

# Building cross-border collaborations to increase diversity and accelerate rare disease drug development – meeting report from the inaugural IndoUSrare Annual Conference 2021

Harvinder Kour Khera, Nisha Venugopal, Ramya T. Karur, Rakesh Mishra, Reena V. Kartha and Harsha K. Rajasimha 

*Ther Adv Rare Dis*  
2022, Vol. 3: 1–15  
DOI: 10.1177/  
26330040221133124  
© The Author(s), 2022.  
Article reuse guidelines:  
sagepub.com/journals-  
permissions

**Abstract:** The inaugural IndoUSrare Annual Conference was held virtually from 29 November to 2 December 2021 and was organized by the Indo US Organization for Rare Diseases (IndoUSrare). The event saw participation from over 250 stakeholders of rare diseases who joined in virtually by audio/video on the Zoom platform from around the world, with a majority of attendees concentrated in the Indian subcontinent and the United States. The conference was held over 4 days from 10:00 a.m. to 12:30 p.m. Eastern Time on each day, which accommodated participation by speakers and attendees from both the eastern and western hemispheres. The agenda over 4 days holistically covered broad topics of interest to different stakeholder groups such as representatives from organizations working toward policy frameworks for rare diseases or orphan drugs (Days 1, 4), biomedical research institutions (Day 2), patient advocacy organizations (Day 3), and patient advocacy and engagement offices within Industry (Day 4). In this meeting report, we summarize the key highlights from each day of this conference, with a perspective on future directions encouraging cross-border multistakeholder collaborations to maximize diversity, equity, and inclusion (DEI) in rare disease diagnosis, research, clinical trials, and treatment access. Each day included a keynote lecture on the theme of the day followed by a series of individual speaker presentations and/or a panel discussion. The goal was to understand current barriers and bottlenecks in the rare disease ecosystem. The discussions also helped highlight gaps and identify potential solutions that can be achieved through building multistakeholder collaborations across international borders, which we believe IndoUSrare is uniquely positioned to do with organizational programs such as rare patient foundation alliance, technology-enabled patient concierge, research corps, and corporate alliance program. The inaugural conference of the then 2+-year-old IndoUSrare organization laid the foundation for ongoing engagement of stakeholders between the two countries – the United States and India. The long-term goal is to scale the conference more broadly and serve as a model for other low- and middle-income countries (LMICs).

Correspondence to:  
**Harsha K. Rajasimha**  
Indo US Organization for  
Rare Diseases, Herndon,  
VA 20171, USA.  
[harshakarur@gmail.com](mailto:harshakarur@gmail.com)  
**Harvinder Kour Khera**  
**Rakesh Mishra**  
Tata Institute for Genetics  
and Society, Bengaluru,  
India  
**Nisha Venugopal**  
**Ramya T. Karur**  
Indo US Organization for  
Rare Diseases, Herndon,  
VA, USA  
**Reena V. Kartha**  
University of Minnesota  
Twin Cities, Minneapolis,  
MN, USA; Indo US  
Organization for Rare  
Diseases, Herndon, VA,  
USA

## Plain language summary

IndoUSrare held its inaugural Annual Conference from 29 November to 2 December 2021. It was focused on the theme of cross-border collaborations for rare disease drug development, with each day dedicated to a specific patient-focused discussion topic,

ranging from patient-led advocacy (Advocacy Day), research (Research Day), rare disease community support and engagement (Patients Alliance Day), to industry collaborations (Industry Day). The 4-day conference was held in virtual mode and attracted over 250 attendees from across the globe. This meeting report provides the key highlights of the event and summarizes learnings and future directions encouraging cross-border collaborations to increase diversity, equity, and inclusion (DEI) in rare disease research and clinical trials.

**Keywords:** clinical trials, collaborations, DEI, diversity, meeting report, orphan drugs, patient advocacy, patient engagement

Received: 18 April 2022; revised manuscript accepted: 26 September 2022.

### Introduction

There are around 10,000 rare diseases that impact over 300 million people around the world.<sup>1,2</sup> Unfortunately, research and awareness of these diseases are lagging, and only less than 350<sup>3</sup> rare disorders have approved treatments. The diagnosis of such diseases is frequently an odyssey for the patients and their families, averaging between 4 to 9 years.<sup>4</sup> Treatments, if available, are often too expensive,<sup>5</sup> and patients must seek help from the government and various non-governmental organizations or crowdfunding sources to be able to afford access. Not everyone is lucky enough to get help.<sup>6,7</sup> Clinical trials can often be the best option for patients with rare diseases for which a drug is under development. However, most clinical trials are conducted in the western world leaving over 90% of the world's population with little opportunity to access or participate. Figure 1 shows a global map of the distribution of all rare disease clinical trials that are registered in the ClinicalTrials.gov portal (accessed 28 June 2022).<sup>8</sup> Supplemental Figures 1 and 2 show a similar distribution when looking for only interventional or observational studies.

There is an utmost need for spreading awareness among the masses for rare diseases as well as initiating more research activities for the development of diagnostics and therapeutics.

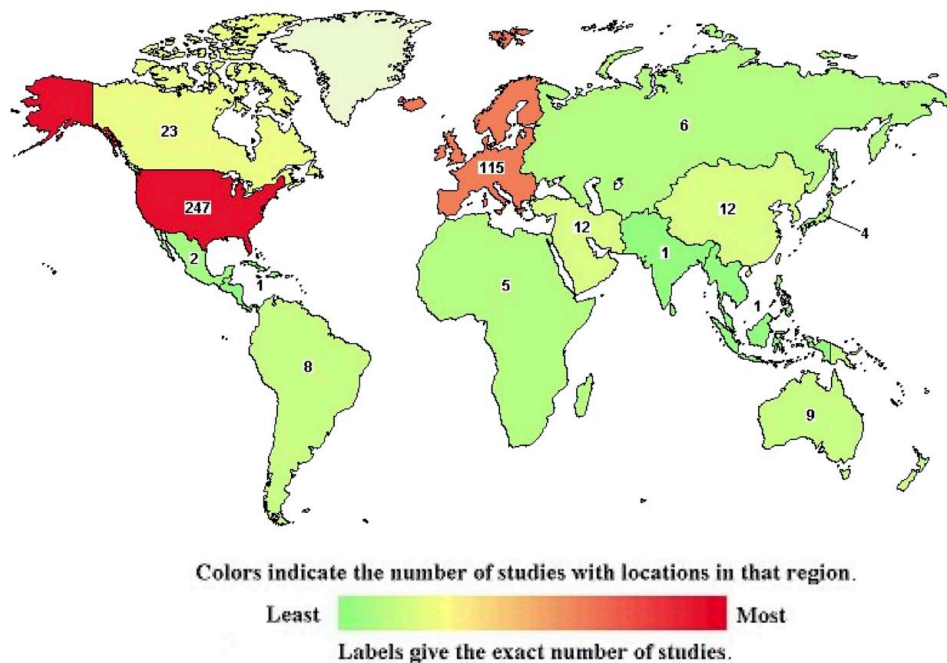
The Indo US Organization for Rare Diseases (IndoUSrare)<sup>9</sup> is a humanitarian non-profit 501(C)(3) tax-exempt public charity organization based in the United States, which addresses the unmet needs of diverse patients with rare diseases globally.

