LIFE SCIENCES INDUSTRY REPORT 2025

PART 6: RARE DISEASE SPACE

Uncover the transformative trends that will drive the life sciences industry ahead, backed by expert commentary and data-driven insights.

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Editors' introduction

There are some 7,000 known rare diseases in the world. Yet, despite determined recent endeavours to attempt to address unmet needs in numerous rare diseases – including the transformative period of rare disease therapeutics post-2010 – the very nature of these diseases means that many complex challenges remain in development of new therapies, as well as the ability to diagnose such diseases earlier.

In Part 6 of the Life Sciences Industry Report, we've collated key thought leadership from 2024 that looks at ways in which to navigate such complexities, dives into both the opportunities that are now available with advanced technologies and coming next generation technologies, and explores the challenges that must yet be overcome.

And, looking to the future of clinical trials in the rare disease space, Part 6 presents also an overview of the potential of gene therapies and of precision medicine in the ongoing search for rare disease solutions.

Part 6 of the Life Sciences Industry Report 2025 aims to provide informed insight into an industry very much at the height of its discovery and development capabilities, on the precipice of truly impressive, paradigm shifting innovation and, vitally, paving the way to broader access to new and earlier rare disease treatments that will permit better quality of life and patient outcomes overall.

The outlook for drug development to treat rare diseases looks encouraging, offering a glimmer of hope to the approximately 400 million people globally who live with these conditions.

Eloise McLennan
Deep Dive Editor

Nicole Raleigh
Web Editor

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Market dominance

The cancer segment dominates the rare disease market with a 37% share.

Top orphan drugs

Trikafta, Darzalex, and Revlimid are among the top orphan drugs driving growth, with high annual sales and therapy costs.

Orphan drug designations

Cancer, neurology, and immunology are the top therapeutic areas for orphan drug designations.

Top companies

Novartis, Roche, and Pfizer lead in the number of orphan drug designations in the US.

Approval trends

There has been a significant increase in orphan drug approvals over the last decade, with 71 in 2023 and 39 in 2024.

Data and insights powered by EVERSANA

Top orphan drugs driving growth in the US

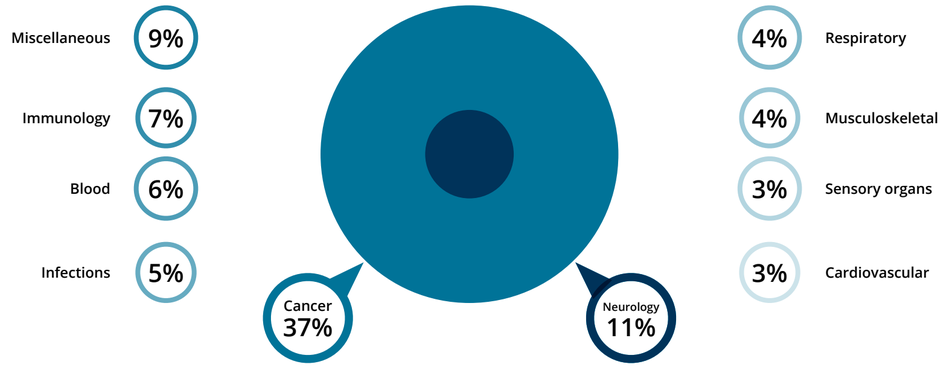
Immunosuppressants followed by immuno-oncology and anti-diabetics constitute the top 3 therapy classes as of 2023

Rank	Product	Molecule name	Company	Approved indication	Annual sales 2023 ($bn)	Annual cost of therapy/ patient ($000')
1	Trikafta	Elexacaftor; Ivacaftor; Tezacaftor	Vertex Pharmaceuticals	Cystic fibrosis in patients aged 2 years	5.54	218
2	Darzalex	Daratumumab	Johnson & Johnson	Multiple Myeloma	5.28	202
3	Revlimid	Lenalidomide	Bristol Myers Squibb	Multiple Myeloma	5.27	471
4	Ofev	Nintedanib Esylate	Boehringer Ingelheim	Idiopathic pulmonary fibrosis	3.11	175
5	Hemlibra	Emicizumab	Roche	Prophylaxis for people with hemophilia a without factor viii inhibitor	2.78	747
6	Imbruvica	Ibrutinib	AbbVie	Chronic lymphocytic leukemia and Small lymphocytic lymphoma	2.67	264
7	Jakafi	Ruxolitinib Phosphate	Incyte	Polycythemia vera, Myelofibrosis, Chronic and acute GVHD	2.59	177
8	Pomalyst	Pomalidomide	Bristol Myers Squibb	Multiple Myeloma	2.36	394
9	Vyndaqel	Tafamidis Meglumine	Pfizer	Cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis	1.86	254
10	Calquence	Acalabrutinib	AstraZeneca	Mantle cell lymphoma, Chronic lymphocytic leukemia or small lymphocytic lymphoma	1.82	182

Source: Evaluate Pharma (Report name on EVP; Accessed on 9th December 2024)

US rare disease market by therapeutic area

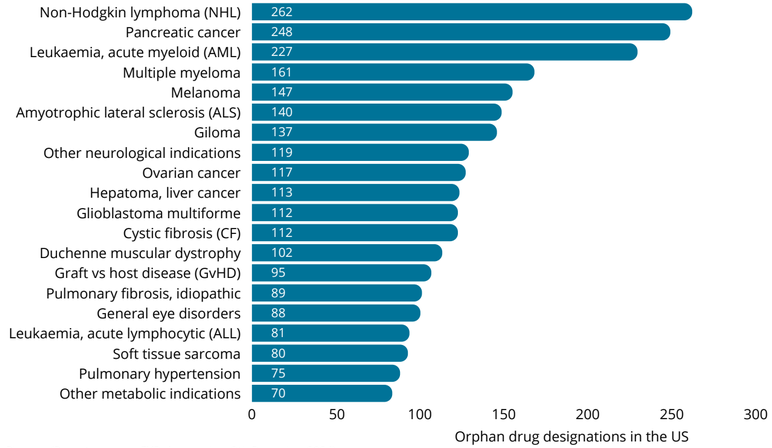
The cancer segment dominated the market with market share of 37%



Source: Evaluate Pharma (Report name on EVP - USA Market Size Rx Sales excluding Generics; Accessed on 29th May 2024)
** Based on forecast on Evaluate Pharma*

