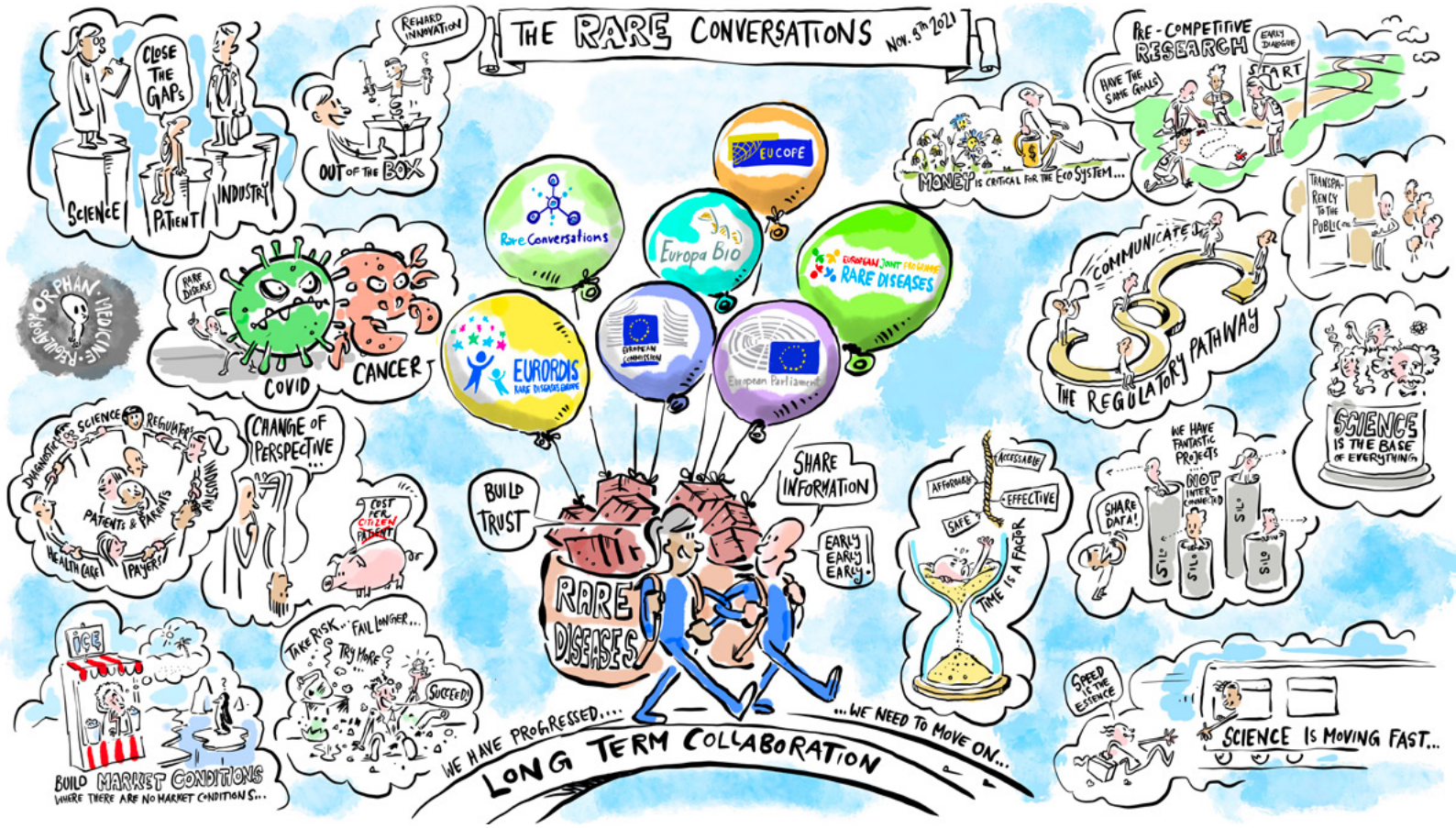
RareConversations

ALEXION
AstraZeneca Rare Disease



Rare Conversations Report 2021

RareConversations

Contents

Executive Summary

Alexion initiated the Rare Conversations series in December 2020 with the belief that – given the impact of the COVID-19 pandemic on the ability to interact face-to-face – this would provide an invaluable platform for exchanging open, diverse opinions and views, involving all relevant stakeholders and discussing the topics important for the rare disease community.

Four Rare Conversations events took place over 2020 and 2021, each in cooperation with a specific partner. The series concluded with the first annual Rare Conversations Conference, which built on the contributions from the previous four events.

- **Take One:** "The impact of COVID-19 on pharmaceutical research and development in rare diseases", in cooperation with EUCOPE.
- **Take Two:** "How to keep rare disease patients at the heart of the discussion", in cooperation with EuropaBio.
- **Take Three:** "The specificities and needs of research in rare diseases", in cooperation with BPI.
- **Take Four:** "HTA: from national to EU value assessment - what provisions for orphan drugs?", in cooperation with EUCOPE.
- **Conclusion:** Rare Conversations Conference, "European rare disease ecosystem: a collaborative path forward", in cooperation with EURORDIS, the European Joint Programme on Rare Diseases (EJP RD), EUCOPE and EuropaBio.

More than 40 different experts took part through the entire Rare Conversations event series, including representatives from research, academia, EU and national institutions, clinicians, health experts, investors, industry and – most importantly – patients. Over 500 people attended the different meetings, participating through surveys and open Q&A sessions. This made the Rare Conversations a genuine opportunity to garner innovative ideas and solutions.

Rare Conversations has helped to build stronger and wider communities, united through their own unique needs, with a common goal – establishing a fit-for-purpose, innovative rare disease ecosystem that brings benefits to patients.

