# EFPIA-EURORDIS JOINT STATEMENT ON PATIENT ACCESS TO MEDICINES FOR RARE DISEASES

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# Executive summary

Despite the success of the 2000 Orphan Medicinal Product (OMP) Regulation, patient access to OMPs across Europe remains imperfect, inequitable, and routinely delayed. These access concerns contributed to spark the current debate around the incentives provided for orphan medicines, which crystallises in the revision of the OMP Regulation. Yet the root causes to impaired patient access to OMPs are complex and multi-faceted; as such, they require tailored and concerted action from all stakeholders. That is why EURORDIS and EFPIA, which share the goal of ensuring broader and faster access to OMPs to all European patients, have joined forces to propose impactful solutions. This joint statement presents the output of a structured dialogue between the two parties, which allowed to identify common proposals to advance this goal (whilst acknowledging areas of divergence).

To increase equity of access across European countries, EURORDIS and EFPIA propose the consideration of a conceptual framework for equity-based tiered pricing (EBTP). EBTP offers to better align medicines' prices with countries' ability-to-pay, which can help to address affordability constraints in lower-income EU Member States without diminishing incentives to invest in new medicines. Because EBTP may only be effective if stakeholders make reciprocal commitments (including the commitment of EU Member States to adhere to the principle of solidarity, to commit to good practices in external reference pricing and to limit parallel trade between lower and higher-income countries), further dialogue on the topic is needed. In addition, EFPIA puts forward an industry commitment to file pricing and reimbursement (P&R) applications across all 27 EU Member States no later than two years after EU marketing authorisation, provided that national P&R systems allow it. EFPIA has also launched an Access Portal that will record timely information on OMPs' P&R status and contribute to better understand the root causes of impaired access.

Addressing shortcomings of and bolstering health technology assessment (HTA) and P&R frameworks can further contribute to enhancing patient access to OMPs. The approval of the EU Regulation on HTA, and inclusion of OMPs in the second wave of implementation, represents a significant opportunity to streamline value assessment processes through cross-country collaboration – if duplication is avoided and methodologies are fit-for-purpose. More routine use of adaptive pathways and real-world evidence (RWE) can help mitigate evidential uncertainty at launch, allowing timely patient access while additional evidence is collected. Because of the importance of EU-wide collaboration for RWE, EURORDIS proposes to establish an EU Fund for RWE, which would coordinate and fund RWE collection efforts. Country-level HTA and P&R processes can also be better adapted to the specificities of rare diseases, by supporting greater use of novel payment and pricing models and ensuring flexibility in the evaluation of and price negotiation for OMPs given their rarity.

Proposals to improve access today would be incomplete without a nod to the future. Improving the lives of rare disease patients requires not only access to the transformative medicines that already exist, but also sustained innovation for tomorrow. EFPIA thus proposes to launch a Moonshot for rare diseases, whereby more coordinated, targeted, and collaborative basic and translational research would allow to unlock a new wave of innovation.

The recommendations contained in this report are not simple solutions to easy problems, nor can they entirely alleviate the access challenge that rare disease patients face. Nonetheless, EURORDIS and EFPIA believe that these proposals collectively represent an important step forward and a foundation for further collaboration. Improving patient access is a joint goal and requires collaboration and commitment from all stakeholders. EURORDIS and EFPIA now invite other stakeholders – the European Commission, Member States, the European Parliament, and civil society including patient organisations, researchers, and clinicians – to match their ambition and join together to advance the interests of rare disease patients in Europe.

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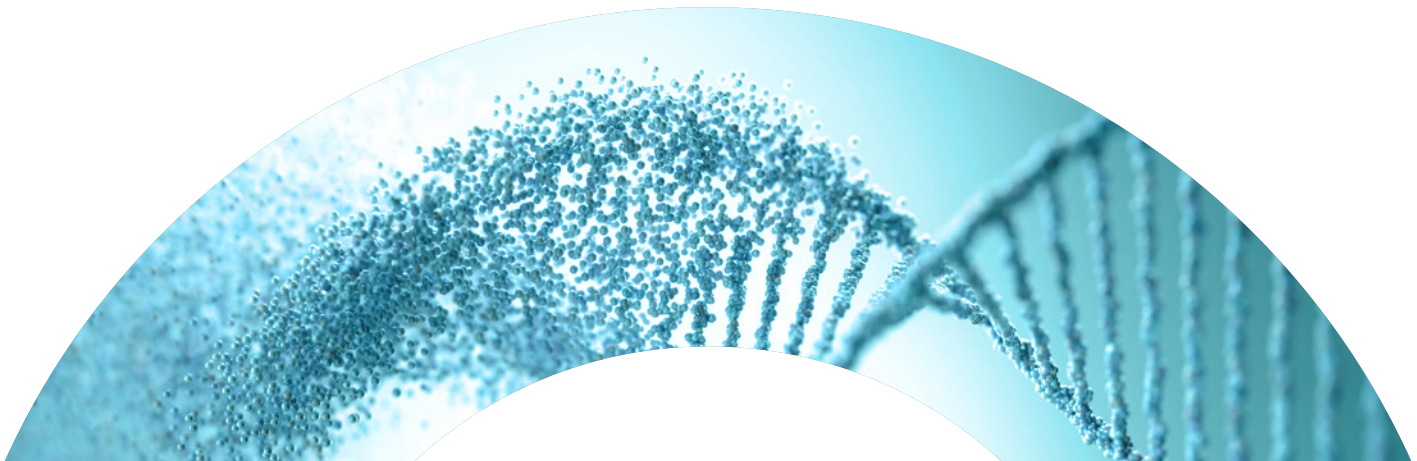