Top 20 indications based on the number of orphan drug designations in the US

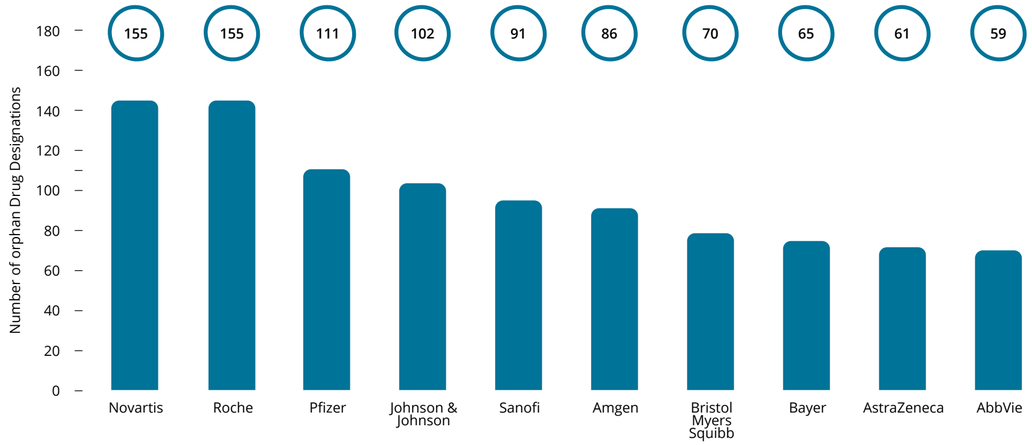
Cancer is the most prominent focus area, with haematologic and solid tumours receiving the highest number of orphan drug designations.



Source: Evaluate Pharma (Report name on EVP; Accessed on 9th December 2024)

Top 10 companies with the most orphan drug designations in the US

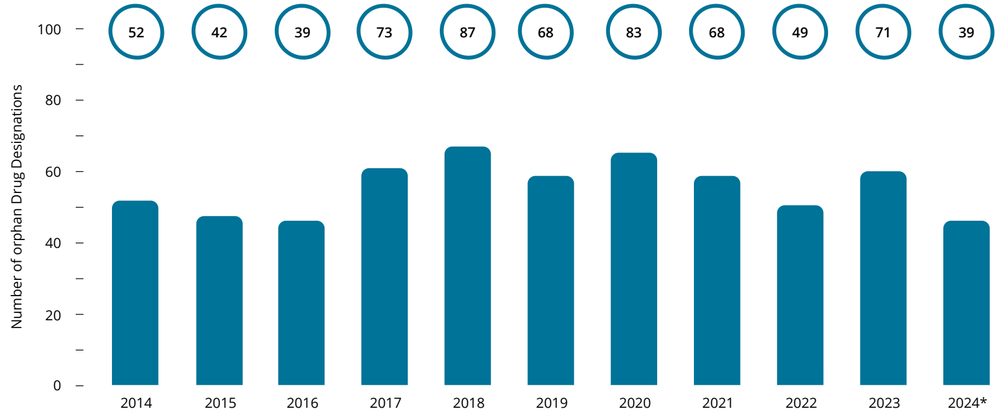
Prominent players operating in the rare disease treatment industry are as mentioned below



Source: Evaluate Pharma (Report name on EVP; Accessed on 9th December 2024)

Annual orphan drug approval in the US

A significant increase has been seen over time, with especially high approval numbers in the recent years of 2020 and 2023.



** 2024 Data is available to date*
Source: Evaluate Pharma; Accessed on 9th December 2024)

*Data and insights powered by **EVERSANA***

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Navigating the complexities of rare disease, diagnostically

As the co-founder of Blueprint Genetics, a proud member of the Quest Diagnostics family, Juha Kkoshenvuo has witnessed firsthand the complexities and nuances involved in rare disease diagnostics and the development of orphan drugs. Quest Diagnostics' collective expertise was encapsulated in the white paper, 'Rare Disease Diagnostics: Advancing Orphan Drug Development through Precision Testing'.

Each year, Quest Diagnostics serves one in three adult Americans and half the physicians and hospitals in the US. Its ethos is that, in the right hands and with the right context, their diagnostic insights can inspire actions that transform lives.

Rare diseases, by definition, affect a small percentage of the population, yet, collectively they present a substantial challenge to the medical community. Each patient's journey to diagnosis and treatment is as unique as their genetic blueprint, often involving a labyrinth of tests and consultations. The Quest Diagnostics white paper sheds light on the evolving landscape of genetic testing and the integral role of multi-omics in revolutionising this field.

Laboratory diagnostics are fundamental to individual health and the health of communities. Quest Diagnostics is working in advanced gene-based and molecular testing, healthcare IT and data analytics, lab services and lab operations, and wellness and population health, to bring lifesaving advanced diagnostics to more people.

The journey from symptom to diagnosis to treatment for rare diseases, though, is fraught with hurdles. With over 7,000 rare diseases identified to date, a significant proportion lack FDA-approved treatments. This gap underscores the urgent need for innovation and strategic approaches in orphan drug research and development, areas where precision diagnostics play a critical role.

Blueprint Genetics is committed to making sense of this complexity. The white paper offers a glimpse into how advanced diagnostic methods, such as Whole Exome Sequencing (WES) and Whole Genome Sequencing (WGS), are shortening the diagnostic odyssey for many patients. Moreover, it discusses the limitations of genetic testing alone and the need for a comprehensive multi-omics approach to obtain a complete understanding of a patient's condition.

The move toward a multi-omics approach – incorporating genomics, epigenomics, transcriptomics (the study of RNA molecules), and proteomics (the study of proteins) – represents the next frontier in rare disease diagnosis. This comprehensive view allows for a deeper understanding of disease mechanisms beyond what genetic information alone can provide.

The white paper also touches on the challenges facing orphan drug development, from understanding disease progression to identifying and validating biomarkers, and the importance of early diagnosis. It doesn't just highlight these challenges; it provides insight into how Quest Diagnostics, through Blueprint Genetics and other assets, is leveraging its advanced diagnostic capabilities to meet these challenges head-on.

While the white paper is rich with information, it's just the tip of the iceberg. Quest Diagnostics' approach, employing cutting-edge technology and a wealth of expertise not only confronts,

but also harnesses, the complexities of rare disease diagnostics for the benefit of drug development and patient care.

The complexities of rare diseases, including their genetic underpinnings, heterogeneous presentations, and often unknown pathophysiology, require a concerted effort from researchers, healthcare providers, and industry stakeholders. The white paper aims to provide a deeper understanding of the current state and future potential of rare disease diagnostics. It's an invitation to explore how these insights can be applied to orphan drug development projects, to ensure that no patient's quest for answers goes unanswered.

Download the white paper today and join the journey towards a future where every rare condition is understood, diagnosed, and treated with the precision it demands.