During the events, certain topics consistently came through as particularly relevant for the rare disease community:

- The impact of COVID-19 on the rare disease community, in both the short and long term.
- The increasing importance of listening to and understanding the patient voices.
- The need for a sustainable model for innovation in order to meet the challenge of defining unmet needs in rare diseases.
- The unique and difficult demands of rare disease R&D: what makes it so special and difficult.
- The need for an adapted approach to value assessment of orphan medicines.
- The partnerships required to sustain the future of the rare disease innovation ecosystem in Europe.

Given the importance of these discussions and the interesting outcomes from the series, this report has been developed to capture some of the key findings and takeaways, so these insights can be shared more broadly and continue to drive further discussion on the unmet needs in rare disease.

Key topics of Rare Conversations

By bringing together the voices of stakeholders representing the broad rare disease community, the Rare Conversations series was able to examine the main priorities and challenges in the rare disease ecosystem. The events covered the entire rare disease value chain. However, as the events covered the entire disease value chain, a number of recurring topics were identified as key to understanding – as well as fully enabling – the rare disease ecosystem.

The impact of COVID-19 on the rare disease community, in both the short and long term

The COVID-19 pandemic outbreak saw people with a rare disease experience delays in their diagnoses and interruptions to their treatment, because the focus was on fighting the pandemic. At the same time, however, the pandemic also provided insights into how to improve the rare disease ecosystem in the future. Regulatory flexibilities, rolling reviews and accelerated administrative procedures; the role of digital tools; involving patients in Health Technology Assessment (HTA) processes; wider acceptance of Real-World Evidence (RWE) could all create a more effective environment.

People with a rare disease have been among the most affected by the COVID-19 outbreak. Restrictive measures, reduced inpatient capabilities and the workload placed on overwhelmed clinicians and caregivers has resulted in delays in diagnosis and disruptions to treatment, impacting daily lives to a greater extent than usual.

Fortunately, the impact of these issues has been partly offset in recent months, thanks to the wider adoption of e-health solutions, homecare services and better management of the pandemic. These exist both in the short term – as a result of the pandemic – and in the long term, with the goal of keeping pace with innovation and bringing new treatments to patients.

Despite the difficulties, rare disease R&D has never halted, although the diversion of resources to this priority means it inevitably slowed it. Yet the way in which the pandemic was managed has highlighted emerging opportunities that Europe should also apply in the rare disease framework.

COVID-19 has shown how regulatory flexibility can become a reality if all stakeholders work together. Yet this need not be solely in times of emergency; the needs of rare disease patients should be treated with similar urgency. Flexibility is particularly important in developing rare diseases treatments that are able to respond to ongoing challenges, and it should be provided for clinical trials in rare diseases. For instance, this flexibility should be applied through adjusted timelines and accelerated administrative procedures, while ensuring appropriate funding and resources for clinical trials' bodies.

The pandemic also accelerated the uptake and adoption of new digital tools, the greater involvement of patients in HTA processes and a wider acceptance of RWE. These solutions all have the potential to reshape the future R&D process for the better, allowing us to consolidate a forward-looking, person-centric rare disease ecosystem, which ensures safe and innovative medicines for EU citizens.

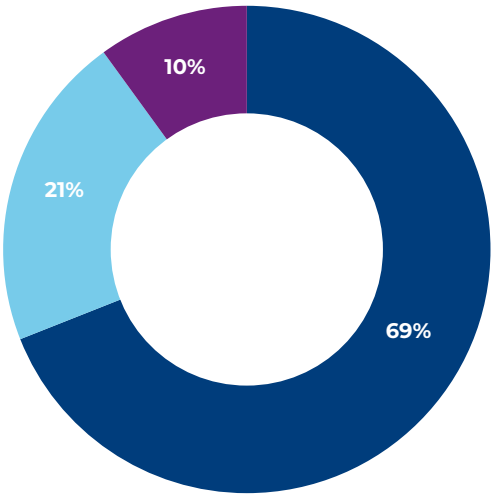
> **Many rare disease patients suffered disruptions to treatment due to COVID-19, often severely impacting their daily lives. However, people have been increasingly embracing e-health solutions; therefore, a lesson of the pandemic should be to broaden the adoption of digital tools.**
>
> **Dimitrios Athanasiou,**
> **Board member of EPF**
> **and member of PDCO**
> Take One, 3 December 2020

> **The rapid availability of vaccines for COVID-19 has shown that collaborative and innovative efforts to combat an existing health threat are possible. The same urgency should be applied to rare diseases and be kept in mind when reforming the regulatory framework.**
>
> **Alastair Kent,**
> **Independent patient advocate**
> Take Two, 4 February 2021

The participants' view:

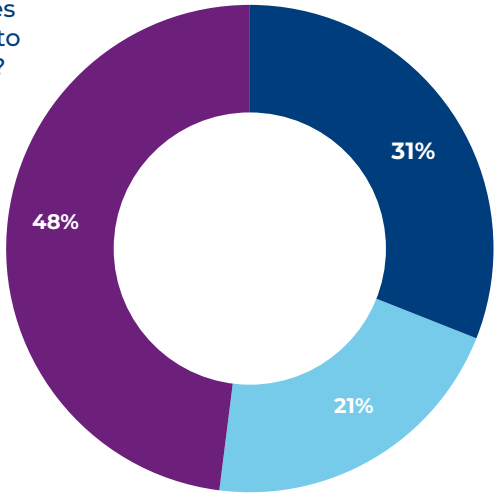
surveys conducted on the topic during Rare Conversations

Which challenges in particular affected rare disease patients during the pandemic?



- Increased difficulties in receiving timely and adequate diagnosis, treatment and care
- Delays or discontinuation of ongoing clinical trials
- De-prioritization of rare disease patients needs

How can we transfer the lessons learned in developing vaccines and treatments for COVID-19 to R&D in the rare diseases area?