# Introduction – Despite the significant advances in the care of rare disease patients afforded by the Orphan Regulation, many patients still do not benefit from timely access to medicines

In Europe, 27 to 36 million people are living with a rare disease, defined as a condition affecting fewer than five in 10,000 people in the EU[1]. These diseases are often debilitating and degenerative conditions; most are of genetic origin, first manifesting in infants or children[2]. Because of the rarity of these diseases, scientific knowledge is limited, patients' ability to get a diagnosis is suboptimal, and many patients still do not have adequate treatment options. This results in important unmet medical needs for these patients. Accordingly, improving patient access to diagnosis, information and care has been recognised as a political priority by Member States and the European Commission (EC)[3].

The 141/2000 (EC) Regulation on orphan medicinal products (OMPs) is part of this political commitment and an important contributor to the care of rare disease patients. The OMP Regulation has brought a wave of innovation that has benefited millions of rare disease patients across Europe. To date, the Commission has authorised more than 200 OMPs and granted an orphan designation to more than 2,000 products[4]. It has been estimated that half of these medicines can be directly attributed to the Regulation[5]. The impact of these OMPs on rare disease patients has been important, with up to 6.3 million European patients having benefited from these innovations[6].

Despite the great success of the OMP Regulation, access to OMPs across Europe remains imperfect and inequitable. Only 37% of OMPs are available across Europe (vs 46% for all medicines)[7]. The level of access to authorised OMPs varies widely across European Member States, from nearly none in Lithuania to nearly complete in Germany[8].

Lack of access is compounded by the unacceptably long delays between marketing authorisation and patient access, which is estimated at 636 days on average for OMPs (vs 511 days for all products)[9]. For patients, every day counts and the impact of these delays to access can be immense. A recent case study in acute myeloid leukaemia assessed the impact on patients of gaining earlier access to a newly authorised treatment in Sweden, the Netherlands, England, and Italy. Results showed that 1,689 more patients could have been treated and have lived altogether 82,920 additional months – that is, about four more years on average for each patient[10].

Such levels of impaired access are not only detrimental to patients but also to broader European Union (EU) goals, including that of supporting the attractiveness and competitiveness of Europe for innovation. Patient access is necessary to improve health within the EU, as well as to ensure equity across EU Member States and between EU citizens. The EU's efforts to 'support a competitive and innovative European pharmaceutical industry' set forth in the European Commission's 2020 Pharmaceutical Strategy for Europe[11], are meaningless and ultimately not sustainable if patients do not benefit from innovation.

# Impaired patient access is a complex and multi-faceted issue which EFPIA and EURORDIS are committed to tackle

EURORDIS and EFPIA see an urgent need to tackle existing inequities in access across Member States by fostering broader and faster access to approved and future innovative medicines. To that end, EURORDIS and EFPIA initiated in November 2020 a structured dialogue with a series of meetings. This structured dialogue aimed at improving patient access to rare disease medicines by identifying areas of alignment and developing proposals to share with other stakeholders. It also provided an opportunity for mutual learning between EURORDIS and EFPIA, acknowledging the existence of areas of misalignment despite a common interest to find concrete solutions to improve access. Six meetings, prepared and facilitated by a third party (Dolon, a consultancy), took place between November 2020 and February 2022.

While there are many root causes to impaired patient access[12, 13], this joint paper outlines several proposals by EURORDIS and EFPIA that aim to address a selected number of these, including[14]:

- the issue of external reference pricing (ERP) and parallel trade across Member States and beyond the EU;
- the differences between rare disease prioritisation and ability to pay across Member States;
- the complexity of navigating health technology assessment (HTA) and pricing and reimbursement (P&R) pathways in the different Member States;
- the challenges to demonstrate the benefits and value of OMPs at the time launch when one-off P&R decisions are taken (due to e.g., residual clinical outcome uncertainty).

EURORDIS further believes that in some cases OMPs' price levels challenge patient access, particularly in lower-income countries, which is an area of misalignment with EFPIA; this topic is not explored in the statement.
This paper lays out three sets of proposals discussed during the dialogues which are supported by both EURORDIS and EFPIA. (Note that these proposals are not representative of the entirety of each party's proposals.)