With an initial focus on the Indian diaspora, their goal is to build cross-border collaborations to connect stakeholders of rare diseases in low- and middle-income regions – such as India – with their counterparts and clinical researchers in the United States. This would allow to improve the diversity of clinical trial participants, accelerate research and development, and improve equitable access to life-saving therapies to diverse populations of rare disease patients. IndoUSrare's mission is to help establish and sustain patient-centric education, awareness, training, research, and engagement programs that are aligned to the US Food and Drug Agency's (FDA) patient-focused drug development (PFDD) paradigm.

### Organization of the inaugural IndoUSrare Annual Conference

The inaugural Annual IndoUSrare Conference was held virtually with the main aim of bringing together all stakeholders on a single platform to understand the current landscape of the rare disease ecosystem, identify barriers and bottlenecks, and discuss the various ways to address these challenges from the perspective of key stakeholders. Speakers were selected by the conference organizing committee based on the quality of the abstracts submitted, speaker biography, and the fit for the topic within the overall goals of the conference.

Each day of the conference was dedicated to a particular theme and included a wide variety of speakers ranging from patients and patient advocacy groups to researchers, industry representatives,



**Figure 1.** Global map of the distribution of all rare disease clinical trials registered on the ClinicalTrials.gov portal. A search for ‘Rare disease’ in ‘Conditions’ yields a total number of 549 studies with the depicted distribution. The maximum number of studies occur in the United States and European Union, and the number of studies in the remaining countries is at least 10 times lower. Supplemental Figure 1 shows a similar distribution when looking for only interventional studies.

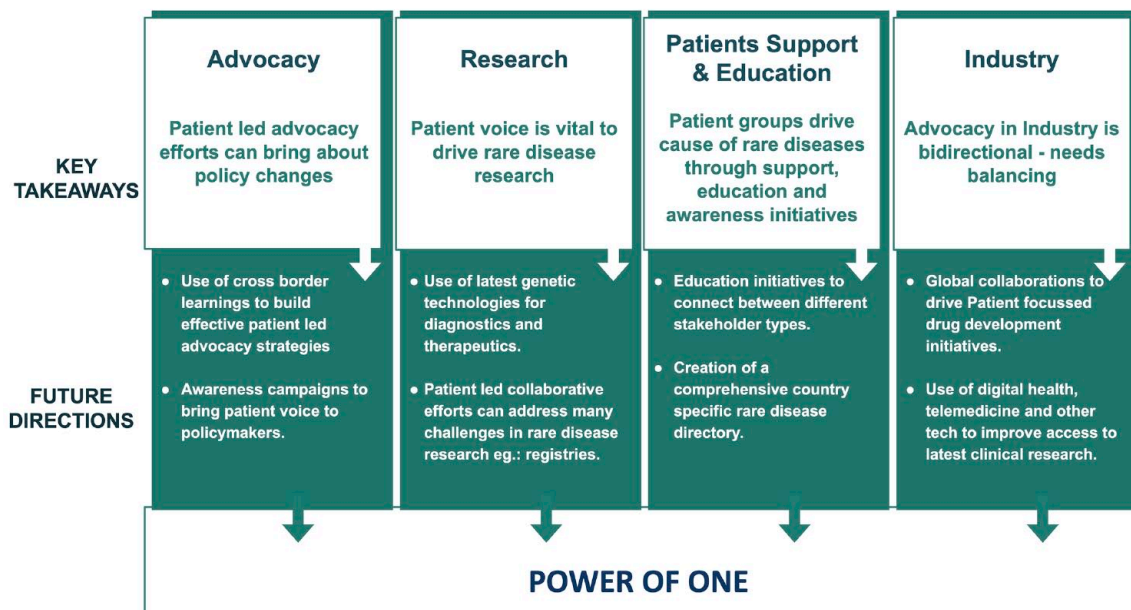
and policymakers. Day 1 – Advocacy Day focused on the role of patient-led legislative advocacy in awareness generation among patients and the public and the effect of policy changes on the community. Day 2 – Research Day featured talks and discussions on patient-led programs and initiatives for advancing research. Day 3 – Patient Alliance Day focused on various programs for patient education, support, awareness, and other initiatives with a particular highlight on the work done by various members of the IndoUSRare Patients Alliance. The final day of the IndoUSRare Annual Conference was on the theme ‘Patient Advocacy in Industry’.

The event was conducted using the Zoom webinar platform and spanned 4 days between 29 November 2021 and 2 December 2021 from 10:00 a.m. to 1:30 p.m. Eastern Standard Time (EST) on each day to accommodate maximum participation from across the world. The conference included keynote lectures, short talks, special sessions, panel discussions on specific topics related to rare diseases, and a keynote address by a legend in the field of rare diseases. The event attracted attendees ranging from patients, advocates,

physicians, researchers, pharma representatives, and policymakers. Figure 2 summarizes the key takeaway points from each day of the conference.

### The flow of the program

The event was kicked off with an opening speech by Dr Harsha Rajasimha (Founder and Executive Chair, IndoUSRare), who highlighted the key gaps in the rare disease community, which are the focus areas of IndoUSRare programs. Expressing his hopes to see India playing an increasing role in rare disease clinical research, Dr Rajasimha spoke of the organization’s core mission and accomplishments: ‘IndoUSRare is aiming to increase the diversity, equity, and global inclusion and build collaborative bridges between the eastern and western hemispheres’. It was followed by a keynote address focused on the National Policy on Rare Diseases by Dr Madhulika Kabra [Professor, Division of Genetics, Department of Pediatrics at All India Institute for Medical Sciences (AIIMS), New Delhi]. The first session featured a panel discussion including Dr Ratna Devi (Patient Advocate, Dakshama Health), Mr Manjit Singh (Lysosomal Storage Disorders Support Society,



**Figure 2.** Key takeaways and learnings from the inaugural IndoUSrare Annual Conference. Each session highlighted the value of patient centricity in all areas pertaining to rare diseases, ranging from academic and clinical research to policy formulation. The talks supported the importance of global collaboration to drive progress in rare diseases and stressed the need to include all stakeholders to bring in their individual voices – ‘The Power of One’.

India), and Ms Swapna Kakani (Patient Advocate for Short Bowel Syndrome and Founder, Alabama Rare), who presented their views and insights. In keeping with the theme, there were also two special talks by Ms Robin Powers (Co-founder, RareAbility) and Ms Gina Cioffi Loud (Senior Manager, Public Affairs for Chiesi Global Rare Diseases).