- Increased cooperation between Member States as well as global collaboration and alignment
- Enhanced incentives and investments into R&D in rare disease treatments
- Regulatory flexibility to fast-track conditional approval of treatements for high need areas

> The COVID-19 experience has demonstrated the positive impact of collaboration in the healthcare space, particularly in times of emergency; we should treat the need of rare disease patients with similar urgency.
>
> **Martine Zimmermann,**
> **SVP, Head of Regulatory Affairs and Quality, Alexion**
> Conference, 9 November 2021

The increasing importance of listening to and understanding the patient voices

People with a rare disease and their families lie at the heart of the rare disease ecosystem. It is vital to involve them and include their views throughout the entire rare disease lifecycle, as those directly affected by rare diseases can provide invaluable insights into their needs and priorities, helping to conduct better clinical trials and research, and improve value assessment.

Rare diseases have an immense impact on the everyday lives of people living with these conditions, preventing them from having a 'normal' life. People with a rare disease suffer from delays in diagnosis: seven years on average. In some regions – even in entire countries – they can lack adequate facilities, while cross-border healthcare can pose physical and linguistic challenges. Moreover, the severity of their condition often prevents them, or their carer, from working or taking an active role in society.

If we are to fully appreciate the difficulties and needs of people with a rare disease, we need a fresh approach. The patients themselves should not simply be at the centre of the discussions on rare diseases, they should be leading them. The reality is that many decisions impacting the lives of people with a rare disease are taken without their involvement. This must change, by engaging with patients through the entire rare disease lifecycle, from diagnosis, R&D, clinical trials and care in appropriate facilities.

Listening to the patient's voice is important to understanding that the emphasis should be wider than simply the financial monetary aspects of support measures; it must encompass the impact on the patients' quality of life and the reduced dependency on society and on social security systems. These should be key considerations when assessing the value of new treatments or revising the regulatory framework. Leveraging the direct experience and expertise of the patient community, as part of a multi-stakeholder approach, can be crucial in improving access and in providing targeted treatments, as well as tackling their everyday challenges.

> **Patients need to be involved even before trials are considered: the progress of patients' involvement in research is too slow. The views of patients are only considered after all the important research decisions have been made.**
>
> **Rob Camp,**
> **Patient Engagement Senior Manager, EURORDIS CABs**
> Take Three, 5 May 2021

> **Rare diseases not only affect people's health – the consequences on their way of living and the impact on the social system also need to be considered. Yet many important decisions on the lives of people affected by rare diseases are taken without involving them. The most important change for the future is to have patients lead the discussion.**
>
> **Stelios Kympouropoulos,**
> **EPP MEP from Greece**
> Take Two, 4 February 2021

It is essential to involve patients from the outset of the value assessment process, since assessors may lack knowledge of a condition, or the HTA reports may fail to grasp the scale of the impact of the disease.

François Houÿez,
Health Policy Advisor, EURORDIS
Take Four, 8 July 2021

The need for a sustainable model for innovation in order to meet the challenge of defining unmet needs in rare diseases

Defining unmet medical needs in rare diseases is challenging. In addition to the availability of therapeutic options, there are numerous other factors that need to be taken into account, including the quality of life of patients or the burden of existing options. This is why it is more important to design a sustainable system for innovation that specifically targets unmet needs, rather than to focus on a narrow definition that risks creating disparities between people living with rare diseases.

Defining unmet need in rare diseases can be difficult, as prioritisation of certain criteria may potentially lead to disparities. Moreover, 'one-size-fits-all' solutions are not appropriate in rare diseases, given the wide range within this category, ranging from ultra-rare diseases to paediatric conditions.

Unmet needs in rare diseases are highly complex and need to take account of a range of factors over and above the availability of treatments. The quality of life of patients, the burden of existing options and the costs for patients all need to be weighed. Even where a therapeutic option is already available, it does not mean that better and more-targeted solutions cannot be found, as existing treatments are rarely transformative or curative.

This is why a narrow definition of unmet need is not the solution for improving patient's lives. In reality, it would be much more effective to focus on the creation of a sustainable model for innovation: a system that fosters increased investments in R&D of rare diseases and enhances partnerships between stakeholders. We should look to a model that modifies the current regulatory process, taking advantage of tools such as rolling reviews and RWE; a system that prioritises the experience and requirements of people with a rare disease.

This model will require more work and additional resources, but it is the only way to tackle high unmet medical need effectively. Such a shift relies on a holistic, reliable and balanced incentives framework for orphan medicinal products, as well as a flexible and coherent regulatory environment. At the same time, it is crucial that all stakeholders – from patients to industry, research to payers – sit together with a common goal of building a new system that is futureproof and fit for purpose.

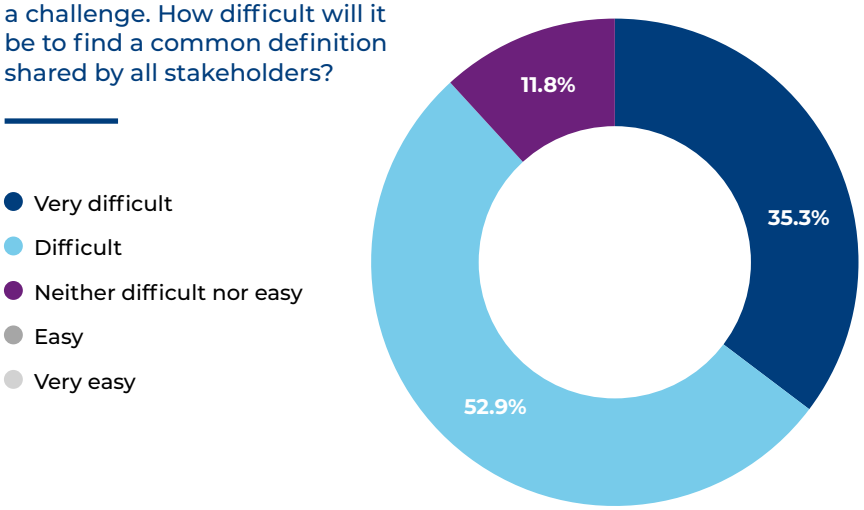
> **Finding new treatments for unmet needs and making them available should be a duty and priority for all stakeholders. This means designing a system fit for purpose. A new European Action Plan for rare diseases should also be implemented.**
>
> **Sara Cerdas,**
> **S&D MEP from Portugal**
> Conference, 9 November 2021