- The first set of proposals (proposal 1 and 2) focuses on enhancing equity of access across Member States through better alignment of OMP prices with countries' ability to pay, an industry commitment to file for P&R in all EU Member States no later than two years after EU marketing authorisation, and the creation of an Access Portal to document the causes of impaired access.
- The second set of proposals (proposal 3, 4 and 5) sets forth several measures to improve HTA and P&R processes, both at EU and Member State level.
- The last set of proposals (proposal 6) focuses on the launch of a Moonshot to stimulate translational research for the development of medicines that will address some of the remaining unmet medical needs of rare disease patients.

While some of these proposals are applicable to all medicines, they are particularly relevant to rare diseases in dealing with their unique specificities.

# Meaningfully improving patient access across the EU will require a plurality of solutions and engagement from all stakeholders

While each proposal intends to address some of the root causes to impaired access, none is sufficient on its own. Instead, multi-factorial causes require a plurality of solutions, as well as concerted actions from all stakeholders, including (but not limited to) the European Commission, Member States, the European Parliament, patients, healthcare professionals and industry. Improving patient access is thus a joint goal that requires collaboration and commitment from all stakeholders. The success of the proposed measures particularly relies on Member States' commitment to make use of the proposed solutions to facilitate faster and broader patient access, in the interest of solidarity, by addressing national and regional access barriers.

EURORDIS and EFPIA see the proposals presented in this statement as a significant step towards achieving the common goal of improving access for rare disease patients across Europe and welcome engagement with other stakeholders to continue exploring these proposals. Further progress could be achieved via multi-stakeholder structured dialogues or as part of the High-Level Forum on Better Access to Health Innovation proposed by EFPIA.

## Part A – EURORDIS and EFPIA put forward several proposals to increase equity of access, including a conceptual framework for Equity Based Tiered Pricing and an Industry Commitment to File

EURORDIS and EFPIA see an urgent need to tackle existing inequities in access across Member States by fostering broader and faster access to approved medicines for rare diseases. To tackle this objective, two proposals have been developed. The first is a proposed approach for Equity-Based Tiered Pricing (EBTP) in Europe.

The second proposal, developed by EFPIA, is an industry commitment to file for P&R in all EU-27 countries no later than two years after EU marketing authorisation provided that national P&R systems allow it, paired with an Access Portal aimed at tracking medicine availability and reimbursement status.

## PROPOSAL 1:

## EURORDIS and EFPIA propose a conceptual framework for international differential pricing (including necessary commitments from all parties): Equity-Based Tiered Pricing

EBTP, also known as international differential pricing, is the strategy of pricing a product differently between countries based on their ability to pay[15]. The intention is to address affordability constraints in lower-income EU countries, without diminishing incentives to invest in new medicines, and ultimately to improve availability of and access to new medicines[16]. EBTP is particularly relevant to therapies for rare diseases as their prices (which are commensurate to the level of innovativeness and the smallness of patient populations) often exceed the ability to pay of lower-income EU countries.

Differential pricing for rare disease medicines has been a cornerstone of EURORDIS's proposals to address access issues[17]. It was explored in early meetings, which resulted in a mutual agreement that EBTP should be a part of the access solution, with a recognition that EBTP cannot solve all access issues on its own[18]. Both parties agreed on the underlying principles and pre-requisites for EBTP, with a political commitment to solidarity being its foundation. A discussion document outlining a potential conceptual framework for EBTP was then developed by EFPIA and explored during its development with EURORDIS in a dialogue[19].

The proposal includes several key elements. First, solidarity among Member States should be demonstrated by their commitment to remove the barriers to EBTP in Europe. This entails that:

- lower prices would be exclusively available to less wealthy Member States;
- wealthier Member States should not include less wealthy ones in their ERP system; and
- medicines sold under an EBTP framework in less wealthy markets should not be diverted to wealthier markets.

Second, EBTP should be paired with a renewed commitment from Member States to complete P&R decisions within 180 days, as set forth in the Transparency Directive[20].

Third, EFPIA believes EBTP should not be seen as an alternative to, but building on the foundation of value-based pricing: prices should always reflect the value medicines deliver to patients, health systems and society.

This approach aims to integrate EBTP within existing legal frameworks and P&R systems, which are predominantly value-based. EURORDIS advocates for a different approach to pricing, which would rely on greater and more structured cross-country collaboration to establish a single EU price anchor[21]. While EURORDIS and EFPIA differ in their preferred methodologies to establish prices, they are both aligned on the key principles for EBTP.

In practice, EBTP would work through country tiering, where the launch price of the medicine in the lower tier must be lower than the lowest price (defined as the "best price") in the upper tier. The scheme would be voluntary for manufacturers (i.e., companies would opt-in for the new launch of one of their products) but would require participation from Member States to effectively benefit patients.