Download the Quest Diagnostics white paper, "Rare Disease Diagnostics: Advancing Orphan Drug Development through Precision Testing" here

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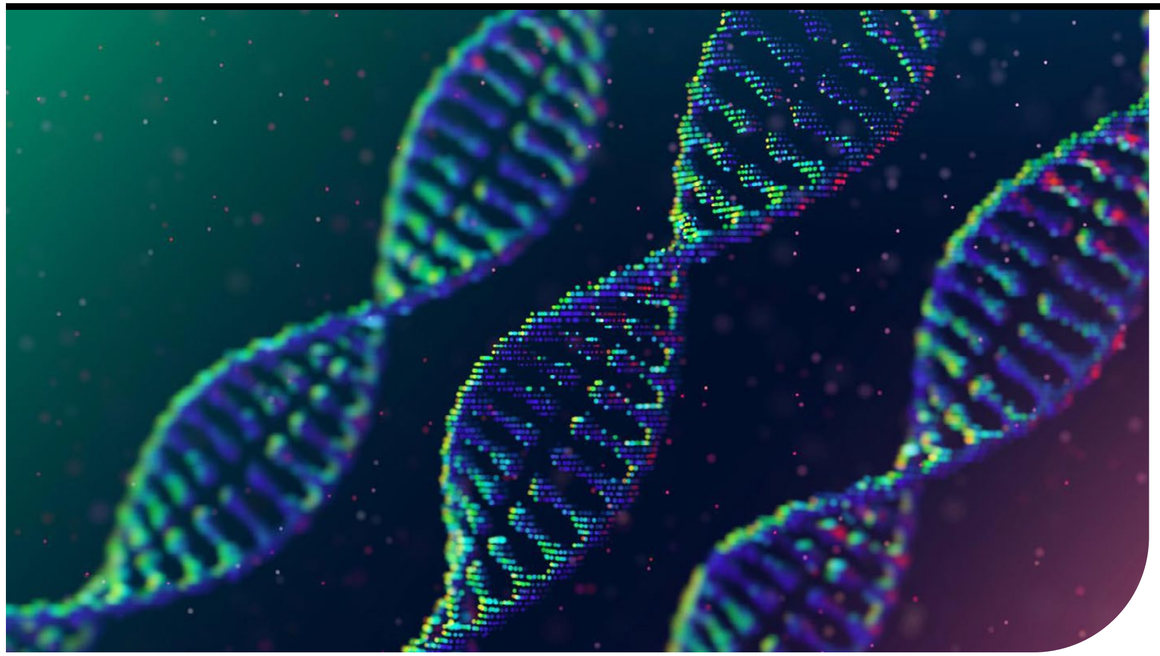


The opportunities and challenges facing rare disease therapies developers

To mark upcoming Rare Disease Day, pharmaphorum asked a panel of experts to give their thoughts on the opportunities and challenges facing developers of rare disease therapies in 2024.

The panel comprised: Jean-Philippe Combal, CEO of Vivet Therapeutics; Dr Jörg Thomas Dierks, CEO of Neuraxpharm; Catherine Pickering, CEO of iOnctura; Jeremy Skillington, CEO, of Poolbeg Pharma; and Miquel Vila-Perelló, CEO and co-founder at SpliceBio.

What does the landscape for rare disease therapies look like in 2024?

Jean-Philippe Combal (JPC): There are global challenges with financing of rare and ultra-rare disease therapies, while in the EU there are uncertainties as to whether payers are able to assess the value of uncertain long-time outcomes.

It's going to be increasingly important to create patient support frameworks to win over payers and collaborate with regulators to find early clinical benefit biomarker approaches for accelerated approvals.

Miquel Vila-Perelló (MVP): We are off to an excellent start, with the approval of three orphan drugs in three different rare disease areas. Hopefully, we can sustain the trend observed in the last decade, whereby approximately 50% of approved drugs are orphan and aimed at rare diseases.

Jeremy Skillington (JS): In 2024, advancements in rare disease therapies continue, with increased focus on precision medicine, gene therapies, and personalised treatment approaches. Research collaborations and innovative technologies play crucial roles in addressing the unique challenges of rare diseases. Access to these therapies may improve, but affordability and availability remain ongoing concerns.

How significant was the first FDA approval of a CRISPR gene therapy in late 2023, and what other promising and cutting-edge developments are on the horizon?

JPC: It was a turning point, but there is much more to be done. The ex-vivo CRISPR-based therapy adoption by patients will be an important next step, while the next cutting-edge step will be in-vivo CRISPR-based therapy - likely for a more limited number of indications.

MVP: It was fantastic news for patients and an endorsement to all gene therapy modalities. The approval demonstrates the pace at which gene therapies are being developed and the clear unmet medical need (10 years from company foundation to first approval). Another development is the recent reports of AAV gene therapies capable of restoring hearing in patients born with mutations in the gene otoferlin. What's significant is the notable therapeutic effect of the approach, considering the fact that the otoferlin gene exceeds the packaging capacity of AAV vectors. The otoferlin gene needs to be split in two and delivered in a dual AAV modality. It demonstrates that gene therapy can work extraordinarily well and that dual AAV gene therapy is feasible in the clinic.

“In principle, any technology that allows us to do more and much faster will have an impact in the understanding and treatment of diseases”

- Miquel Vila-Perelló

JS: The first FDA approval of a CRISPR gene therapy in late 2023 marked a significant milestone, showcasing the potential of gene editing for treating genetic disorders. This breakthrough has spurred further research and development in the field. Ongoing efforts include expanding CRISPR applications, improving precision, and addressing ethical considerations. Additionally, advancements in RNA-based therapies, stem cell treatments, and AI-assisted drug discovery show promise in shaping the future of medical interventions.

How has AI contributed to our understanding and treatment of rare diseases, and how will it affect research in the future?

JPC: It will and can certainly help in rare disease, although it’s difficult to understand the impact on the treatment of rare diseases today. It could help protocol design through the design of virtual arms or real-world data analysis, for example.

Catherine Pickering (CP): AI has already demonstrated its potential in improving the efficiency of diagnosis and treatment. The use of AI can bypass some conventional limitations associated with rare diseases. Namely, it can optimise traditional randomised control trials, and may eventually reduce costs for drug research and development. Recent advancements have enabled researchers to train models based on large datasets and then fine-tune these models on smaller datasets typically associated with rare diseases.

JS: AI has significantly contributed to rare disease research by analysing vast datasets, identifying patterns, and accelerating the discovery of potential treatments. Machine learning algorithms aid in the interpretation of genetic data, facilitating the identification of disease-related mutations. In the future, AI is expected to enhance drug repurposing, streamline clinical trials, and enable more personalised treatment strategies, ultimately improving outcomes for individuals with rare diseases. AI has also contributed to finding eligible patients for approved therapies by mining large claims datasets.