Dr Reena Kartha (Director of Research Programs, IndoUSrare) introduced the theme for Day 2, providing an overview of the collaborative research projects undertaken by IndoUSrare to address the gaps in rare disease research globally with a specific focus on India and other low- and middle-income countries (LMICs). Dr Thangaraj [Director, Centre for DNA Fingerprinting and Diagnostics (CDFD), India] and Dr Vinod Scaria [Principal Scientist, CSIR Institute of Genomics and Integrative Biology (CSIR IGIB)] presented their research on population genetics in India. Clinician-researchers Dr Julie Saba [Professor of Pediatrics, University of California, San Francisco (UCSF)] and Dr Anaita Udwadia Hegde (Consultant Pediatric Neurologist at SRCC Narayana Healthcare, and President, Association of Child Neurology, India) presented their

perspectives and experiences. The need and value of patient-led research programs in rare diseases were highlighted by Professor Lara Bloom (President & CEO, The Ehlers-Danlos Society), Ms Sophia Zilber (Patient Registry Director, Cure Mito Foundation), and Mr Nathan Peck (CEO, Cure VCP Disease, Inc.).

Dr Nisha Venugopal (Program Manager, IndoUSrare) introduced the IndoUSrare Patient Alliance program, highlighting the key values of the program of driving cross-border collaborations to connect patient foundations to cost-effective research and resources in India and connect patient groups in the Indian subcontinent to the latest cutting-edge clinical research and resources. The session featured talks by patient advocacy group leaders in India and the United States (Mr Samir Sethi, President, Indian Rett Syndrome Foundation), Ms Gitanjali Sehgal [Co-founder, Families of Spinal Muscular Atrophy (India) TRUST], Mr Shani Weber (Community Education Director, The Ehlers-Danlos Society), Ms Rubby Chawla (President, Indian Patients Society for Primary Immunodeficiency), Mr Marc Yale (Advocacy & Research Coordinator, International Pemphigus Pemphigoid Foundation), Ms Beth Bowerman

(Research Services Coordinator, National Ataxia Foundation Support and Education for Ataxia Patients), who shared their experiences in spreading awareness and leading patient support in their respective disease areas. Dr Arun Shastry, PhD (Chief Scientific Officer, Dystrophy Annihilation Research Trust, India) also brought in the experiences of setting up and leading a successful patient-owned and patient-led research initiative in India. Dr Anish Bhatnagar (CEO, Soleno Therapeutics), Ms Kate Delaney (Senior Director, Global Patient Advocacy and Engagement, BioMarin Pharmaceutical Inc.), David Rintell, EdD (VP, Head of Patient Advocacy at BridgeBio Pharma, Inc), and Anil Raina, MPIB [General Manager (India) – Sanofi Genzyme] emphasized the role of patient advocacy in the life science industry in the United States and India. The concluding highlight of the conference was a fireside chat of Dr Rajasimha with Frank Sasinowski, JD, MPH (Director, Hyman, Phelps & McNamara, P.C., Vice Chair, EveryLife Foundation for Rare Diseases, and founding Board Director at IndoUSrare) who spearheaded regulatory innovation to accelerate the review and approval of orphan drugs since 1983. The conversation highlighted the need for the development of new standards for regulatory review and approvals of orphan drugs.

### Key themes

Several key themes that emerged during the conference have been summarized in the sections below:

#### *Role of patient-led legislative advocacy for rare diseases*

All sessions on Advocacy Day highlighted the importance of advocacy in the diagnosis, treatment, management, and prevention of rare diseases with a particular focus on (a) priorities for advocates and patients and leveraging the voice of the masses, (b) research and clinical trials as priorities for rare diseases, (c) applying the learnings from global advocacy efforts in India, and (d) how new born screening can save lives.

The speakers and panelists shared success stories of how patient-led efforts have brought about policy changes. Mr Manjit Singh shared his journey as a parent of two sons diagnosed with Hunter syndrome, and his efforts for the inclusion of health services for specially-abled

children in the country via judicial cases in India. Dr Ratna Devi summarized her rare disease advocacy efforts at the national, regional, and global levels, including her work at PAIR (Patient Academy for Innovation and Research), which focuses on capacity building of patient groups.<sup>10</sup> Ms Swapna Kakani shared her life story as a patient with a rare chronic disease, short bowel syndrome, and highlighted how patient advocacy can change the viewpoint of policymakers by increasing awareness about rare diseases. Ms Robin Powers shared her journey of becoming an advocate and her perspectives as a patient with hypermobile Ehlers-Danlos syndrome who went on to obtain a degree in biochemical pharmacology of rare diseases, highlighting how people suffering from rare diseases are ‘specially-abled’.

#### *India's National Policy on Rare Diseases*

In her keynote address, Dr Madhulika Kabra provided a holistic view of rare diseases in India, highlighting current developments and underscoring the areas that are lagging, such as research and collaborations among all stakeholders. The National Policy on Rare Diseases (NPRD 2021)<sup>11</sup> released by the Government of India in March 2021 has a special focus on using a comprehensive integrated strategy to prevent the birth of children with rare diseases. The policy provisions allow for access to affordable health care for patients with rare diseases through various government schemes and voluntary crowdfunding to the eight Centres of Excellence (COE). These COEs are recognized across India within existing institutions with the mandate to provide education and training and to promote screening, diagnostics, and prevention by genetic counseling, prenatal screening, and diagnosis. Dr Kabra highlighted the availability of numerous short- and long-term courses in India that increase the pool of skilled clinicians in medical genetics and genomics to work toward diagnosis, treatment, and prevention of rare diseases.

#### *Clinician perspectives on rare disease research in India*

Rare disease patients in India face a variety of challenges such as the presence of very few patient groups, limited interaction between patients, and a lack of focus on research for new treatments. From her perspective as a pediatric neurologist dealing with patients affected by rare conditions,

Dr Anaita Hegde spoke about the issues faced by clinicians in the areas of rare disease research, and the hurdles to scaling up at all levels, that is, patient, hospital, and professional arenas. She highlighted her experience conducting whole-exome sequencing in 1200 patient samples, which identified 764 positive cases, of which 206 represented rare epileptic encephalopathies, 175 rare movement disorders, and 142 neuromuscular disorders.

*Genetic epidemiology of rare diseases in the Indian context*

India is home to a substantial population of rare disease patients – an estimated 70 million people are affected by rare genetic disorders in India, with over 36,000 affected individuals in even the least populated state of Sikkim.<sup>12</sup> During his keynote lecture which provided an overview of the genetic basis underlying the occurrence of recessive diseases due to the presence of founder events in the population, Dr Thangaraj attributed the high prevalence of rare diseases in specific ethnic groups, particularly the recessive gene mutations expressed in the Indian population, to the structure and the inherent diversity of the Indian population, and the practice of endogamy (marriage within the group).<sup>13</sup> He also emphasized the need to spread awareness about rare pediatric genetic disorders. He summarized his work on identifying novel mutations in mitochondrial DNA associated with ophthalmoplegia and premature aging, as well as mutations leading to encephalopathy, seizures, and stroke-like episodes.<sup>14</sup> Speaking of future directions, Dr Thangaraj summarized CDFD's plans to have a mission program in rare pediatric genetic disorders to provide coordinated care for patients along with their work to advance diagnosis and research. Patients would be recruited through collaborators and care provided with the use of telemedicine, while whole genome or whole-exome sequencing is performed, and a web resource portal and database of the variants are created. Further analysis of the variants would be carried out using in-silico methods followed by functional evaluations to further characterize disease biology and identify therapeutic targets.