To avoid negative impacts from ERP (EU Member States being referenced ex-EU), net prices would remain confidential across Member States. It would thus be the company's responsibility to ensure the "best price" rule is applied across tiers. A verification process would be implemented via an independent auditor (separate from industry, the European Commission, and national payers). The auditor would monitor compliance by participating manufacturers with the "best price" rule and by Member States with the application of ERP principles and ensuring that non-extraterritoriality[22] is observed. Patient groups would also have a role in monitoring whether EBTP delivers improved access to medicines for patients.

EBTP is intended to benefit all stakeholders. Patients across the whole of the EU would get faster and better access to life-altering medicines. Member States would pay prices that reflect both the value of these medicines and their ability to pay. The EU would advance its goal to reduce access delays and health inequalities across Member States. Industry would be able to generate revenue from their products as they are being made available earlier on, which would help compensate for the lower prices granted to the less wealthy Member States.

Importantly, the EBTP conceptual framework outlined by EFPIA relies upon reciprocity of commitments among stakeholders, including the commitment of EU Member States to adhere to the principle of solidarity and commit to good practices in ERP.

The proposed industry commitments would therefore be contingent on the implementation of corresponding commitments from other parties necessary for the EBTP framework to achieve the intended impact[23].

EURORDIS and EFPIA look forward to engaging on this topic and its underlying principles with other key stakeholders, including patients, the European Commission, Member States, the European Parliament, healthcare professionals and civil society.

## PROPOSAL 2:

## EFPIA launches an industry Commitment to File and European Access Portal[24]

EFPIA's Member Companies have formally expressed their commitment to further explore the root causes of impaired access and to address the root causes of unequal and delayed patient access in collaboration with EU Member States and other stakeholders.

First, industry commits to filing P&R applications across all 27 EU Member States no later than two years after EU marketing authorisation, provided that national P&R systems allow it. This commitment applies to all newly EU authorised medicines, including OMPs.

Considering this significant commitment, industry calls for the Commission and Member States to progress solutions to access hurdles such as amending ERP systems and preventing the unintended consequences from parallel trade between lower- and higher-income Member States and to ensure the appropriate conditions are there for the proposed access solutions to become effective.

Second, industry's commitment to file for P&R is paired with a European Access Portal, launched in April 2022. The aim of the Access Portal is to record timely information on the P&R status of medicines across access pathways and the reasons for unavailability and delays in all Member States. The Access Portal will collect information related to the marketing authorisation date, the access pathway (including early access pathway), the P&R filing and completion date, and reasons for delays or non-application within each country. Companies will be responsible for providing this information in the Access Portal. Information collected through the Access Portal will be disclosed at the aggregate level, therapeutic level or anonymised product level (where relevant) through regular published reports. It is hoped that this Access Portal will provide valuable information to better understand the root causes of unavailability and delays, and how this changes over time[25].

EURORDIS welcomes these proactive industry commitments as positive steps towards improved patient access.

# Part B – EURORDIS and EFPIA advocate for improved HTA and P&R processes, with the view to enhance and expedite patient access

EURORDIS and EFPIA have identified several opportunities to improve HTA and P&R processes, with the view to achieve broader and faster patient access to OMPs. Underpinning all these proposals is the fundamental need for stakeholders to recognise the inherent differences of rare diseases.

Three proposals are put forward. Proposal 3 centres on the potential benefits of EU-level and cross-country collaborations, such as the recent EU Regulation on HTA. Proposal 4 proposes potential approaches to better managing the evidential uncertainty frequently associated with rare diseases: real-world evidence (RWE) and adaptive pathways. Proposal 5 focuses on country-level adaptations to HTA and P&R systems, beyond RWE and adaptive processes, aimed at accelerating and broadening patient access. This includes proposals for novel payment and pricing models and for increased flexibility in light of the evidential challenges that are typical for rare diseases.

## PROPOSAL 3:

### EURORDIS and EFPIA support enhancing EU-level and cross-country collaborations for OMPs

During the dialogue, EURORDIS and EFPIA explored the benefits and drawbacks of collaboration along the HTA and P&R processes for OMPs access, either led by EU institutions or coordinated at Member State level. Most attention was devoted to recent EU developments on the Regulation on HTA.

The (EC) Regulation 2021/2282 on HTA was enacted in January 2022[26]. This new framework includes joint activities across EU Member States around clinical assessments, scientific consultations, horizon scanning, and further voluntary cooperation. Joint clinical assessments (JCA) will be mandatory and focus on the assessment of clinical evidence, whereas economic considerations will remain country specific. Member States will conduct their own appraisal of the evidence and draw their own conclusions on the value of the health technology but will be required to communicate how the JCA reports were used. The first implementation phase (2025-2027) will focus on oncology medicines and advanced therapeutic medicinal products (ATMPs), including those indicated for rare diseases.

