of Biosciences* highlights some of the work being done in India and points towards an optimistic future where we may see drugs being developed and produced in India. Recent remarkable developments in new therapeutic approaches, such as mRNA therapeutics, *in vivo* gene therapy, etc., present unprecedented opportunities to make state-of-the-art therapeutic options available to our people.

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It is heartening to see that clinicians and scientists including social scientists have contributed to this volume covering areas such as policy, disease registry, epidemiology, diagnosis, patient management, current drugs, future drug discovery, and basic biology of rare diseases. The articles describe the current state of knowledge as well as the developments taking place in India. It gives me great hope that we may be able to produce affordable drugs for many rare diseases in India in the near future.

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