MVP: One thing that is yet to be understood is if AI can significantly improve the odds of identifying drugs that eventually make it across the finish line. In principle, any technology that allows us to do more and much faster will have an impact in the understanding and treatment of diseases. However, a fundamental challenge in the drug development industry is that this hypothesis can only be tested in the clinic, and I think it will take more time to see if AI can deliver on its promise.

Jörg Thomas Dierks (JTD): It is notoriously difficult to understand rare diseases, even within the medical and scientific community, and misdiagnosis is common. AI can be a valuable tool in reducing the time taken to reach an accurate diagnosis and can help with gaining a greater understanding of rare diseases.

How are collaborations between researchers, pharmaceutical companies, and patient advocacy groups shaping the landscape of rare disease research and treatment?

CP: Collaborations are supporting earlier, faster, and more accurate diagnosis of rare diseases. This, in turn, facilitates more efficient rare disease research, clinical trials, and treatment. Ultimately, rare disease communities are very important in supporting patients, advocating for better research, care and treatment, connecting patients and doctors with resources, and influencing regulatory policy.

MVP: Collaborations between biopharmaceutical companies and patient advocacy groups (PAGs) play a crucial role in the development of novel drugs for rare diseases. PAGs, with their close connections to patient communities, can help facilitate patient identification and recruitment for clinical trials, and can even conduct Natural History Studies that are fundamental to understanding the progression of the disease and associated relevant endpoints – such as the Foundation Fighting Blindness did with the ProgStar study in Stargardt disease. More importantly, foundations help us understand what is really important for the patients, and what we need to achieve to improve their quality of life.

JS: Collaborations among researchers, pharmaceutical companies, and patient advocacy groups are vital in advancing rare disease

research and treatment. These partnerships facilitate information sharing, accelerate drug development, and address the unique challenges of rare diseases. Patient advocacy groups provide valuable insights, ensuring that research aligns with patient needs. Collaborative efforts enhance data sharing, streamline clinical trials, and promote a more comprehensive understanding of rare diseases, ultimately improving the development and accessibility of treatments.

JTD: Collaborations and support from stakeholders are of great benefit to finding treatments for rare diseases, including receiving help from patient advocacy groups to gain valuable insights on the patient experience from the patients/sufferers themselves.

What are the challenges for clinical trial recruitment for rare diseases?

MVP: Recruiting patients for clinical trials for rare diseases is, by definition, challenging due to the small number of individuals affected by these conditions, which makes it difficult to reach, identify, and enrol enough participants to ensure statistically significant results. These patients are also dispersed around the globe, which complicates their access to trial sites. Finally, many rare diseases are not well-known and have not been deeply studied and characterised, resulting in a lack of awareness or information about available trials for both patients and healthcare providers, further limiting recruitment possibilities.

JPC: Patient education is important because choosing a gene therapy is like choosing an entirely new destination.

It's important patients understand the risks and benefits throughout the treatment journey. This starts as early as the decision to be screened, being screened, deciding to be injected, to being injected with a co-medication. This awareness must continue throughout the follow-up period, which will be vital as we learn more about long-term durability and safety.

JS: Clinical trial recruitment for rare diseases faces challenges such as limited patient populations, geographical dispersion, and often a lack of awareness about these conditions. Identifying eligible participants becomes challenging due to the rarity of the diseases, potentially leading to prolonged trial durations. Additionally, logistical and financial barriers can hinder patient engagement. Collaboration between researchers, patient advocacy groups, and healthcare professionals is crucial to overcoming these challenges and improving the efficiency of clinical trial recruitment for rare diseases.

CP: Because of the low numbers of patients with rare diseases, it can be challenging to recruit into clinical trials. Further, under legislation passed in 2023, the FDA will require diversity plans for Phase 3 clinical trials conducted in the US. This will enable historically underrepresented patients a stronger opportunity to have investigational access to treatments, but it also places extra challenges on clinical trial recruitment. Drug developers can seek exemptions for the required diversity plan if certain conditions are met.

JTD: The patient population in rare diseases is much smaller by definition than in more prevalent diseases. The pool of potential trial participants is therefore proportionally smaller and can be geographically spread out. Due to the complexities of rare diseases and factors such as slow diagnosis or misdiagnosis, trial recruitment is challenging, and it can often take longer for regulators to consider and approve trials and treatments. Sufferers also have a very complex patient journey, as they typically have to visit several specialists to receive a proper diagnosis. Consequently, patient associations are often very active and supportive, due to the need to give rare disease patients a 'voice', and so these channels can help support clinical trial recruitment.

Do you think it will be easier or harder for rare disease biotechs to secure financing in 2024? What advice can you give your peers?

CP: Coming off one of the most challenging periods for IPOs in recent history, 2024 has gotten off to a promising start. Projects with sound scientific rationale, and convincing preclinical and clinical data are a necessity in a funding environment that has become much more risk averse. Investors are showing a preference for mid-to-late-stage data, so,

many biotechs will stay private for longer, instead favouring other strategies to raise capital alongside equity financing, including venture debt and non-dilutive funding, such as grants, partnerships, and mergers.

JS: 2024 is expected to be easier than 2023, which was a tough year, but likely more challenging than pre-pandemic years. There is plenty of capital available that has not been deployed and investor confidence appears to be recovering, albeit slowly. While interest in innovative treatments persists, securing financing remains competitive. Peers should emphasise robust and compelling data, engage in strategic partnerships, and effectively communicate the societal and medical impact of their work to attract investors. Staying informed about funding trends, leveraging collaborative networks, and showcasing the clinical and commercial potential of their initiatives will be key for rare disease biotechs seeking financing.

MVP: Judging by the optimism earlier this year at the JP Morgan Healthcare Conference in San Francisco, 2024 will provide more opportunities to secure financing. The best advice I have received and tested to be true is that you need to be determined and giving up is not an option: there are patients waiting for us to bring much needed treatments across the finish line.

JPC: Being cautiously optimistic, it could be easier if inflation is reduced and data is supportive – otherwise, it will remain hard.