EURORDIS is pleased that ATMPs and oncological medicines, including their rare indications, are part of the first implementation phase of the Regulation.

EURORDIS would further support prioritising OMPs for very low prevalence conditions (e.g., less than 1 in 10,000 patients) in the first implementation phase, as these medicines would benefit greatly from pooled capabilities and expertise. EFPIA welcomes the staggered approach to implementation, which may help to establish high quality outputs and help all stakeholders to build trust in the EU HTA framework.

EURORDIS and EFPIA support the activities proposed in the EU Regulation on HTA. They agree that EU-level collaboration on JCA has the potential to lead to broader and/or accelerated access if:

- HTA agencies pool their capabilities and develop a common understanding of the benefits of a new medicine,
- methodological guidelines allow for flexibility in evidence requirements in light of the challenges posed by rarity[27],
- there is no duplication between what is being done at EU and national levels respectively,
- there is a reliable commitment to use the joint assessment as the basis of national decisions, and
- the drafting of JCAs at European level does not lead to any de facto patient access delays at national level[28, 29].

EURORDIS and EFPIA see the Regulation's adoption and implementation as an opportunity, including for OMPs. There are, however, ongoing concerns that will need to be addressed during the current implementation phase. These include the risk of JCAs not reflecting the specificities of OMPs as requested in the Regulation, the chance of duplication with country-level HTAs, and the non-binding nature of the JCAs (lack of a formal obligation for Member States to replace national clinical assessments by the JCAs and to effectively use the JCAs in local pricing and reimbursement decisions).

As a result, both parties are willing to work with all stakeholders to overcome these concerns and ensure that the Regulation's implementation will result in more timely and broader patient access. Specifically, EFPIA has highlighted some key areas of focus relating to the feasibility of this future new system. This entails national adaptations of processes and timelines to optimise the use of EU-level activities, sufficient capacity and appropriate resourcing for joint scientific consultations, fit-for-purpose methodologies given the rarity of OMPs that will lead to high quality outputs, and meaningful inclusion of manufacturers, patients and clinical experts throughout the process[30]. An open, transparent and collaborative approach involving all stakeholders, including patients and industry, is a key success factor. It is therefore important that the right consultation process and appeal mechanisms are put in place.

Beyond the EU Regulation on HTA, other forms of cross-country collaborations were also discussed as part of the dialogue. These include joint negotiations, joint procurement coordinated by Member States and European procurement (led by the Commission), which are key parts of EURORDIS's vision. While EURORDIS and EFPIA are not aligned on the topic, both recognise the potential benefits of Member State-led cross-border collaborations in specific circumstances. For example, EFPIA recognises the potential benefits of joint procurement in the case of serious cross-border health threats and the potential for consistent pricing and payment arrangements in the context of cross-border care for ultra-rare disease patients when therapeutic options in patients' best interest are concentrated in a few highly specialised centres in selected countries[31]. EURORDIS favours exploring new European-level procurement methods more broadly, especially for therapies administered in few highly specialised centres[32].

## PROPOSAL 4:

## EURORDIS and EFPIA call for greater use of adaptive pathways and RWE in value assessments, and for increased resources to enhance their effect

Evidential uncertainty at the time of marketing authorisation frequently adds to the complexity of HTA and pricing negotiations for rare disease medicines. The challenge of small populations is exacerbated for ATMPs given the relatively short duration of trials compared to the expected long-term effects of these treatments[33].

There is consensus between EURORDIS and EFPIA on the potential to mitigate this uncertainty through adaptive pathways and greater use of RWE in specific cases. This has the potential to complement the understanding of a medicine's effectiveness, optimal clinical use, outcomes in specific target populations, and expected budget impact. Adaptive processes of value assessment using RWE can be leveraged to manage evidential uncertainty over time, enabling earlier patient access to these medicines while evidence is being collected. A recent example is the conditional reimbursement pathway underpinned by ring-fenced funding for OMPs in the Netherlands. The scheme allows for patient access per the EMA label with incomplete data while RWE is generated for later assessments of clinical outcomes and value[34].

RWE collection requires multi-stakeholder and cross-national collaborations, especially for rare diseases. This is because rare diseases affect a small number of patients in a single country, so pooling data at a regional level is necessary to generate a robust understanding of the treatment effect. Recent EU developments and initiatives – including the Innovative Medicines Initiative (IMI), DARWIN EU, GetReal Institute, RWE4DECISIONS, European Digital Health, and the European Rare Disease Research Coordination and Support Action (ERICA) – have improved the opportunities for cross-country collaboration on generating and using RWE. Furthermore, well-established European Reference Networks (ERNs) have the potential to contribute to the coordination of RWE collection.