> **Rare diseases still have huge unmet need and are one of the health priorities in the EU that cannot wait; research and development of new treatments is crucial to addressing them.**
>
> **Claudia Gamon,**
> **MEP, Renew Europe**
> Take Three, 5 May 2021

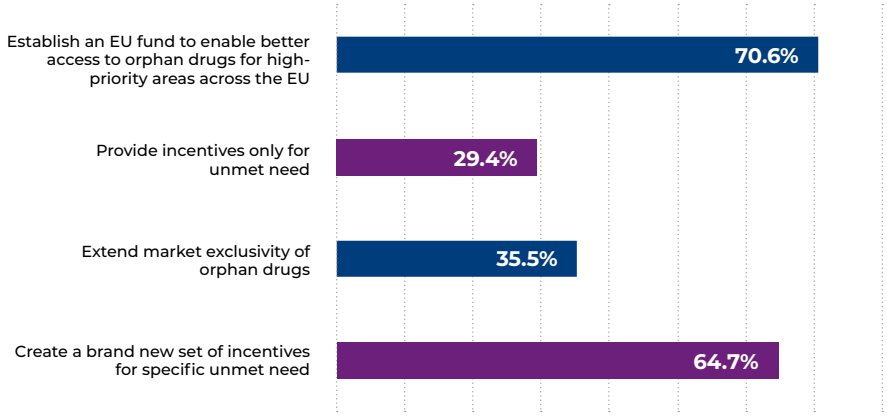
The participants' view:

surveys conducted on the topic during Rare Conversations

Defining 'unmet medical need' in the rare disease field represents a challenge. How difficult will it be to find a common definition shared by all stakeholders?



If research investments focused on unmet medical need had to be incentivised in a special way, which tools or mechanisms should be prioritised? (Multiple choices available)



The pandemic has shown us all how it feels to have no treatment options – the everyday reality for rare disease patients. To tackle this unmet need, investment in R&D for rare diseases need to be increased and partnerships reinforced. Furthermore, a reliable and balanced incentives system for orphan medicinal products (OMPs), involving all stakeholders, should be implemented.

Matthias Wilken,
Managing Director Market Access, Markets and Supply, BPI
Take Three, 5 May 2021

The unique and difficult demands of rare disease R&D: what makes it so special and difficult

R&D in rare diseases presents scientific and economic peculiarities that make it more challenging to undertake successfully. Overcoming these difficulties requires blending a number of opportunities, including greater public investment in research, public-private partnerships, earlier patient involvement and the use of new digital solutions.

Rare diseases endure a complex journey to treatment: for the majority, there is a great deal of uncertainty, no clinical studies exist as yet and scientific research into specific diseases often lacks funding. Pharmaceutical companies encounter difficulties investing in (ultra-) rare disease research, because these conditions – by definition - only affect very small populations and the cost of clinical trials is very high, reducing the likelihood of achieving a return on investments. These scientific and economic reasons make it particularly difficult to translate research into development.

Compared to the relative lack of difficulty of developing treatments for more common diseases, this lack of knowledge and resources explains why the level of investment is so important for supporting R&D in rare diseases, particularly among small- and medium-sized enterprises (SMEs). Innovation in rare diseases needs additional incentives to close the knowledge and economic gap with their more common counterparts. A societal approach is needed, one that covers the cost through a comprehensive reimbursement framework. Such a method has proven successful over recent decades, given that research in the rare disease space has already advanced considerably: for some conditions, life expectancy has dramatically increased, and for others the granular expertise has improved.

It will also be important to involve patients much earlier in the research process, even before clinical trials are being considered or before an organisation chooses a specific area for research. Desirable as it is, a patient-centric approach currently remains the exception rather than the norm. In part, this reflects certain practical challenges in determining the ideal ways to involve rare disease patients at the research stage; these will need to be resolved.

There is no 'one-size-fits-all' approach available for encouraging R&D in rare diseases, it requires a blend of several elements: increased (public) investment in R&D and greater patient involvement as well as more public-private partnerships such as the Innovative Medicines Initiative (IMI). The European Reference Networks (ERNs) provide an excellent example of successful cooperation, triggering the potential for research and involving patients directly. However, the challenge of moving the ERNs closer to industry and enhancing collaboration remains. Other

> **Proper access to medicines and treatments is essential for all patients; however, doing this for rare disease patients represents a challenge. They often face specific barriers, included the fact that private investment in R&D is not guaranteed. This is why I have always supported public funding of such research at both EU and Member State level.**
>
> **Maria da Graça Carvalho, MEP, EPP**
> Conference, 9 November 2021

> **There is still a lack of knowledge about rare diseases compared to more common conditions. This is why the level of investment is important, particularly for SMEs.**
>
> **Bernard Grimm, Healthcare Director, EuropaBio**
> Take Two, 4 February 2021

initiatives, however, such as the European Joint Programme on Rare Diseases (EJP RD), have provided a template and demonstrated that working together is possible.

Last, new digital solutions involving patients in HTA processes and a wider acceptance of RWE, offer the potential to reshape and improve the future R&D process. This in turn will support a forward-looking, person-centric ecosystem that ensures further innovative medicines.

The participants' view:

surveys conducted on the topic during Rare Conversations

What is the current state of the European research ecosystem for rare diseases?