About the interviewees

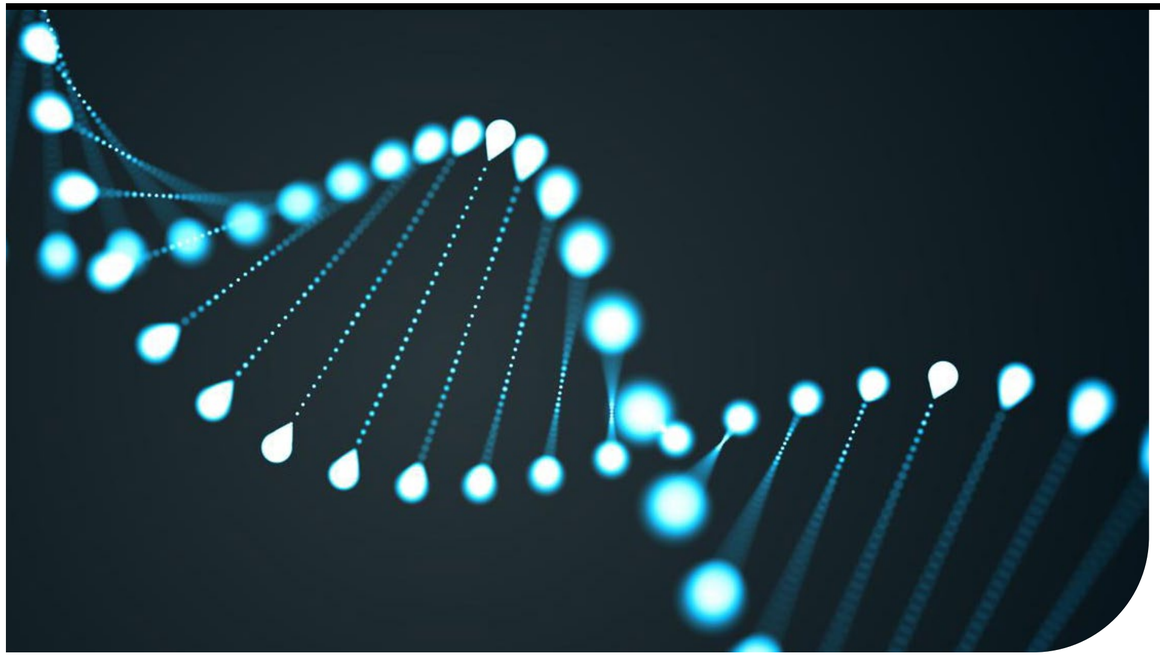
Jean-Philippe Combal has 26 years of experience in the pharma & biotech industries. He is a highly skilled senior executive with a broad range of experience leading global development and a successful track record of innovation and development in the area of orphan drugs. While chief operating officer of GenSight Biologics, he successfully contributed and participated to an investment round of more than $80m, including a successful IPO, and piloted the advancement of two major gene therapy programmes from non-clinical to phase 3 pivotal trials, as well as regulatory and launch readiness strategies. Combal earned his PhD in Toxicology and PharmD from Paris XI University and holds a Master's in Strategic Marketing from ESCP Paris, as well as a General Management Programme from the centre of executive development at INSEAD.

Dr Jörg Thomas Dierks has 30 years of healthcare experience and has held several senior executive positions in the pharmaceutical industry. He joined Neuraxpharm in 2018 from his previous post as CEO of Meda, a Swedish specialty pharmaceutical company, which he held from 2013. Dierks had been the chief operating officer for Meda from 2005 and also assumed the role of chief scientific officer for a period of time. He was instrumental in growing the business over many years and led its sale to Mylan in 2016 for $10bn. Before joining Meda, Dierks was chief operating officer at Viatris, a pharmaceutical company based in Germany. He graduated from Johannes-Gutenberg-Universität zu Mainz with a degree in Human Medicine. This included working for a year in a hospital in Koblenz in 1986, earning him the title of Medical Doctor. One year later, Dierks was awarded the title of Doctor of Medicine. He also studied business administration for scientists at the Fernuniversität Gesamthochschule in Hagen.

Catherine Pickering holds a PhD in Medicinal Chemistry and an MBA. During her career, she has held various licensing and business development positions in pharma and biotech. Before founding and building iOnctura, she led the global oncology and immuno-oncology licensing and business development function at Merck. During her time at Merck, she was also an integral member of the oncology franchise leadership team, a cross functional team responsible for creating the strategy and managing the oncology business.

Jeremy Skillington began his biotechnology career in the Business Development group of Genentech, Inc in California in 2002. At Genentech, he was responsible for executing over 40 licensing, investment, and collaboration transactions. Returning to Ireland in 2009, Skillington led Business Development and was a member of the Senior Management team at Opsona Therapeutics Ltd, before becoming a founder and CEO of mmune-oncology company TriMod Therapeutics Ltd. In 2014, he joined German investment fund HS Lifesciences GmbH to provide start-up and business development support to portfolio companies ImmunoQure AG and Ethris GmbH. Skillington joined Inflazome at its founding in 2016 and was instrumental in their acquisition by Roche in September 2020 for €380m (£325m) upfront and significant downstream milestones. He studied Biochemistry at the National University of Ireland, Galway where he was awarded his PhD. He performed his post-doctoral research at the University of California, San Francisco in the lab of Professor Rik Derynck.

Miquel Vila-Perelló co-founded SpliceBio and serves as CEO. He has broad experience in biotechnology, chemical biology, and protein chemistry, as well as in the managing of research teams and projects. After obtaining his PhD at the University of Barcelona, Vila-Perelló carried out postdoctoral studies at The Rockefeller University. He later became a Research Scholar at Princeton University, where he managed the Protein Center at the Department of Chemistry. Over the last ten years, he has contributed to the discovery and development of novel protein ligation technologies. He has authored more than 23 publications, including patent applications, and has a proven track record for the leadership of scientific teams and non-dilutive fundraising.



Looking to the future of clinical trials: Gene therapy, precision medicine, and the ongoing quest for rare disease solutions

Next-generation technologies in medicine have significantly expanded our ability to identify and address rare diseases, propelling forwards the development of more effective and targeted treatments.

Recent research efforts worldwide have yielded noteworthy progress, influencing the lives of individuals grappling with numerous rare disease types. The period post-2010 has witnessed an unprecedented surge in the approval of treatment options, marking a transformative era in rare disease therapeutics.

The current landscape is evolving as the medical community delves into the realms of gene therapy and precision medicine, representing a new frontier in research. Recognising the pivotal forces that instigated this initial wave of change is crucial, as it lays the foundation for ongoing improvements that push the boundaries of what is achievable for patients today. Advances in these cutting-edge technologies hold promise for continued breakthroughs, offering hope to those affected by rare diseases.

The call for improved rare disease treatment options

In 1983, when the Orphan Drug Act was signed into law, there were 16 orphan drug designation requests. By 2019, the number of orphan drug designation requests had increased significantly to over 700 annually. That growth is attributable to many factors, but perhaps most importantly the powerful impact of advocacy. When patients and families, patient organisations, clinical development organisations, clinicians, and researchers joined to create one voice calling for improved rare disease treatment options, the result had a meaningful impact.

This surge in orphan drug designation requests since the inception of the Orphan Drug Act in 1983 underscores the growing recognition of the importance of rare disease research and treatment development. Advocacy has played a pivotal role in driving this progress, amplifying the voices of those affected by rare diseases and advocating for policies that incentivize and support research and development in this area.