Because of the importance of EU-wide collaboration for RWE, EURORDIS proposes to establish an EU Fund for RWE[35]. The Fund would provide a platform for Member States to align research questions for post-approval data collection for selected OMPs with residual decision-relevant uncertainty at the time of EU marketing authorisation.

The Fund would initially focus on very small populations and complex treatments, given the level of evidential uncertainty at launch associated with these therapies. It is an instrument that would allow for the sustainable and coordinated collection of RWE in a targeted, efficient, and harmonised way across Europe.

The evidence collected through the EU Fund could then inform discussions at regulatory and P&R levels (e.g., in future EU JCAs, in national P&R decisions, or as part of EURORDIS's proposed EU Table of Negotiations). This proposal for an EU Fund is to be further discussed with EFPIA, which does not have a dedicated position on EURORDIS's proposal.

EURORDIS and EFPIA encourage countries' adoption of adaptive pathways and systematic use of RWE in HTA and P&R decisions[36, 37, 38]. This means that Member States' P&R processes would be able to cope with residual decision-relevant uncertainty at the time of launch, allow for iterative assessments of value using RWE, and on that basis, be willing to revise P&R decisions based on the medicine's re-assessment of value. In some cases, for example when the RWE collected focuses on clinical outcomes and is applicable across countries, the re-assessment of value could be coordinated with EU-level JCA to avoid inefficiencies and duplication.

EURORDIS and EFPIA will continue to work together on defining what an EU-level infrastructure for RWE could look like. They further welcome multi-stakeholder dialogues to advance a common understanding of the infrastructure, processes and standards, and cross-border collaboration required to facilitate the systematic RWE collection for rare diseases.

## PROPOSAL 5:

## EURORDIS and EFPIA support the adaptation of country-level HTA and P&R frameworks to the specificities of rare diseases

EFPIA has developed a series of country-level proposals, beyond adaptive processes and RWE, to address challenges within Member State P&R frameworks in order to enable more timely and equal patient access across the EU. These proposals broadly aim to better adapt HTA and P&R frameworks to the inherent challenges posed by orphan medicines.

These proposals, which were discussed with EURORDIS during the dialogues, should be advanced through multi-stakeholder discussions, e.g., at Member State level or in the context of the proposed High-level Forum on Better Access to Health Innovation.

One proposal aims to overcome barriers through a more systematic use of novel payment and pricing models, such as outcomes-based payments, over-time payments, indication and combination-based pricing, and subscription payments[39]. These models can address clinical and financial uncertainty, affordability constraints, or issues linked to medicines being used across indications and combinations, and thus ultimately contribute to accelerating patient access. Such challenges are particularly common for ATMPs, for which clinical uncertainty, financial risk, and issues of affordability are exacerbated. Novel payment and pricing models could offer more targeted solutions to support patient access to ATMPs while mitigating these key concerns[40, 41].

Furthermore, there is an established need for HTA and P&R frameworks to recognise the inherent challenges and constraints of drug development in small populations and to ensure flexibility in the evaluation of and price negotiation for OMPs[42].

The challenges inherent to the development of medicines for small populations (including lack of disease knowledge, difficulty of generating robust evidence, higher costs of development per patient, higher prices necessary to provide sufficient returns) mean that it is more difficult for most OMPs to demonstrate an added benefit and/or value-for-money based on conventional frameworks.

This is because current approaches focus on rigid clinical benefit and cost-effectiveness evaluations, such as evaluations based on cost per quality-adjusted life years. Conventional HTA methods need to be adapted to rarity, mainly by offering flexibility on evidential uncertainty and by introducing context-specific willingness-to-pay thresholds. Many countries include, or plan to implement, process adaptions for rare diseases (e.g., increased thresholds for ultra-rare conditions in Norway and Sweden, simplified evidence requirements and automatic added benefit in Germany[43]), which EURORDIS and EFPIA welcome.

Flexibility in P&R processes would also entail refraining from reimbursement restrictions within the EMA label, in order to avoid that access is denied to patients who may benefit from a therapy[44]. Wherever possible, all eligible patients within the authorised EMA label should be considered for reimbursement[45], considering the difficulty of generating evidence in all patient subgroups in low prevalence diseases.

These proposals will not only help improve patient access but also support a sustainable environment for innovation to continue to address the greatest areas of unmet medical need. That is because these proposals have the potential to increase manufacturers' confidence that medicines will be reimbursed for all eligible patients, thus reducing uncertainty around the economic viability of developing the medicine.

## Part C – Because improved access today must go hand in hand with innovation for tomorrow, EFPIA propose to discuss a Moonshot for rare diseases

Beyond improving patient access to today's OMPs, there is a need to encourage tomorrow's innovation, to address rare disease patients' remaining unmet medical needs.

Targeted efforts to advance basic science in a collaborative way can lead to the innovation that will fill those therapeutic gaps.