- Europe is a global leader, with cutting-edge research infrastructure targeting rare diseases.
- **Important elements of the research ecosystem for rare diseases are already in place or are emerging, such as the European Reference Network, the European Joint Program on Rare Diseases or the European OMP Regulation; however, more progress is needed.**
- Europe does not have a clear research strategy for rare diseases and is not yet ready to address the unmet needs.

Which solutions does Europe need to become the future powerhouse of rare disease research?

- Increased investments from the European Commission and Member States into basic research that targets areas of high unmet need.
- A fully operating model for the European Reference Networks that enables sustainable multiyear funding and provides an effective interface for R&D partnerships with the industry.
- **A renewed incentive framework for orphan drugs that provides additional measures for attracting investments in the areas of highest unmet need and to continuing support for ongoing cross-industry research efforts.**
- New platforms to enable and support philanthropic and patient-drive research initiatives focused on addressing areas of highest unmet need.

Having all stakeholders working together is a vitally important aspect of research in rare diseases: indeed, in the EJP RD, the benefit of this approach can already be seen. However, such research needs to be better translated into benefits.

Daria Julkowska,
Scientific Coordinator at EJP RD
Take Three, 5 May 2021

What is still missing is bringing research and healthcare much closer together, powered by data and data analytics. What are needed are joint research programmes, like the EJP RD, but capable of going a step further and funded by public money.

Yann Le Cam,
CEO, EURORDIS
Conference, 9 November 2021

The need for an adapted approach to value assessment of orphan medicines

An EU, multi-stakeholder approach can improve the value assessment process for orphan medicines by bringing together expertise to complement and enrich the assessors' knowledge. EU HTA is a step in the right direction, but the full potential of other tools – such as RWE and the use of data – also need to be fully leveraged.

Value assessment of orphan medicinal products (OMPs) at EU and Member State level offers relevant opportunities for the rare disease ecosystem, particularly regarding access. However, it is important that the process for rare diseases differs from that used for regular diseases. This is because the specificities of rare diseases are not well recognised by many HTA bodies, as they tend to run counter to their existing processes, which are usually focused on more common diseases. A European, multi-stakeholder approach to value assessment – involving researchers, regulators, patient groups, payers, national authorities and industry – would ensure proper expertise for this process and strike the right balance between different needs.

Involving patients from the outset of the value assessment process is vital, as they can bring the insights into the specific condition that HTA bodies may lack and help them grasp the impact of the disease. Input from patients with personal experience of the conditions could help overcome these shortcomings.

An EU-wide HTA is a step in the right direction for ensuring that patients suffering from the same condition in different Member States enjoy the same access to treatments. It also provides a huge improvement for patients in terms of transparency. It would also assist SMEs by reducing their administrative burdens and costs. However, in order for the new EU HTA to be successful, Member States must, in practice, consider any recommendations it makes.

> We need common understanding on a value framework, but it needs to be one that takes into account opportunity costs. Existing value frameworks have always been weak on the cost aspects. Factoring this in may help bring payers and HTA bodies on board.
>
> **Michael Schlander, Professor of Health Economics, University of Heidelberg**
> Conference, 9 November 2021

> HTA for rare diseases should differ from value assessment for normal diseases. They should take into account that there are only meaningful treatments for 5% of the indications, and that it takes patients an average of seven years to receive their diagnosis. The key factors in assessing different regulatory systems are providing incentives for innovation and the use of real-world evidence.
>
> **Simu Thomas, Vice President, Global Health Economics & Outcomes Research, Alexion**
> Take Four, 8 July 2021

There are also other ways to help adapt value assessment procedures. In particular, RWE and data offer huge potential for extending the time available for demonstrating the benefits of a therapy for a rare disease, particularly where large-scale clinical trials may not be feasible. Enhancing the potential of ERNs – where industry should be involved more – and ensuring dialogue with stakeholders to identify potential bottlenecks and opportunities are also opportunities. Indeed, the use of RWE is one of the key differentiators between the EU and the US regulatory systems; this sees most orphan drugs being developed for the US market, partly attributable to the EU's more complex regulatory process and a lack of harmonisation between Member States. Pan-European data collection should be the future: this is where Patient-Reported Outcomes (PROS) could be relevant. These should capture data in an easy-to-use, easy to substantiate format. Once validated, the data would provide a far more robust measure of outcomes and level of evidence.

By using real-world evidence, the time to prove the benefit of a medication for rare diseases, for which large scale clinical trials might not be feasible, can be increased. In France, the promise of a benefit will now be recognised. This marks a major improvement, since it previously took a long time to change the level of recognised benefits.

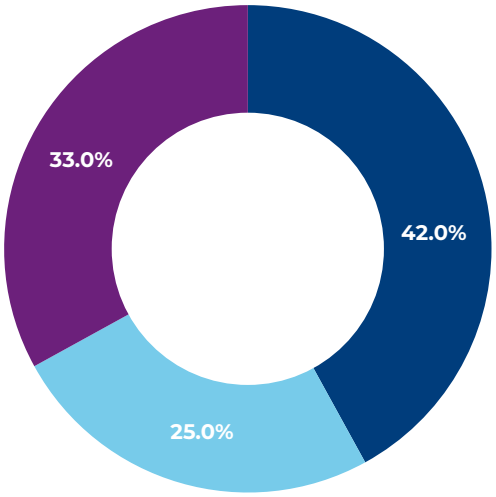
Olivier Blin,
President, OrphanDev
Take Four, 8 July 2021

The participants' view:

surveys conducted on the topic during Rare Conversations

How could the issue of access equity to orphan drugs in Europe be solved?