Through tireless efforts, advocacy groups have raised awareness, mobilised communities, and influenced policymakers to prioritise rare diseases on the global health agenda. The collaborative efforts of patients, families, advocacy organisations, and the medical community have fostered a supportive ecosystem for rare disease research and clinical trials, paving the way for transformative advancements in diagnosis, treatment, and, ultimately, the lives of those living with rare diseases.

The undiagnosed journey through the healthcare system

Despite advancements in genotype–phenotype correlation and gene discovery, the undiagnosed journey within the healthcare system persists for most rare disease patients, highlighting the urgent need for early and accurate diagnoses, access to emerging treatments, and enhancements in quality and quantity of life. As research efforts continue to drive new treatment options, the environment for patients can be further improved using the

Given the difficulty rare disease patients face in finding suitable care, fostering trust between patients and principal investigators becomes vital for sustained engagement during a trial.

same approach that first brought change: to collectively solve challenges with the spirit of patient advocacy. Clinical trial teams, working together with all relevant stakeholders, play a vital role in this by:

- Expanding the reach of trials and potential treatment options to new clinical sites
- Educating healthcare practitioners and patient communities about clinical esearch participation
- Connecting patients to sites, sites to patients, and patients to patients through traditional grassroots outreach and new digital platforms
- Sharing transparent trial progress information with participants

Success in rare disease trials

Some of the differences between rare disease trials and other types of research studies are found in the site selection approach, level of protocol complexity, and extended durations between study visits. It is important for clinical research teams to consider these factors and make adjustments at the start of a rare disease trial. Ensure a strong start by unifying stakeholders, offering sufficient support tools, and creating a platform to share successes along the way:

1. Unify stakeholders.

In rare disease research, the distinctive site selection process involves identifying patients, rather than primary investigators. Sites with rare disease research expertise often maintain robust relationships with sponsors. The crucial approach is to unite all stakeholders, including patients, caretakers, sites, key opinion leaders (KOLs), contract research organisations (CROs)/ vendors, and the sponsor.

2. Offer support tools.

Enrolment in rare disease studies tends to be slow, leading to extended gaps between screening visits. Providing sites with support materials is crucial for easy access to protocol information, addressing challenges such as inclusion/exclusion criteria. Given the difficulty rare disease patients face in finding suitable care, fostering trust between patients and principal investigators becomes vital for sustained engagement during a trial, facilitated by support tools that enhance communication pathways.

3. Share successes.

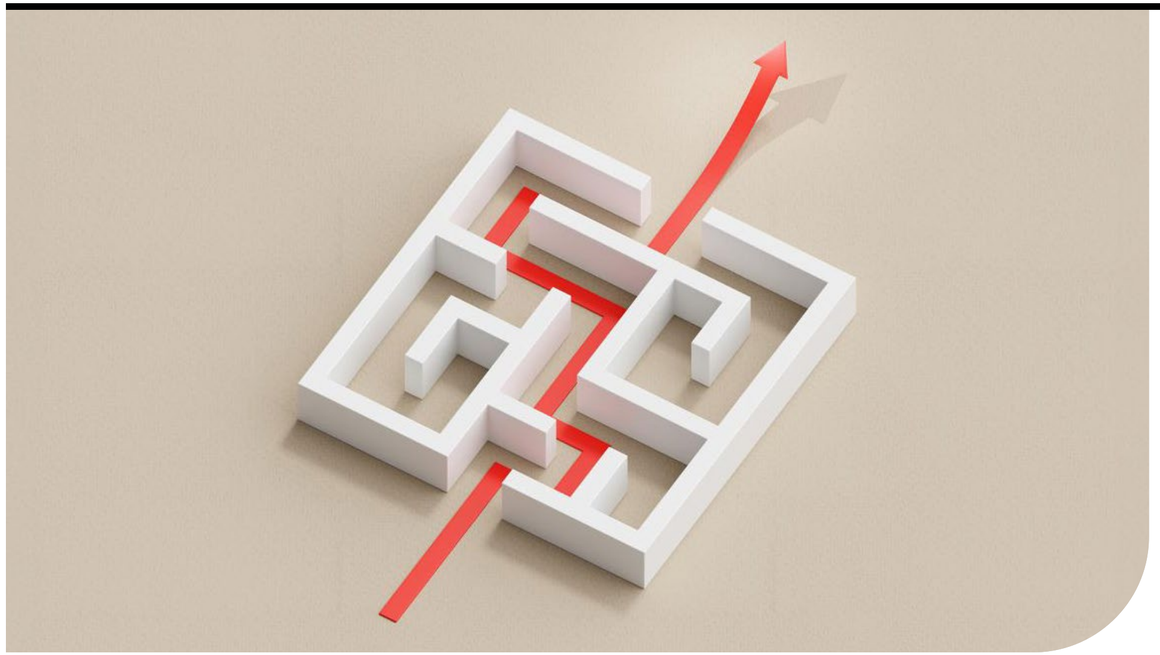
Facilitating communication and success-sharing among research sites is highly beneficial. Regular webinars or face-to-face meetings for study coordinators to exchange ideas foster a motivated and impactful community. Sustained collaboration among rare disease research sites remains crucial.

The landscape of rare disease research has witnessed remarkable strides in recent years, with the advent of cutting-edge technologies and an exponential growth in approved treatment options. While the momentum in genotype-phenotype correlation and gene discovery is evident, challenges persist in providing timely diagnoses and accessible treatments for the majority of rare disease patients.

Emphasising collaborative efforts among stakeholders, including patients, caretakers, sites, key opinion leaders, and sponsors remains paramount for advancing our understanding and addressing the unique challenges posed by rare diseases in contemporary research.

About the author

Meredith Gartner is a programme director for Advanced Clinical and has previous experience as a project manager, clinical research associate and clinical project assistant. Gartner has been in the industry for ~18 years with experience working on multiple clinical trials in oncology, immuno, cellular (gene, CAR-T) therapy, rare disease, endocrine/metabolic, neurological, psychological, urology, vaccine, and infectious disease trials.



Part One: Overcoming challenges and seizing opportunities in global market access for rare and complex conditions

The outlook for drug development to treat rare diseases looks encouraging, offering hope to the 300 million people globally facing the significant challenges of these often-overlooked conditions.

However, for pharmaceutical manufacturers, navigating the path to effectively launch these transformative therapies in global markets is complex. Companies must address a multitude of evolving access challenges, including varying approaches to reimbursement across the globe, choosing the optimal pricing strategy that works globally and at the individual country level, and the increased demand for risk sharing outcomes-based access agreements that rely on the generation of real-world evidence.