In his talk titled, 'From personal genomes to populations and back', Dr Vinod Scaria emphasized the lack of awareness, the lack of easily available and affordable systems to offer genetic testing to aid clinicians, and the lack of understanding of the

distribution of mutations as well as the common mutations in various genetic diseases in the country. He highlighted areas of interest at IGIB which include Mendelian genetics, epigenetics, pharmacogenomics, and genetic epidemiology of diseases. He emphasized the value of genomics in P5 medicine (Preventive, Precise, Predictive, Personalized, and Participatory), and spoke about creating an ecosystem for clinical genomics in India – a pan-India clinical network with 280 clinicians and 70+ centers in partnership with existing programs such as Genomics for Understanding Rare Disease, India Alliance Network (GUARDIAN),<sup>15</sup> Genomics for Public Health in India (IndiGen),<sup>16</sup> and Genomics and other omics technologies for Enabling Medical Decision (GOMED).<sup>17</sup> He also spoke of various other initiatives at IGIB toward genomics-based solutions for rare disease diagnoses. IGIB holds the largest database on genome sequencing which includes databases like South Asian Genomes and Exomes (SAGE)<sup>18</sup> and the Arab, Middle East, and North Africa genome (al mena).<sup>19</sup> Dr Scaria also elaborated on the various programs at IGIB that work to address the lack of a comprehensive system for screening or diagnosis of genetic diseases in India.

*Exploring gene therapy for rare disorders*

The diseases caused by mutations in genes can be treated by gene therapy, that is, by introducing a functional copy of the mutant gene into the cells or tissues especially when the defect is in a single gene. New methods for genome engineering like Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) and base editing allow the researchers to fix an existing allele. Gene therapy is being explored as a potential treatment for many rare disorders with a genetic basis. Dr Julie Saba summarized her work on sphingosine phosphate lyase insufficiency syndrome (SPLIS), which is an inherited recessive rare genetic disorder of sphingolipid metabolism caused by inactivating mutations in SGPL1.<sup>20</sup> SGPL1 encodes the enzyme sphingosine phosphate lyase (SPL). Dr Saba discovered the SGPL1 gene 25 years ago and is currently working on therapy for the disease, which has a multifactorial pathogenesis.<sup>21</sup> Possible treatments are either supplementation with Vitamin B6 (the enzyme's cofactor) or gene therapy. High doses of Vitamin B6 are beneficial in SPLIS patient-derived fibroblasts.<sup>22</sup> Later on, they successfully treated four patients with high doses of Vit B6 and observed a rise in lymphocyte

levels. Her group also investigated gene therapy with adeno-associated virus-mediated delivery of the SPL gene in the *Sgpl1* knockout mouse model and observed positive effects in terms of prevention of nephrosis and overall survival.<sup>23</sup>

#### *Patient-centric collaborations and partnerships driving research for rare diseases*

Patients and patient advocacy groups play an essential role in driving research – they can help recruit patients for clinical trials, encourage participation in natural history studies, identify cohorts of individuals with a variety of phenotypic expressions, and educate patients, the public, the media, and health care professionals about upcoming research and training initiatives and the value and potential of patient registries.<sup>24</sup> Detailing a disease's natural history, assessing the clinical effectiveness of therapies, analyzing the safety of treatments, and evaluating or enhancing the quality of care are the four basic uses for patient registries. Registries frequently collect additional individual-level data not typically captured in traditional clinical settings, which might help clinical trial designers better reflect the needs of the patient population.<sup>25</sup> The conference highlighted several success stories of patient registries and patient-led collaborative research.

The Cure Mito Foundation's Leigh Syndrome Global Patient Registry<sup>26</sup> was launched in September 2021 in collaboration with the Coordination for Rare Diseases at Sanford (CoRDS)<sup>27</sup> to understand the patient population and to share clinical trials and research opportunities with patients. As of November 2021, it had 120 participants from 21 countries, making it the first global registry for Leigh syndrome. The registry collects information on diagnosis and genetic mutation, symptoms, loss of milestones, health care utilization, and caregiver burden. Other research initiatives at the Cure Mito Foundation are the collection program for electronic medical records for Leigh syndrome conducted along with AllStripes, and their participation in the Rare Disease Cures Accelerator Data and Data Analytics Platform (RDCA-DAP), an FDA-funded initiative providing centralized and standardized infrastructure to support and accelerate rare disease characterization. The Cure Mito Foundation is dedicated to advancing education and research for Leigh syndrome.

Cure VCP Disease, Inc.<sup>28</sup> has maintained a VCP disease patient registry since June 2018. VCP stands for Valosin-containing protein-p97 gene. Mutant VCP does not degrade proteins properly, affecting the central nervous system, peripheral nervous system, and skeletal system in many ways. To strengthen patients' voices through the use of patient data, Cure VCP, Inc. is involved in many studies like their Global Patient Registry with CoRDS, a retrospective natural history study with AllStripes, a prospective natural history study with National Children's Hospital, and a prospective remote video assessment study with Casimir, LLC (<http://casimirtrials.com/>).

Professor Lara Bloom spoke about how patient-centric collaborations and partnerships can drive research. Speaking about the importance of patient engagement, she emphasized that it is necessary to involve the patient's voice from the very beginning of any process and that the patient or caregiver be considered an equal stakeholder in the process. In 2018, the Ehlers-Danlos Society<sup>29</sup> was awarded a grant from PCORI (Patient-Centered Outcomes for Research Initiative) to form the Ehlers-Danlos Syndrome (EDS) and Hypermobility Spectrum Disorders (HSD) Community Coalition which brought together all stakeholders including individual patients, health care professionals, and patient organizations to put forth research priorities and successfully bridge the gap between the community and organizations. This program was well received and is still actively working toward the priorities identified. The 'Ahead Coalition' brings together stakeholders to help infants, children, and young patients with HSD and EDS achieve a quicker and more accurate diagnosis. The EDS and HSD global registry has over 15,000 individuals registered. The registry has helped recruitment for HEDGE (Hypermobility Ehlers-Danlos Genetic Evaluation), a patient-led global initiative to understand the genetic markers of hypermobile EDS. Prof. Bloom attributed the success of these landmark initiatives to the importance given to patient engagement at every stage of the work.

Dr Arun Shastry spoke about DART's<sup>30</sup> aim to achieve the total annihilation of muscular dystrophies. In addition to conducting several awareness and advocacy programs, DART has a state-of-the-art research facility that works on studying the efficacy of antisense oligonucleotides based exon

skipping in *in vitro* and *in vivo* models, genomics studies to understand variants in Duchenne Muscular Dystrophy (DMD) in India, and a proteomics lab that works to understand muscle regeneration capacity. DART recently showed successful results for multiple exon skipping for DMD in a single patient study. They have now received approval to start a phase II/III multicentre trial for exon skipping and are recruiting patients in nine centers across India. Their research aims to provide affordable and accessible therapeutic options to dystrophy patients in the country.