- Increase collaboration between payers, HTA, patients and industry at national and EU level
- Establish a European solidarity fund to provide access to ultra-orphan drugs addressing areas of high unmet need
- Develop dedicated and adapted access and HTA pathways for orphan drugs in all EU Member States



The partnerships required to sustain the future of the rare disease innovation ecosystem in Europe

Partnerships represent the key to an innovative rare disease ecosystem. The impact of a spirit of cooperation in the last 20 years has seen the instigation of successful initiatives such as the ERNs, the IMI and the EJP RD. This underlines the value of partnerships at all stages of the rare disease pathway, from R&D to access. For this reason, it is essential to continue, – and where appropriate, expand – this collaborative approach. This will maximise the capacity to identify innovative treatment options and bring them to the patients that most need them.

In the last 20 years, the rare disease ecosystem has established a solid foundation, built on a series of many elements – not just the OMP Regulation – with a spirit of cooperation throughout. However, a huge appetite remains for advancing the agenda to tackle fundamental challenges such as unmet need. This spirit of multi-stakeholder collaboration will be crucial for ensuring the future of an innovative ecosystem for rare diseases throughout their entire lifecycle.

A number of initiatives have demonstrated the value of multi-stakeholder collaboration: Public-Private Partnerships (PPPs), including the IMI and the ERNs; research initiatives such as EJP RD and the International Rare Diseases Research Consortium (IRDiRC), and multi-stakeholder platforms such as the European Expert Group on Orphan Drugs Incentives.
The common thread linking these seemingly diverse initiatives is the involvement of all relevant actors, particularly through the proactive involvement of patients and the sustained focus on their needs.

Partnerships play a vital role in rare disease R&D by helping to identify the most promising opportunities for focusing (limited) resources. Such partnerships help 'join the dots' between researchers and industry, helping translate basic research into the development of new treatments and to find pathways to accelerate innovation. It is therefore vital to take advantage of the PPP opportunities created by the upcoming Innovative Health Initiative (IHI) and the expanded ERNs to advance the agenda for rare disease research.

Collaboration is crucial in the rare disease field: the Expert Group on Orphan Drugs Incentives provides a positive model for a multi-stakeholder forum to discuss rare disease incentives from an interdisciplinary perspective.

Alexander Natz,
Secretary General, EUCOPE
Take One, 3 December 2020

Coordination between patients, payers and HTAs is vital: where this is happening – such as in BeNeLuxA – it is beginning to bear fruit. This is proof that such collaboration is essential in ensuring timely access to potentially transformative therapies.

Simone Boselli,
Director of Public Affairs, EURORDIS
Conference, 9 November 2021

Such collaboration is equally essential in the regulatory environment. Consolidated stakeholder interaction, such as the ERNs or the European Network for Health Technology Assessment (EUnetHTA), has seen significant progress in the field of rare diseases, and this model should be further expanded. Since the drug development process is not perfect, dialogue is essential: sharing relevant information between those involved can help make regulatory pathways faster and more efficient.

Where multi-stakeholder coordination does happen, it brings results in terms of patient access to new treatments. In this field, fragmentation remains an issue that must be addressed; it is essential to have all stakeholders around the table, using their expertise to provide insights to various workstreams that are required to make access a reality.

Partnerships are the only way to understand each other's viewpoints and perspectives, and to working together to tackle existing issues. The ultimate goal must be to ensure a future-proofed innovative ecosystem for the rare disease community.

The feeding in of rare disease therapies lifecycle data is the one of the objectives of the ERNs, but to achieve this, the ERNs need to be sustained. If they are to deliver, they need resources.

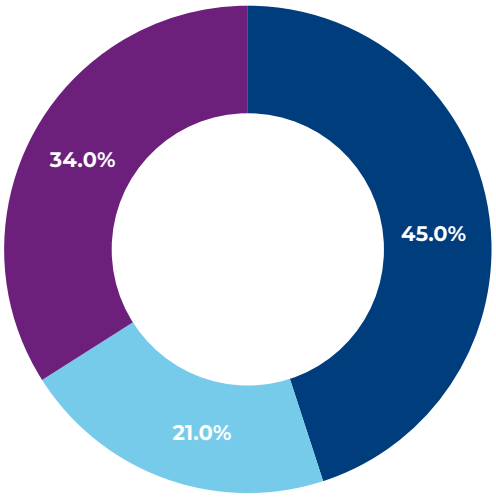
Maurizio Scarpa,
Coordinator at MetabERN
Conference, 9 November 2021

The participants' view:

surveys conducted on the topic during Rare Conversations

What should a future European Rare Disease Partnership focus on?

- Closing the research gaps and strengthen discoveries in areas of high unmet need
- Championing the implementation of the European Health Data Space for rare diseases
- Reconciling access challenges for orphan medicines through one dedicated initiative at the EU level



Rare diseases will be one of the areas for partnership, building on the work already done. It will include industry involvement as stakeholders, alongside patients and regulators. This will be essential for establishing new regulatory pathways suitable for encouraging translation into treatments.

Carmen Laplaza Santos,
DG RTD, European Commission
Conference, 9 November 2021

ALEXION
AstraZeneca Rare Disease

Overview of events

Episode One

The impact of COVID-19 on pharmaceutical research and development in rare diseases

In cooperation with

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

On 3 December 2020, 'Take One' of the Rare Conversations event series saw stakeholders from patient organisations, regulatory bodies and industry come together to discuss the impact of COVID-19 on the R&D process in the field of rare diseases. The event saw an animated, engaging discussion that examined the challenges that had arisen during an exceptional year.

The panel discussion featured:

- **Dimitrios Athanasiou**, Board member of the European Patients Forum (EPF) and member of the EMA Paediatric Committee (PDCO)
- **Dr Thomas Lönngren**, former Head of the EMA
- **Dr Alexander Natz**, Secretary General of EUCOPE
- **Dr Martine Zimmermann**, Senior Vice President Global Regulatory Affairs at Alexion.

The event was moderated by **Maciej Gajewski**, Executive Director and Head of Public Affairs and Policy at Alexion.