## PROPOSAL 6:

### EURORDIS and EFPIA call for a Moonshot for basic and translational research for adult and paediatric rare disease

EFPIA has suggested a Moonshot to develop science for rare diseases, thus supporting innovation in underserved areas. Typically, a Moonshot refers to an open-science model aimed at making knowledge generated from scientific research transparent and accessible through shared collaborative networks. A recent example is the cancer Moonshot launched in 2016 with an ambition to reduce cancer deaths in the United States by 50%, by accelerating scientific discovery, fostering greater collaboration and improving data sharing[46].

In many rare and paediatric diseases, limited understanding of disease pathophysiology and of potential drug targets precludes any investment. The Moonshot for rare diseases aims to establish a mindset of concerted effort towards developing the basic science and accelerating the translational research that are prerequisites for clinical development[47].

This shared goal would encourage all stakeholders to work together on defined areas of priority based on better coordination of basic research, investment, and infrastructures. The model would be built on public-private partnerships, leveraging existing European initiatives such as the IMI and its successor, the Innovative Health Initiative (IHI), as well as enabling collaboration opportunities for industry in any Commission programme dealing with rare diseases (e.g., ERNs for rare disease and potential European Rare Disease Partnership in Horizon Europe).

This proposal has the potential of contributing to faster, better, and more efficient and coordinated development of innovative products. EURORDIS is fully supportive of this initiative; EURORDIS and EFPIA will actively partner to design and implement the Moonshot.

## CONCLUSION:

### The fact that EURORDIS and EFPIA have for the first time issued a joint statement is testament to the importance of the proposals put forward

EFPIA and EURORDIS are independent organisations, with diverse memberships and differing agendas, that share a mutual interest in advancing patient access to medicines for rare diseases.

To engage in these structured dialogues and to seek opportunities for change has required effort, courage, and compromise on both sides. The recommendations contained in this report are not simple solutions to easy problems, nor can they entirely alleviate the access challenge that rare disease patients face. Yet both parties believe that these proposals collectively represent an important step forward and a foundation for further collaboration.

There is much work to be done, and both organisations are committed to further developing the ideas contained in this document and translating them into practice. EURORDIS and EFPIA hope that the proposals put forward will inform ongoing and future policy discussions (including the revision of the OMP Regulation and of the general Pharmaceutical Legislation, Horizon Europe, and the EU Health programme).

EURORDIS and EFPIA now invite other stakeholders – the European Commission, Member States, the European Parliament, and civil society including patient organisations, researchers, and clinicians – to match their ambition and join together to advance the interests of rare disease patients in Europe.

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[13] EURORDIS report. Breaking the access deadlock to leave no one behind. A contribution by EURORDIS and its Members on possibilities for patients' full and equitable access to rare disease therapies in Europe. January 2018. Available from: https://www.eurordis.org/accesspaper

[14] Root causes are not listed in order of importance

[15] European Commission. Study on enhanced cross-country coordination in the area of pharmaceutical product pricing. Final report. December 2015

[16] EURORDIS report. Breaking the access deadlock to leave no one behind. A contribution by EURORDIS and its Members on possibilities for patients' full and equitable access to rare disease therapies in Europe. January 2018. Available from: https://www.eurordis.org/accesspaper

[17] Ibid

[18] It is important to note that EBTP would not address all root causes of access delays. Delays to patient access would still occur as a result of other structural issues – solutions to which are discussed in the rest of the paper

[19] EFPIA. A shared approach to supporting Equity Based Tiered Pricing. Discussion document. April 2022. Available from: https://www.efpia.eu/media/636837/a-shared-approach-to-supporting-equity-based-tiered-pricing.pdf

[20] Official Journal of the European Communities. Council Directive of 21 December 1988 relating to the transparency of measures regulating the pricing of medicinal products for human use and their inclusion in the scope of national health insurance systems (89/105/EC). Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:31989L0105&from=EN

[21] In Breaking the Access Deadlock, EURORDIS advocates for increased collaboration among Member States for price setting and for an alternative to value-based pricing to calculate a European "bedrock price". This common "bedrock" baseline price would be negotiated in an EU Table of Negotiations and further adjusted based on several elements, including countries' ability to pay. The move away from value-based pricing and establishment of an EU Table of Negotiations to determine prices are areas of misalignment between EFPIA and EURORDIS.

[22] Non-extraterritoriality refers to the fact that national price controls should not apply beyond a Member State's jurisdiction. In other words, the auditor would also need to verify Member States' compliance with the application of ERP principles and ensuring that non-extraterritoriality is observed.