#### *Importance of patient support, awareness, and education*

To enable enhanced care and effective patient interaction with health care professionals and policymakers, and to drive patient-centric research, there is a considerable need for boosting awareness and education of both health care professionals and patients about many aspects of rare diseases. Various patient advocacy groups working toward these aspects of awareness, patient education, and support shared their experiences during the conference. These have been summarized in the section below.

The Indian Rett Syndrome Foundation (IRSF)<sup>31</sup> is a national association of parents, families, doctors, scientists, health professionals, and caretakers of children with Rett syndrome and was established in 2010. Rett syndrome is a unique neurodevelopmental disorder that is first noticed in infancy and primarily affects girls but in rare cases, can also be seen in boys. It is often misdiagnosed as autism, cerebral palsy, or global developmental delay. He emphasized that the disease has no curative treatment. However, some treatments can be given to help in tackling comorbidities. IRSF President, Mr Samir Sethi spoke about the challenges faced by rare disease patients and their families due to the existing barriers in the public health system in India, and the work done by the foundation to help families of patients with Rett syndrome to address these challenges. He highlighted why India is a good destination for clinical trials and expressed his hope that organizations such as IndoUSrare can help address this gap and connect India to the latest research in the West, bringing clinical trial and compassionate access program opportunities to the country.

Families of SMA Trust (FSMA)<sup>32</sup> is involved in various programs including awareness, programs

for patient support, and education. Co-Founder, Ms Gitanjali Sehgal provided insights from the experience of the family of an SMA patient (her niece), and stated that SMA is considered to be the leading genetic cause of childhood deaths in the world. Despite the availability of approved treatments, many patients cannot afford access to the three different currently approved therapies for the disease, due to the exorbitant costs. Ms Sehgal's talk highlighted the need for a comprehensive approach involving all stakeholders to provide an ecosystem that is supportive of patients' needs.

The IndoUSrare Annual Meeting provided a forum for mutual learning for organizations from across the world to learn from each other's experiences. Numerous organizations in the United States and Europe have been working toward supporting specific patient needs through their programs. One such organization is the Ehlers-Danlos Society (EDS), which works to address many of these needs. Ms Shani Weber spoke about how a patient group can educate health care professionals and help them to be more aware of ways to diagnose, treat, and support the rare disease patient community. Stressing the importance of how rare disease patient groups can make a difference through education, support, awareness, advocacy, and support of research, she summarized five programs at EDS that address these gaps. EDS organizes conferences and support group meetings and has a dedicated helpline and a message board on Inspire to connect and support the community. Of special note, the society was the first case where the project ECHO was adapted for a rare disease. Based on the idea of 'All Teach, All Learn', project ECHO follows a hub and spoke model for knowledge sharing networks which are led by expert specialist teams. EDS ECHO has specific programs for clinicians, pediatric specialists, and specific types of EDS, advocacy for community members, and one for community leaders and educators.

Indian Patients Society for Primary Immunodeficiencies (IPSPI)<sup>33</sup> is a national Primary Immunodeficiency Disorder (PID) organization formed in 2004 having a medical advisory team of nationwide experts. It is the National Member Organisation (NMO) of the International Patient Organisation for Primary Immunodeficiencies (IPOPI), UK.<sup>34</sup> Founder and President, Ms Rubby



Chawla gave an overview of the programs for support and education for the Primary Immunodeficiency Disorder (PID) patient community in India including awareness campaigns and programs for Continuing Medical Education (CMEs) for the medical fraternity. She highlighted the work done by the Society to address challenges faced by the PID community in India during the Covid-19 pandemic, including the lack of access to treatments and medicine due to the extreme risk of exposure and high costs, and lack of awareness of vaccine safety.

The International Pemphigus and Pemphigoid Foundation (IPPF)<sup>35</sup> offers numerous programs to support the Pemphigus and Pemphigoid patient community. Pemphigus and Pemphigoid are a set of chronic and rare autoimmune diseases that need active treatment for management, yet the diseases are very frequently misdiagnosed. Mr Marc Yale spoke about the support programs which include their Peer Health Coach program, patient education webinars and conferences, and local, regional, and international support groups. They provide a number of resources for patients including printed and educational magazines, a map of physicians specializing in the disease across the world, and a community support platform. They work actively to advocate for the Pemphigus and Pemphigoid community at both state and federal levels in the United States. They also have programs for educating professionals, and clinical trial education. In addition, they support research programs including their natural history registry.

The programs at the National Ataxia Foundation (NAF)<sup>36</sup> offer support and education for Ataxia patients working toward the organization's vision of a world without Ataxia. Ms Beth Bowerman (Research Services Coordinator, NAF) stressed the importance of patient education for clinical trial readiness, including connecting all stakeholders to support this effort, ensuring adequate recruitment for clinical trials, and bringing the patient voice to the drug development process. Toward this end, NAF has established the Drug Development Collaborative (DDC) which works toward Ataxia specific resources and information to help patient readiness for participation in clinical trials; and the Clinical Trial Readiness Initiative which is a series of educational materials and programs for the community, support groups, patients, and caregiver panels.

#### *Role of patient advocacy in industry*

In recent years, the biopharmaceutical companies developing orphan therapies in the United States have found the need for roles such as chief patient officer or leadership roles in patient advocacy within the companies. These roles champion the patient perspectives and needs within the organization and have internal mandates to put patients' interests at the center of all strategic planning activities. Patient advocacy organizations now have a primary point of contact at such biopharmaceutical companies and industry.<sup>37,38</sup> Speaking about the importance of patient advocacy within the orphan drugs Industry, Dr David Rintell (VP, Head of Patient Advocacy at BridgeBio Pharma, Inc) said 'Advocacy is bidirectional' meaning one should advocate for patients' perspective within the company while also representing a company to the advocacy groups and patient families. This can foster the growth and support of both patients and the industry. He also expressed the importance of diversity in clinical trials. Ms Kate Delaney (Senior Director, Global Patient Advocacy and Engagement BioMarin) also emphasized the importance of balancing partnerships between industry and the patient advocacy community. Advocacy impacts drug development across different research and clinical stages. In the research stage, patient advocates provide a unique point of view on the impact of their condition. In the clinical development stage, the advocacy community can be valuable partners to increase trial awareness, bring the patient perspective to key program decisions (like clinical endpoints, eligibility criteria, etc.), help in patient enrollment and retention, and clarify the risk/benefit trade-off of the therapy. In the review stage, the community can help regulators better understand the impact of the therapies on their lives outside of what is captured by the study data.