Episode Two

How to keep rare disease patients at the heart of the discussion

In cooperation with

EuropaBio

On 4 February 2021, 'Take Two' of the Rare Conversations event series took place, focusing on the importance of keeping rare disease patients at the heart of the discussion. Panellists representing the patient, regulatory, health and industry communities discussed how to define unmet needs and address them. They also examined the conditions needed to improve the R&D and regulatory frameworks to promote innovation that benefits rare disease patients, the needs of the patient community and how to ensure that they remain high on the healthcare agenda.

The panel discussion featured:

- **Simone Boselli**, Director of Public Affairs at EURORDIS
- **Bernard Grimm**, Healthcare Director at EuropaBio
- **Dr Denis Horgan**, Executive Director of EAPM
- **Alastair Kent**, Independent patient's advocate
- **Dr Stelios Kympouropoulos**, Member of the European Parliament from Greece, sitting with the EPP
- **Dr Cees Smit**, Patient expert on haemophilia.

The event was co-moderated by **Maciej Gajewski**, Executive Director and Head of Public Affairs and Policy at Alexion, and **Walter Atzori**, Head of Patient Advocacy International at Alexion.

Episode Three

The specificities and needs of research in rare diseases

On 5 May 2021, 'Take Three' of Alexion's Rare Conversations event series debated on the specificities and needs of research in rare disease. R&D of new treatments in rare and ultra-rare diseases poses its own distinct challenges, due to gaps in knowledge and understanding of the conditions, small patient populations, difficulties in recruiting for and conducting clinical trials, and needs for high investment. The panellists discussed the steps needed to deliver further success for the benefit of people with a rare disease.

The panel discussion featured:

- **Inês Alves**, President of ANDO Portugal and ERN BOND ePAG member
- **Rob Camp**, Patient Engagement Senior Manager in EURORDIS Community Advisory Board
- **Claudia Gamon**, Member of the European Parliament from Austria, sitting with Renew Europe
- **Dr Daria Julkowska**, Scientific Coordinator of the EJP RD
- **Dr Gianluca Pirozzi**, SVP, Head of Development and Safety at Alexion
- **Prof Dr Franz Schaefer**, ERKNet Coordinator and Professor of Paediatrics at Heidelberg University Hospital
- **Dr Matthias Wilken**, Managing Director Market Access, Markets and Supply, at BPI.

The event was co-moderated by **Maciej Gajewski**, Executive Director and Head of Public Affairs and Policy at Alexion, and **Walter Atzori**, Head of Patient Advocacy International at Alexion.

In cooperation with

Episode Four

HTA: from national to EU value assessment – what provisions for orphan drugs?

In cooperation with

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

'Take Four' of Alexion's Rare Conversations event series took place on 8 July 2021. Panellists, including researchers, regulators, patient's groups and industry representatives, discussed the current rules and methodologies used in value assessment mechanisms for orphan drugs at European and Member State level. It then examined the positive impact that EU collaboration could bring about for these frameworks.

The panel featured:

- **Prof Olivier Blin**, President of OrphanDev
- **Josie Godfrey**, Director of JG Zebra Consulting
- **François Houÿez**, Health Policy Advisor at EURORDIS
- **Adam Hutchings**, Managing Director of Dolon
- **Dr Alexander Natz**, Secretary General at EUCOPE
- **Dr Juozas Olekas**, Member of the European Parliament from Lithuania, sitting with the S&D
- **Dr Simu Thomas**, Vice President, Global Health Economics & Outcomes Research, Alexion.

The event was moderated by **Maciej Gajewski**, Executive Director and Head of Public Affairs and Policy at Alexion.

Conference

European rare disease ecosystem: a collaborative path forward

In cooperation with

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On 9 November 2021, Alexion hosted the Rare Conversations conference. This event saw regulators, patients, research, academia, EU institutions, industry and investors develop inspiring ideas for advancing the future of rare diseases. The event included high-level discussion on how to enable the ecosystem, and then narrowed its focus to address three key areas: research and development, regulatory approval, access. Over four sessions, speakers examined the entire value chain for rare diseases and orphan drugs.

Welcome remarks

Tamar Thompson,
Vice President and Head
of Corporate Affairs, Alexion

The ‘Rare Conversations’ series had been created to ensure that the needs and voices of the rare disease community were not drowned out in the understandable clamour created by the COVID-19 pandemic. While we could not have predicted it at the time, this now seems a prescient decision. Nearly two years on, the pandemic is still with us, and understandably still dominating the healthcare agenda. Yet the needs of people with rare diseases, their families and carers also remain as real as ever.

Keynote speech

Soraya Bekkali,
Senior Vice President, International Commercial Operations, Alexion

We all acknowledge that the European Orphan Drugs Regulation has provided an important stimulus for companies and investors alike. For the past 20 years, the industry has been increasingly more open to take risk in researching medicines for rare diseases, which we often knew little about. We can say that some of those diseases are no longer orphan, while they are and remain certainly rare.

We have built a very strong foundation in Europe, which has helped companies such as Alexion to bring much needed medicines to patients. Looking at the bigger picture, the industry has developed an impressive pipeline of around 2500 medicines with orphan drug designation. This scientific advancement in rare diseases has also benefitted broader patient populations. And that is real hope for the future. So together, we must ensure that we maintain this great momentum for the benefit of patients.

Opening session: Setting the agenda for partnerships in rare diseases

The opening session set the scene for the importance of collaboration and partnership in the rare disease ecosystem. Panellists discussed how to use partnerships to maximise existing opportunities and to remove barriers so as to bring benefits to people affected by rare diseases.

The opening session's panel featured:

- **Dr Sara Cerdas**, Member of the European Parliament from Portugal, sitting with the S&D
- **Bernard Grimm**, Healthcare Director, EuropaBio
- **Yann Le Cam**, Chief Executive Officer at EURORDIS – Rare Diseases Europe
- **Dr Pierre Meulien**, Executive Director, Innovative Medicines Initiative (IMI)
- **Dr Andrzej Jan Rys**, Director Health systems, medical products and innovation, DG SANTE.