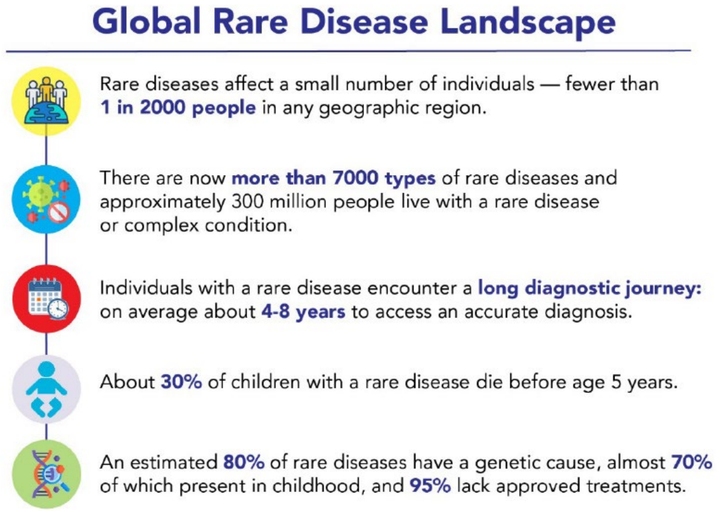
Growing global opportunities in the rare and orphan drug market

Today, 36 million people in the European Union (EU) and 30 million in the US with a rare disease face the harsh reality of a lengthy diagnostic journey, limited research into and awareness of their conditions, and a lack of approved treatments. Currently, less than 5% of all rare diseases have approved therapies available on the market.

IMAGE: Data Source: The Lancet Global Health

There are strong expectations that drug spending and growth will accelerate globally over the next few years, though the pace will differ by country, as will key drivers such as volume and price. By 2028, specialty medicines are projected to account for over 40% of total global spending on medicines, with more than half of that expenditure occurring in leading developed markets. This growth is partially being driven by the increased number of drugs being developed and receiving regulatory approval to treat rare diseases.

In the US, for example, the Food and Drug Administration (FDA) Center for Drug Evaluation and Research (CDER) demonstrated its commitment to hastening the development of treatments for patients with rare diseases. By launching the Accelerating Rare disease



Successful launch or patient access is not guaranteed by regulatory approval of a drug.

Cures (ARC) Program to promote scientific and regulatory innovation in 2022, over half of all the novel drugs and biologics approved by the FDA were aimed at preventing, diagnosing, or treating rare disease by 2023.

As of Q2 2024, the FDA approved 15 new drugs targeting rare diseases, including several for rare cancers. Additionally, the US Orphan Drug Approval Law, enacted more than 40 years ago, continues to encourage pharmaceutical companies to develop treatments for rare diseases by providing incentives such as extended market exclusivity and enhanced tax credits.

In the EU, the Committee for Orphan Medicinal Products (COMP), the European Medicines Agency's (EMA) committee responsible for recommending orphan designation of medicines for rare diseases, has introduced incentives to develop new treatments that include reduced regulatory fees, expedited review processes and an additional two years of market exclusivity for approved drugs treating rare diseases. In the first three months of 2024, EMA had already granted orphan drug designation to 22 drugs affecting 25 different rare diseases.

Navigating country-specific reimbursement landscapes

Successful launch or patient access is not guaranteed by regulatory approval of a drug. Finding the right balance between embracing innovation and ensuring affordable access to costly, yet transformative, therapies for rare disease remains a challenge for manufacturers.

Successful go-to-market strategies need to take into account several key factors, such as the high costs of medications, the potential lack of clinical trial data and the specific challenges associated with curative treatments. Additionally, the reimbursement processes for drugs differ greatly depending on the region, often influenced by whether a health technology assessment (HTA) is mandated by payers.

Throughout the world, there is wide variability in HTA requirements. To harmonise the description of an HTA from country to country, an international joint task group provides this definition: an HTA is a "multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. The purpose is to inform decision-making to promote an equitable, efficient, and high-quality health system."

HTA informs decision-making related to drug pricing and reimbursement recommendations by taking into consideration efficacy and safety data from registration trials, patient health-related quality of life (HRQoL) measurements, life-expectancy impacts, and cost data. HTAs support coverage and reimbursement decisions, clinical guidelines, and policy decisions that contribute to better patient outcomes and the efficient use of healthcare resources.

Overall HTA recommendations are shaped by societal and divergent cultural values, resulting in very different practices among international HTA jurisdictions. HTA may be mandated at national or regional levels in Europe and countries such as Australia and Canada. Additionally, collaboration among national HTA bodies is increasing, as evidenced by the upcoming Joint Clinical Assessment (JCA) in the EU, which will be implemented in January 2025.

In contrast to many developed countries, the US does not have a national HTA programme to broadly evaluate, guide coverage, and pricing decisions. Each private and public payer independently makes its own coverage decisions and conducts separate price negotiations.

The road to successful global market access remains intricate and multifaceted. The supportive regulatory environments in both the US and the EU signal a commitment to advancing treatments for rare conditions, yet, the challenge lies in ensuring that these innovative therapies are not only approved, but also accessible and affordable for patients who need them. Looking ahead, fostering collaboration among stakeholders, including manufacturers, payers, regulators and patient advocacy groups, will be crucial in overcoming these challenges. By aligning efforts to streamline processes and enhance understanding of the true value of these therapies, we can transform the lives of the millions affected by rare diseases and create a more equitable healthcare landscape for all. In part two, navigating pricing, real-world outcomes, and accessibility issues will be covered.

About the author

Gillian Molloy serves as VP of market access, EU/UK, at AscellaHealth. Molloy brings almost 20 years of experience in the life sciences industry to her role, in both the European and US markets. She has held commercial and market access leadership positions at Baxter, Novartis Oncology, and AstraZeneca, as well as trade relations and formulary strategy leadership roles at UnitedHealth Group. At AscellaHealth, Molloy provides strategic innovation and consultative market access support to pharmaceutical manufacturers and healthcare organisations. Prior to moving into the life sciences industry, Molloy held a chief pharmacist position in the Mater Misericordiae University Hospital, Dublin. She holds a BSc in Pharmacy and an MSc in Hospital Pharmacy from the University of Dublin, Trinity College, as well as an MBA from University College Dublin Michael Smurfit Graduate Business School. Molloy also has a Diploma in Health Economics from the National University of Ireland Whitaker School of Government and Management.

Investment outlook: Key takeaways from LSX USA

Investment and strategic partnerships are the lifeblood of innovation in healthcare, driving groundbreaking discoveries and accelerating the development of life-changing therapies. And so, it was no surprise that the 2024 LSX USA Congress in Boston attracted life sciences innovators and decision-makers from around the world, eager to explore the latest trends shaping the industry.

Among those attendees was pharmaphorum's editor-in-chief, Jonah Comstock, who took to the floor to uncover the trends and talking points set to influence investment decisions in the coming months.