#### *Charitable access programs (CAP)*

Several companies and non-governmental organizations (NGOs) operate charitable or humanitarian programs in an attempt to meet the requirements of patients who are unable to obtain licensed medicines. Mr Anil Raina (General Manager, Sanofi Genzyme – India) highlighted that Sanofi Genzyme has had its footprints in India since 1999 through its charitable access program (CAP). It is currently marketing treatments for patients affected by rare diseases (Cerezyme, Myozyme, Fabrazyme, Aldurazyme),

multiple sclerosis (Aubagio, Lemtrada), and cancer (Jevtana). Sanofi Genzyme is currently supporting over 130 patients with Gaucher, Pompe, Fabry, or MPS type1 diseases through the India CAP. He outlined the development of an ecosystem for rare diseases as follows: (a) increasing access to treatment through CAP and Centres of Excellence, (b) improving diagnosis and management through preceptorship programs, diagnostic support, and capacity building, and (c) promoting awareness and advocacy via patient societies, public relation campaigns, expert forums, billboards, and so on.

Ms Gina Cioffi Loud provided insights from her previous non-profit rare disease advocacy experience as the National Executive Director of the Cooley's Anemia Foundation. In addition, she highlighted Chiesi's leadership as the world's largest pharma company certified as a Benefit Corporation (B Corp) and their work in this regard to achieve United Nations Sustainability Goal 3 – Health for all at all ages.

#### *Rare disease advocacy and orphan drug regulations*

Mr Sasinowski (Director, Hyman, Phelps & McNamara, P.C., Vice Chair, EveryLife Foundation for Rare Diseases, and founding Board Director at IndoUSrare) shared his experiences and observations during the time when President Ronald Reagan signed the US Orphan Drug Act of 1983 and how he has been continuously involved with the approvals of new orphan drugs by the FDA since then. Based on his experience with the US FDA, he advised pursuing similar strategies in India so that authorities could become more flexible in approving new therapies for rare diseases. He emphasized that the same criteria used for the review and approval of drugs for common conditions cannot be applied to an orphan drug because of inherent problems of having fewer people affected by a rare medical condition and the problems with clinical trial conduct. Hence, flexibility in the drug approval process is the key to ensuring maximum patients benefit from approved therapies. This requires marked changes in the country's legislation, regulations, and policies. In conclusion, Mr Sasinowski advised all to think beyond the definition of rare diseases – he urged regulators to set new standards for orphan therapies and not apply the same standard expectations borrowed from common

conditions. Patient-focused drug development and active participation in FDA activities should be the way forward. He also encouraged each patient or advocate to think of themselves as 'warriors' in the rare disease arena by taking those small steps toward making a difference in the community – highlighting the 'Power of One' in rare diseases.

#### **Major challenges in the field of rare diseases**

Challenges highlighted during the conference include lack of awareness among all stakeholders, barriers to achieving a timely and accurate diagnosis, the 'zip code' of a patient being a major factor in access to treatments or clinical trials, and the unaffordable high cost of orphan therapies for most patients when available. Although most of these issues are universal, there is a stark contrast in the magnitude and impact of these challenges faced by rare disease patients in LMICs like India,<sup>39,40</sup> and globally underrepresented populations like the Indian diaspora. Existing non-governmental organizations and patient advocacy groups are doing more than their fair share of the work raising awareness among patients affected by rare diseases and the public; these groups are usually formed by the patients or their family members and are often focused on a particular rare disease or a subset of related rare diseases. Most organizations operate within a single country while trying to include patients from all over the world through digital patient engagement.

Another major hindrance in the field is the lack of active funding for scientific research in understanding the natural history of the disease to enable the development of affordable diagnostics and therapeutics. Of the 10,000+ rare diseases<sup>2</sup> known to date, less than 5% have any available approved treatments.<sup>3</sup> This is due to the long timelines of rare disease research from basic research in the lab, to translational research, and clinical research to assess the safety and efficacy of orphan therapies. This means a diminished interest from funders of commercial pharma since the market is very small, and the expected return on investment is generally perceived as too little too late. Governmental tax and regulatory incentives can go a long way in addressing this in LMICs, as has been demonstrated by the US Orphan Drug Act of 1983.<sup>41</sup> In addition, government funding for extramural academic research

by LMICs could play a major role in initiating and conducting the much-needed local research involving patients with rare diseases. More collaborations between researchers in different countries can maximize the impact of limited research funding by leveraging existing resources and data.

Data on the prevalence and incidence of rare diseases is available in the United States and European Union from databases such as the Genetic and Rare Diseases Information Centre (GARD)<sup>42</sup> and Orphanet.<sup>43</sup> However, such data is unknown in many countries for most rare diseases. Estimates are sometimes obtained from retrospective studies conducted locally and extrapolated by individual hospitals or institutions on smaller cohorts. There is a critical need to understand the prevalence and incidence of rare diseases in densely populous LMICs such as India.

### Limitations and potential solutions identified

One of the major limitations in conducting the research related to rare genetic diseases that came up was the severe lack of global diversity, equity, and access in clinical trials. This is especially important in the case of rare diseases where a very small number of people are affected by a particular disease, and clinical trials often fail because of poor patient recruitment. India accounts for only 2% of global clinical trials even though it is home to over 18% of the total population globally. Dr Harsha Rajasimha and Dr Anish Bhatnagar moderated a panel discussion among the life science industry's patient advocacy leaders – Ms Kate Delaney, Dr David Rintell, and Mr Anil Raina. The panelists highlighted the challenges in bringing global clinical trials to India, including the lack of patient registries, natural history studies, and a dearth of information on the prevalence, incidence, or economic burden of rare diseases in the country.

Digital health and remote monitoring technologies, integration with electronic medical records, patient registries, natural history studies, remote electronic informed consent, electronic patient-reported outcomes, telemedicine or video calling, and N-of-1 clinical trials were noted as recent technological advances that are expected to have a dramatic impact. These advances offer the opportunity to decrease the cost of clinical research and offer much hope for patients worldwide to access

novel therapeutic interventions from rural, hard-to-reach geographies, including from most LMICs with access to the Internet.

The critical role of engaging the legislative and executive branches of the government in various countries was highlighted, and the exemplary work of rare disease legislative advocates (RDLA) at the federal and state levels in the United States was acknowledged. India and other countries need to develop state-level and national-level networks of advocates to inform and educate policy-makers about patient stories and unmet needs.

It has become essential to foster research and innovation that can lead to faster discovery and development of affordable diagnostics and therapeutics for the rare disorders relevant to a community. India has demonstrated a high level of effectiveness in pre-clinical, computational, statistical, and animal model research that can be better leveraged by international collaborators. The repurposing of existing approved therapies for other diseases is another area requiring improvement so that people suffering from rare diseases can access affordable diagnostics and treatments on time.

Genome sequencing is now available at a population scale and more recently, genome editing technologies (such as CRISPR-CAS9) have begun to increase the accessibility of gene therapy and DNA diagnostics to reach a large population. For instance, the rapid widespread availability of genetic testing services in both public and private sectors in India was highlighted. Although research and development of gene therapies are still in the nascent stages in the Indian subcontinent, patients are expressing desperation and a sense of urgency in accessing potential gene therapies currently in development in the United States or elsewhere. Informing the patients about the possible risks and benefits of gene therapies and connecting them to ongoing clinical trials is a critical gap that IndoUSrare can fill.