The opening session was co-moderated by **Tamsin Rose**, Friends of Europe, and **Maciej Gajewski**, Executive Director and Head of Public Affairs and Policy at Alexion.

Breakout session 1: Translate basic research into development through alliance building

The first breakout session set out to examine ways of converting early-stage research into clinical development. The key to positive outcomes appears to lie in cooperation between stakeholders, which has seen PPPs become successful in translational research, both at EU level and around the world.

The session featured:

- **Dr Rianne Ellenbroek**, Investment Manager FIRST fund at BioGeneration Ventures
- **Dr Daria Julkowska**, Scientific Coordinator at EJP RD
- **Carmen Laplaza Santos**, Head of Unit Health Innovations & Ecosystems, DG RTD
- **Dr Gianluca Pirozzi**, SVP, Head of Development and Safety at Alexion
- **Prof Dr Alessandro Prigione**, Department of General Paediatrics, University Children's Hospital, Düsseldorf
- **Declan Noone**, President of the European Haemophilia Consortium (EHC)
- **Anton Ussi**, Operational Director, EATRIS.

The three breakout sessions were co-moderated by **Julia Wahl**, Managing Economist at Copenhagen Economics, and **Maciej Gajewski**, Executive Director and Head of Public Affairs and Policy at Alexion.

Breakout session 2: Multi-stakeholder cooperation for an efficient regulatory environment

Cooperation between stakeholders is important for maximising the potential of the regulatory environment. This is a vital step for accelerating approvals of new products and reducing the time to market. The response to COVID-19 has shown that, even within the constraints of the existing regulatory process, a faster process is possible where there is high unmet need.

The panel for this breakout session featured:

- **Dimitrios Athanasiou**, Board member of the European Patients Forum (EPF) and Member of the EMA Paediatric Committee (PDCO)
- **Tilly Metz**, Member of the European Parliament from Luxemburg, sitting with the Greens
- **Dr Alexander Natz**, Secretary-General at EUCOPE
- **Prof Dr Maurizio Scarpa**, Coordinator at the ERN for Rare Hereditary Metabolic Diseases (MetabERN)
- **Dr Martine Zimmermann**, SVP, Head of Regulatory Affairs and Quality, Alexion.

Breakout session 3: A common path to enable access to new orphan drugs

A particular issue for orphan drugs is the delay in reaching patients, frequently created by market access issues. The solution often lies in better coordination between stakeholders. The purpose of this session was to identify ways of overcoming these issues and accelerating access following approval and market entry. It also examined how to improve collaboration between stakeholders during the value assessment of orphan drugs.

The panel assembled to discuss this topic featured:

- **Simone Boselli**, Public Affairs Director at EURORDIS – Rare Diseases Europe
- **Dr Maria da Graça Carvalho**, Member of the European Parliament from Portugal, sitting with the EPP
- **Wendy Erler**, VP, Head Patient Insights and Advocacy at Alexion
- **Max Newton**, Engagement Manager (Global Supplier & Association Relations) at IQVIA
- **Prof Michael Schlander**, Professor of Health Economics at the University of Heidelberg.

Rare Conversations: Conclusions

The objective of the inaugural 'Rare Conversations' series was to bring together as many voices as possible to discuss the future of Europe's rare disease ecosystem. It saw the rare disease community identify solutions and opportunities for improving this ecosystem, for addressing existing challenges and for making the environment one that is fit-for-purpose and encourages innovation.

From the outset, it was clear the 'Rare Conversations' event series would focus on cooperation, engagement and sharing between diverse stakeholders, while ensuring that patients and their needs remained the keystone.

Throughout each of the events, the common theme is that there are huge opportunities for greater collaboration and further concrete partnerships. These will be vital for future research and development, for finding ways to accelerate regulatory processes to address the huge unmet need in rare diseases and to make real progress on access. Successful initiatives such as the ERNs, the IMI and the EJP RD are clear examples of what the spirit of cooperation can achieve; sustaining this momentum is vital.

An EU multi-stakeholder approach will also be pivotal in improving the value assessment of orphan drugs by aggregating the available expertise to complement and enhance the assessors' knowledge and understanding. A dedicated rare disease EU HTA, combined with RWE, should be fully developed. The COVID-19 pandemic has shown the potential of these tools, and of regulatory flexibilities and rolling reviews. If applied to rare diseases, these tools would help reduce delays in diagnosis and treatments for people with a rare disease.

In fact, patients and their families must always be at the heart of the rare disease ecosystem. If we are to clearly understand their priorities and how to tackle unmet medical needs, it is crucial to build this around them and include their views throughout the entire rare disease lifecycle. Unmet medical needs represent a particular challenge, since there are several factors – over and above the availability of therapeutic options – that need to be taken into account, including quality of life considerations and the burden of existing options. This is why innovation must be sustainable, and why rare disease R&D must be properly enabled through greater public investments in research, earlier involvement for patients, PPPs and wider use of new digital solutions.

This collaborative approach discussed during these 'Rare Conversations' is also required ahead of the revision to the European Regulation on orphan medicinal products. Only by working together will it be possible shape an updated framework capable of fully enabling the rare disease ecosystem and shaping it for the coming 20 years.

The themes touched on during the entire event series deserve further reflection and thorough discussion if we are to maximise value of the insights gathered. There are many remaining topics that would benefit from a deeper dive.

The 'Rare Conversations' will continue during 2022, with fresh events and innovative formats, providing further food for thought while always listening to the different voices active in this field. At the same time, the events will retain their original spirit and continue to pursue their ultimate goal: improving the lives of rare disease patients.

RareConversations

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