In this special episode of the pharmaphorum podcast, Jonah sat down with Deep Dive editor Eloise McLennan to discuss key takeaways from the LSX conference. From evolving investment trends like AI in biotech and digital to emerging areas such as precision psychiatry, they explore the cautiously optimistic investment landscape, the delicate balance between early- and late-stage investments, and the importance of building honest, productive relationships across the healthcare ecosystem.

Tune in to hear their in-depth analysis of the latest investment and partnership trends shaping the future of healthcare innovation.

You can listen to episode 131 of the pharmaphorum podcast in the player below, download the episode to your computer, or find it - and subscribe to the rest of the series - in iTunes, Spotify, Amazon Music, Podbean, and pretty much wherever you get your other podcasts!

Rare diseases: The urgent need for health equity and accelerated access

Rare diseases are complex, but the need is urgent. Alexion's Eunice Alvazzi discusses the shared responsibility in achieving access to innovation in rare diseases

An estimated 400 million people globally are affected by rare diseases. While each condition individually may be rare, in Europe alone, there are approximately 36 million people living with a rare disease. Rare diseases are often severe, progressive and life-threatening, and the path to diagnosis can be lengthy and convoluted. The limited medical and scientific knowledge about individual rare diseases and limited access to specialist care pose unique challenges to healthcare professionals and health systems, creating considerable health inequity for rare disease patients.

Once a diagnosis has been ascertained, people living with a rare disease continue to face barriers to care; of the estimated 10,000 rare diseases, more than 90% currently have no meaningful treatment options. Even when an appropriate treatment exists, access isn't guaranteed. There are significant disparities between EU countries in how quickly patients can access innovative orphan medicines, and across the globe, people living with rare diseases face challenges navigating access in countries where there is no rare disease infrastructure and access has not previously existed for rare disease medicines.

One way to begin to address these disparities is to ensure that there is strong data and evidence demonstrating the clinical and economic value of the medicine for rare disease patients and the health care system.

Traditional value assessments fuel health inequity

National healthcare systems and value assessment processes for rare diseases need to evolve to address the disparities – and, therefore, inequities – in how quickly patients can access innovative rare disease medicines.

To overcome access challenges, the complexities of rare diseases must be taken into consideration. For example, while the UK Rare Disease Framework established in 2021 emphasises the importance of enhancing access for patients with rare diseases, progress in patient access has been limited due to a lack of updates to the value assessment framework for rare diseases medicines.

One of the factors driving inequity is that traditional value assessments do not comprehensively capture the full impact on the quality of life for people living with complex rare conditions and their carers. An openness to embracing novel approaches and actively involving patients is required to accelerate access to rare disease medicines.

Developing compelling evidence on the burden of rare disease

Rare diseases impose a high social and economic burden for patients and their families, health care systems and society overall, yet demonstrating this can be difficult and there is a scarcity of cost of illness (COI) studies. The main issue to address in the COI analysis of rare diseases is the lack of primary and/or aggregated data, making it challenging to estimate the economic burden.

For example, evidence may be limited to only the patient and fail to account for the broader impact on the quality of life of parents caring for a gravely ill or disabled child throughout their life – or adequately represent the financial burden of rare diseases on families and wider society.

Markers of disease progression may also be unidentified or unmapped, making arguments for time-critical intervention difficult to evidence.

Many agencies responsible for assessing the quality and efficacy of medical treatments are now actively seeking inclusion of patient-reported outcomes data in health technology assessment (HTA) submissions, including burden of disease data that could better inform

decision-making by presenting a more complete picture of the impact of a rare disease. Thus, it is especially important for industry and clinical trial investigators to actively seek out and respond to patient feedback on meaningful outcomes and incorporate novel clinical trial endpoints that can be used to develop cost-effectiveness arguments.

Increasing patient participation in evidence development

With rare diseases being inherently unique and not well understood, conducting clinical research in these areas is often complex, particularly with small patient population sizes. Establishing meaningful clinical endpoints also may be problematic due to the nature of evidence that it is possible and ethical to produce.

Successful approaches often involve working closely with regulatory decision makers at an early stage to define and establish novel outcome measures that patients have identified as uniquely meaningful to them. Collecting real-world evidence from registries can also provide new and complementary information for regulatory submissions, as well as generating the long-term data required as part of post-marketing surveillance.

Additionally, new digital technologies are increasingly being employed to generate compelling outcome data and include the patient voice. For example, Alexion was one of the first companies to use video evidence of patients in regulatory submissions to demonstrate the impact of an outcome measure for a rare metabolic disease – an approach that is now considered standard practice.

Partnering to improve access to medicines

Given the acknowledged challenges in accelerating access to innovation in rare disease, as a global rare disease community, we must together champion equitable access for all. It is incumbent on all stakeholders working in this complex area to proactively identify and work to remove access barriers at local and regional levels and to build the capabilities of healthcare systems across the world to best serve the significant unmet needs of people living with rare diseases.

Achieving access to medicines is at one end of the journey – but creating a favourable environment for innovation to flourish is the essential starting point. The European Orphan Medicinal Products (OMP) regulation was introduced to address the lack of R&D and subsequent lack of treatments for rare diseases. After two decades, it is appropriate to review the framework, but the proposed update of the OMP regulation could unravel the innovation incentives that the original regulation helped create. The rare disease community needs policies that encourage steps forward, not back.

The best possible chance of improving access to innovation for rare disease patients is through partnership. As an industry, we must continue to invest in innovations and forge new collaborations to improve accessibility to treatments and solve affordability challenges together with payers. We must proactively engage in dialogue with access decision makers, sharing our perspectives, identifying the challenges and then problem solving and forging unified commitments together. People living with a rare disease deserve health equity – and it is our shared responsibility to make this happen today and for future generations.

About the author

Eunice Alvazzi is the global head of haematology, nephrology, and neurology value and pricing at Alexion, AstraZeneca Rare Disease, a global biopharmaceutical company focused on developing life-changing therapies for people living with rare diseases. She is passionate about advancing patient access for rare disease patients.

About Alexion

Alexion, AstraZeneca Rare Disease, is the group within AstraZeneca focused on rare diseases, created following the 2021 acquisition of Alexion Pharmaceuticals, Inc. As a leader in rare diseases for more than 30 years, Alexion is focused on serving patients and families affected by rare diseases and devastating conditions through the discovery, development, and commercialisation of life-changing medicines.

Alexion focuses its research efforts on novel molecules and targets in the complement cascade and its development efforts on haematology, nephrology, neurology, metabolic disorders, cardiology, and ophthalmology. Headquartered in Boston, Massachusetts, Alexion has offices around the globe and serves patients in more than 50 countries. For more information, please visit www.alexion.com.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