The life science industry has demonstrated numerous success stories in therapy development for ultra-rare diseases such as cystic fibrosis, spinal muscular atrophy, and lysosomal storage disorders. The highly regulated industry has also created new roles such as chief patient officer and patient advocates within the companies in the last decade. These roles in the US

biopharmaceutical companies are helping in the meaningful engagement of patients throughout the patient-focused drug development process. It is encouraging to see biopharmaceutical companies with a presence in LMICs developing similar roles in other countries.

Dr Rajasimha emphasized the need for clinical trials to transcend international borders, especially in emerging markets such as India. He further advised patient families on the proper channels to engage with regulatory agencies and biopharmaceutical industry for information on therapies via patient advocacy groups, sponsor company websites, and direct email communication to the contacts provided in the latest clinical trials on ClinicalTrials.gov<sup>44</sup> or the Clinical Trial Registry of India (CTRI).<sup>45</sup>

### Role of IndoUSrare in addressing some of the gaps

IndoUSrare is uniquely placed to address many of the various challenges and gaps highlighted during the conference through various programs that are focused on building collaborations among stakeholders across geographic boundaries to raise awareness, engage patients, accelerate research, and therapy development. IndoUSrare aims to catalyze this acceleration of advocacy and technology innovation by building strategic partnerships and collaborative bridges for all stakeholders of rare diseases in the United States with those in the Indian subcontinent to break through existing silos that prevent collaboration. IndoUSrare is in the early stages of operationalizing a corporate advisory council to engage industry stakeholders to help address common challenges around patient education, investigator engagement, disease epidemiology data in the geographies of interest, and unique challenges associated with maximizing the engagement of persons affected by rare diseases in India or those in diaspora from India globally. Recent projects of IndoUSrare include a collaborative study conducted with the non-profit, Rare-X to understand the feasibility of patient-owned health data registries in India,<sup>46</sup> a perspective article on the impact of COVID-19 on rare disease research and clinical development,<sup>47</sup> and the currently ongoing epidemiology project in collaboration with the GRID Council, India, which aims to scientifically estimate the prevalence and incidence of a subset of rare diseases represented by our member organizations in India,

the United States, and globally. IndoUSrare's technology-enabled patient concierge is helping connect remote patients of Indian origin with informational, educational, diagnostic, research resources, and expertise that may not be locally accessible in the patient's proximity. A directory of important resources and expertise for the management of rare diseases was suggested as invaluable for stakeholders to access and search. The IndoUSrare Research Corps is currently a group of over 50 key opinion leaders and experts that include health care providers and researchers from renowned centers and research institutes in India and the United States. This initiative aims to accelerate the process of identifying patients with specific rare diseases or gene mutations in India, to better understand the natural history and disease heterogeneity, and to characterize geographic and ethnic differences in these specific diseases.

IndoUSrare is solely focused on addressing the barriers and bottlenecks that have led to massive health inequities in access to affordable diagnostics and life-saving therapies for all rare disease patient populations globally.<sup>48</sup>

### Conclusion

The conference highlighted the major challenges, numerous success stories, and possible solutions in the field of rare diseases. Genomic technology has never come this close to finding curative therapies for many monogenic diseases. Leveraging the latest technologies to address the challenges such as those highlighted during this event is the need of the hour to make previously unaffordable therapeutics available to the masses and improve the lives of all patients with rare diseases globally.

### Declarations

#### *Ethics approval and consent to participate*

Ethical approval and informed consent were not required for this review.

#### *Consent for publication*

Not applicable.

#### *Author contributions*

**Harvinder Kour Khara:** Conceptualization; Writing – original draft; Writing – review & editing.

**Nisha Venugopal:** Data curation; Investigation; Methodology; Project administration; Resources; Validation; Writing – original draft; Writing – review & editing.

**Ramya T. Karur:** Data curation; Formal analysis; Project administration; Validation; Writing – review & editing.

**Rakesh Mishra:** Formal analysis; Resources; Supervision; Writing – review & editing.

**Reena V. Kartha:** Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Supervision; Writing – review & editing.

**Harsha K. Rajasimha:** Data curation; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Writing – review & editing.

### Acknowledgements

The authors acknowledge all the speakers at the IndoUSrare Annual Conference for their time, insights, and for reviewing a draft of this report. The authors also acknowledge all IndoUSrare staff, volunteers, patient alliance members, community engagement leaders, organizational partners, donors, and supporters of IndoUSrare including all Advisors, Research Corps Members, and industry collaborators.

### Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The authors gratefully acknowledge general organizational support for the Indo US Organization for Rare Diseases through contributions from individual donors, fundraisers, and donations and grants from corporate charitable programs at Takeda Pharmaceutical Company Limited (DON-000187, GRN-000210), Ultragenyx Pharmaceutical Inc. (DON-HASS-1051), and Amicus Therapeutics.

### Competing interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### Availability of data and materials

Not applicable.

### ORCID iD

Harsha K. Rajasimha  <https://orcid.org/0000-0002-2703-9939>

### Supplemental material

Supplemental material for this article is available online.


### References

1. Nguengang Wakap S, Lambert DM, Olry A, *et al.* Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database. *Eur J Hum Genet* 2020; 28: 165–173.
2. CACCA, Council DA and Platform RX. The power of being counted, <https://rare-x.org/case-studies/the-power-of-being-counted/> (2022, accessed 22 July 2022).
3. Kaufmann P, Pariser AR and Austin C. From scientific discovery to treatments for rare diseases – the view from the National Center for Advancing Translational Sciences – Office of Rare Diseases Research. *Orphanet J Rare Dis* 2018; 13: 1–8.
4. Isono M, Kokado M and Kato K. Why does it take so long for rare disease patients to get an accurate diagnosis? – a qualitative investigation of patient experiences of hereditary angioedema. *PLoS ONE* 2022; 17: e0265847.
5. Smith AG. The cost of drugs for rare diseases is threatening the U.S. health care system. *Harvard Business Review*, <https://hbr.org/2017/04/the-cost-of-drugs-for-rare-diseases-is-threatening-the-u-s-health-care-system> (2017, accessed 22 July 2022).
6. Tisdale A, Cutillo CM, Nathan R, *et al.* The IDEaS initiative: pilot study to assess the impact of rare diseases on patients and healthcare systems. *Orphanet J Rare Dis* 2021; 16: 1–18.
7. Yates N and Hinkel J. The economics of moonshots: value in rare disease drug development. *Clin Transl Sci* 2022; 15: 809–812.
8. List of rare disease clinical trials, [https://clinicaltrials.gov/ct2/results?cond=rare+diseases&age\\_v=&gndr=&type=&rslt=&Search=Apply](https://clinicaltrials.gov/ct2/results?cond=rare+diseases&age_v=&gndr=&type=&rslt=&Search=Apply) (accessed 22 July 2022).
9. Rare Disease Organization Connecting India and US – IndoUSrare, <https://www.indousrare.org/> (accessed 22 July 2022).
10. PAIR Academy, <https://www.pairacademy.org/> (accessed 22 July 2022).
11. Ministry of Health and Family Welfare, Government of India. National Policy for Rare Diseases, <https://main.mohfw.gov.in/sites/default/files/Final%20NPRD%2C%202021.pdf> (2021, accessed 22 July 2022).