[23] EFPIA. A shared approach to supporting Equity Based Tiered Pricing. Discussion document. April 2022. Available from: https://www.efpia.eu/media/636837/a-shared-approach-to-supporting-equity-based-tiered-pricing.pdf

[24] EFPIA. Addressing patient access inequalities in Europe: The Industry commitment to file pricing and reimbursement applications across Europe and the European Access Portal. April 2022. Available from: https://www.efpia.eu/media/636830/addressing-patient-access-inequalities-in-europe.pdf

[25] IQVIA Report. EFPIA Patient WAIT Indicator 2020 survey. April 2021. Available from: https://efpia.eu/media/602652/efpia-patient-wait-indicator-final-250521.pdf

[26] Regulation (EC) 2021/2282 on health technology assessment. Available from: https://ec.europa.eu/commission/presscorner/detail/en/ip_21_6771

[27] See for example Recital 24 of the EU Regulation on HTA: "Methodologies for performing joint clinical assessments and joint scientific consultations should be adapted to include specificities of new health technologies for which some data may not be readily available. This may be the case for, inter alia, orphan medicinal products, vaccines and advanced therapy medicinal products."

[28] EFPIA report. Policy principles on cross-country collaborations on medicines' pricing and access. January 2019. Available from: https://efpia.eu/media/412513/policy-principles-on-cross-country-collaborations-on-medicines-pricing-and-access.pdf

[29] EFPIA statement in response to the Council compromise agreement on the Commission Proposal for a Regulation on Health Technology Assessment. 26 March 2021. Available from: https://www.efpia.eu/news-events/the-efpia-view/statements-press-releases/efpia-statement-in-response-to-the-council-compromise-agreement-on-the-commission-proposal-for-a-regulation-on-health-technology-assessment/

[30] EFPIA statement on adoption of health technology assessment regulation. 12 December 2021 Available from: EFPIA statement on adoption of Health Technology Assessment Regulation

[31] EFPIA White Paper on the effectiveness of public procurement of medicines in the EU. 12 October 2021. Available from efpia_white-paper_public-procurement.pdf

[32] To EURORDIS, increasing collaboration at EU-level also links to the Commission's Cross-border Healthcare Directive, which requires recognition by Member States of the place where products are being delivered and calls for proper legal requirements allowing for patients to seek care in other Member States.

[33] RARE IMPACT. A review of the challenges and proposals for improving patient access to advanced therapeutic medicinal products. Available from: https://rareimpact.eu/why-rare-impact

[34] National Health Care Institute. Conditional inclusion of orphan drugs, conditionals and exceptionals in basic health care. Available from: https://english.zorginstituutnederland.nl/

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[36] Ibid

[37] RARE IMPACT. Improving patient access to gene and cell therapies for rare diseases in Europe. A review of challenges and proposals for improving patient access to advanced therapeutic medicinal products in France. V1 January 2020. Available from: RARE-IMPACT-Country-Assessments-France_v1_2020-04-28.pdf (rareimpact.eu)

[38] EFPIA blog. Using registries in real world evidence: Paving the path for success. 4 October 2016. Available from: https://www.efpia.eu/news-events/the-efpia-view/blog-articles/using-registries-in-real-world-evidence-paving-the-path-for-success/

[39] EFPIA report. Addressing healthcare challenges | Novel pricing and payment models: new solutions to improve patient access. July 2020. Available from: https://efpia.eu/media/554543/novel-pricing-and-payment-models-new-solutions-to-improve-patient-access-300630.pdf,

[40] EFPIA report. Shifting the paradigm for ATMPs: Adapting reimbursement and value frameworks to improve patient access in Europe. January 2022. Available from: https://www.efpia.eu/media/636632/atmps-white-paper-cell-and-gene-therapies-related-market-access-issues.pdf

[41] RARE-IMPACT report. Improving patient access to gene and cell therapies for rare diseases in Europe: Challenges and solutions for improving patient access to advanced therapies medicinal products at the European Union level. October 2020. Available from: https://rareimpact.eu/site/wp-content/uploads/2020/11/RARE-IMPACT-European-Assessment_v1_2020-11-23.pdf

[42] Nicod et al. Are supplemental appraisal/reimbursement processes needed for rare disease treatments? An international comparison of country approaches. Orphanet Journal of Rare Diseases. (2020) 15:189

[43] Ibid

[44] As medicines for rare diseases are developed for a small number of patients, restricting the number of patients beyond the EMA label negatively impacts not only patient access but also potential revenue for manufacturers, and in the long run incentives for innovation in rare diseases

[45] Annemans et al. Recommendations from the Working Group for Value Assessment and Funding Processes in Rare Diseases. Orphanet Journal of Rare Diseases, 2017, 12:50

[46] National Cancer Institute. Cancer Moonshot. Available from: https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative

[47] Dolon report prepared for EFPIA. Addressing unmet medical needs in extremely rare and paediatric-onset diseases: how the biopharmaceutical innovation model can help identify current issues and find potential solutions. July 2021. Available from: https://www.efpia.eu/media/602878/addressing-unmet-needs-in-extremely-rare-and-paediatric-onset-diseases-how-the-biopharmaceutical-innovation-model-can-help-identify-current-issues-and-find-potential-solutions.pdf

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