12. Rare diseases India, <http://www.rarediseasesindia.org/> (accessed 22 July 2022).
13. Nakatsuka N, Moorjani P, Rai N, *et al.* The promise of discovering population-specific disease-associated genes in South Asia. *Nat Genet* 2017; 49: 1403–1407.
14. Paramasivam A, Meena AK, Pedaparathi L, *et al.* Novel mutation in C10orf2 associated with multiple mtDNA deletions, chronic progressive external ophthalmoplegia and premature aging. *Mitochondrion* 2016; 26: 81–85.
15. Sivasubbu S and Scaria V. Genomics of rare genetic diseases – experiences from India. *Hum Genomics* 2019; 13: 1–18.
16. Genomics for Public Health in India – IndiGen, <https://indigen.igib.in/> (accessed 22 July 2022).
17. Genomics other omics tools for enabling Medical Decisions (GOMED), <http://gomed.igib.in/> (accessed 22 July 2022).
18. Hariprakash JM, Vellarikkal SK, Verma A, *et al.* SAGE: a comprehensive resource of genetic variants integrating south Asian whole genomes and exomes. *Database* 2018; 2018: 1–10.
19. Koshy R, Ranawat A and Scaria V. al mena: a comprehensive resource of human genetic variants integrating genomes and exomes from Arab, Middle Eastern and north African populations. *J Hum Genet* 2017; 62: 889–894.
20. Weaver KN, Sullivan B, Hildebrandt F, *et al.* Sphingosine phosphate lyase insufficiency syndrome. In: Adam MP, Everman DB, Mirzaa GM, *et al.* (eds) *GeneReviews [Internet]*. Seattle, WA: University of Washington, Seattle, 2020.
21. Saba JD. Fifty years of lyase and a moment of truth: sphingosine phosphate lyase from discovery to disease. *J Lipid Res* 2019; 60: 456–463.
22. Zhao P, Liu ID, Hodgin JB, *et al.* Responsiveness of sphingosine phosphate lyase insufficiency syndrome to vitamin B6 cofactor supplementation. *J Inherit Metab Dis* 2020; 43: 1131–1142.
23. Zhao P, Tassew GB, Lee JY, *et al.* Efficacy of AAV9-mediated SGPL1 gene transfer in a mouse model of S1P lyase insufficiency syndrome. *JCI Insight* 2021; 6: 145936.
24. Merkel PA, Manion M, Gopal-Srivastava R, *et al.* The partnership of patient advocacy groups and clinical investigators in the rare diseases clinical research network. *Orphanet J Rare Dis* 2016; 11: 1–10.
25. Boulanger V, Schlemmer M, Rossov S, *et al.* Establishing patient registries for rare diseases: rationale and challenges. *Pharmaceut Med* 2020; 34: 185–190.
26. Registry Cure Mito Foundation. Patient registry, <https://www.curemito.org/registry> (accessed 22 July 2022).
27. Coordination for Rare Diseases at Sanford (CORDs) Registry, <https://research.sanfordhealth.org/rare-disease-registry> (accessed 23 July 2022).
28. Cure VCP disease Inc, <https://www.curevcp.org/aboutus> (accessed 23 July 2022).
29. The Ehlers- Danlos society, <https://www.ehlers-danlos.com/> (accessed 22 July 2022).
30. Dystrophy Annihilation Research trust (DART), <https://dartindia.in/> (accessed 23 July 2022).
31. Indian Rett Syndrome Foundation (IRSF), <https://www.rettsyndrome.in/> (accessed 23 July 2022).
32. Families of Spinal Muscular Atrophy (India) TRUST, <http://fsmaindia.org/> (accessed 23 July 2022).
33. Indian Patients Society for Primary Immunodeficiency, <https://www.ipspiindia.org/> (accessed 22 July 2022).
34. International Patient Organisation for Primary Immunodeficiencies, <https://ipopi.org/> (accessed 22 July 2022).
35. The International Pemphigus Pemphigoid Foundation (IPPF), <https://www.pemphigus.org/> (accessed 23 July 2022).
36. National Ataxia Foundation, <https://www.ataxia.org/> (accessed 23 July 2022).
37. Berry SA, Coughlin CR 2nd, McCandless S, *et al.* Developing interactions with industry in rare diseases: lessons learned and continuing challenges. *Genet Med* 2020; 22: 219–226.
38. Stein S, Bogard E, Boice N, *et al.* Principles for interactions with biopharmaceutical companies: the development of guidelines for patient advocacy organizations in the field of rare diseases. *Orphanet J Rare Dis* 2018; 13: 1–10.
39. Rajasimha HK, Shirol PB, Ramamoorthy P, *et al.* Organization for rare diseases India (ORDI) – addressing the challenges and opportunities for the Indian rare diseases’ community. *Genet Res* 2014; 96: 9.
40. Chan AYL, Chan VKY, Olsson S, *et al.* Access and unmet needs of orphan drugs in 194

- countries and 6 areas: a global policy review with content analysis. *Value Health* 2020; 23: 1580–1591.
41. Orphan Drug Act USA, <https://www.govinfo.gov/content/pkg/STATUTE-96/pdf/STATUTE-96-Pg2049.pdf> (accessed 22 July 2022).
  42. Genetic Rare Diseases Information Center (GARD) an NCATS Program providing information about rare or genetic diseases, <https://rarediseases.info.nih.gov/> (accessed 22 July 2022).
  43. The portal for rare diseases orphan drugs – Orphanet, <https://www.orpha.net/consor/cgi-bin/index.php> (accessed 22 July 2022).
  44. Database of privately publicly funded clinical studies conducted around the world, <https://clinicaltrials.gov/> (accessed 22 July 2022).
  45. Clinical Trials Registry India (CTRI), <http://ctri.nic.in/Clinicaltrials/login.php> (accessed 22 July 2022).
  46. Patient-owned health data registries – India feasibility study report RARE-X, <https://rare-x.org/case-studies/patient-owned-health-data-registries-india-feasibility-study-report/> (2021, accessed 23 July 2022).
  47. Venugopal N, Kartha RV, Baranova A, *et al.* Impact of COVID-19 on rare disease research and clinical development: a global perspective. *Translational Genomics* 2021; 2: e1–8.
  48. Addressing massive health inequities on rare disease day. *ET Health World*, February 22 2022, <https://health.economictimes.indiatimes.com/news/industry/addressing-massive-health-inequities-on-rare-disease-day/89736862> (accessed 23 July 2022).

Visit SAGE journals online  
[journals.sagepub.com/  
home/trd](https://journals.sagepub.com/home/trd)

 SAGE journals