DOLON

Rare DISEASE DAY 2024

What does it take to see continued rare disease innovation in Europe?

While innovation in rare disease has brought transformative change to the lives of many patients, significant unmet need remains. In Europe today, a substantial number of patients with rare diseases lack an approved treatment option, experience shortcomings with current treatments or cannot access an approved treatment.

Continued innovation in rare disease is essential to addressing remaining unmet needs. To mark Rare Disease Day 2024, we explore four critical elements to sustaining rare disease innovation in Europe. These are outlined below, building on work recently published by Dolon team members.

#1 Great science

#2 Clear incentives

#3 Supportive P&R

#4 Strong community

Requirement #1: Great Science

"...[some of] the factors that drive which drugs get developed relate to the relative degree of disease knowledge and treatment ability in that indication. Across all the areas of unmet need requiring innovation, only a small subset of disease areas are [currently] 'clinically viable'."

— Isabelle Laurence and colleagues in 'Rare innovation: How it happens, when it doesn't, and what can be done to sustain it.' *Publication commissioned by Alexion.*

The fact that 95% of approximately 6,000-10,000 known rare diseases still lack any approved treatment[1,2] is down to a combination of clinical and economic hurdles to innovation. First and foremost, innovation requires excellent science – without which there is no question of industry investment in developing and launching a novel therapy.

Scientific discovery is progressive and often difficult to predict. Basic research – often supported by public funding and performed in academic institutions – plays an essential role in generating the foundational scientific understanding and technological capability which form the building blocks for future drug development. Industry generally enters the stage once scientific leads are established to transform original science into a clinically tested and approved product, in what is invariably a long and risky process.

In our recent publication exploring the factors which drive drug development[3], we examine how rarity exacerbates the scientific challenges to innovation. Indeed, with what little is known about most rare diseases and their populations, great underlying science is even more important, and challenging, to attain.

Public policy plays a critical role in driving scientific discovery to expand the field of clinically viable areas for innovation. Though in isolation this is not enough to drive rare disease development in Europe, it is an essential pre-requisite.

Requirement #2: Clear incentives

"Europe must create an ecosystem that actively nurtures innovation and encourages greater investment from pharmaceutical companies in pioneering therapeutic advancements."

— Lindsay Kreill and colleagues in 'Revision of the General Pharmaceutical Legislation: Impact Assessment of European Commission and EFPIA proposals.' *Publication commissioned by EFPIA.*

Companies – like people – must make choices about where to invest their limited resources, based on assessments of where they can achieve the greatest impact for society and their shareholders. When pharmaceutical companies invest, they first and foremost consider where there is great science and unmet need, but then within those areas must make choices about which options to pursue.

In view of the considerable economic challenges to therapeutic development for rare diseases, continued innovation is heavily dependent on whether investment is sufficiently incentivised. Recognition of this led to the establishment of the EU Orphan Regulation nearly 25 years ago, with the hope to encourage innovation in rare disease.

The importance of incentives in driving investment and innovation in Europe was underlined by our recent modelling of the impact of curtailing intellectual property (IP) protections – as has been proposed by the European Commission. In a recent Dolon analysis commissioned by EFPIA, and quoted by the Financial Times, we found that changes to a form of IP called regulatory data protection would substantially reduce industry's inclination to invest, translating to a 22% drop in development between 2022 and 2035[4]. Shortly before that, we published our impact assessment of proposed revisions to the Orphan Regulation, which we estimated would decrease rare disease innovation by 12% in the same period[5].

Continued orphan innovation relies on a balanced legislative environment for medicines that ensures availability, affordability, and access alongside clear incentives which support industrial competitiveness. Prolonged uncertainty around these incentives will erode industry confidence and, ultimately, orphan development in Europe.

Requirement #3: Supportive P&R

"The pioneering nature of ATMPs means that the costs of developing [and manufacturing] these products are especially high, making products potentially economically unviable if prices do not reflect value."

— Adam Hutchings in 'Innovative contracting for ATMPs in Europe: Recent learnings from the manufacturer experience.' *Publication commissioned by Alliance for Regenerative Medicine.*

Whether a medicine exists matters little for patients who cannot receive it because it is not reimbursed. Reimbursement is also key for manufacturers who rely on the sale of medicines to recover their considerable investment in development and to support their future pipeline.

Continued innovation and access in rare disease in Europe relies on country-level pricing and reimbursement (P&R) approaches that can recognise and reward promising orphan developments – though this is by no means simple. Indeed, many extremely novel, transformative treatments fall foul of traditional P&R systems designed for chronic therapies in common conditions.

One such example is cell and gene therapies. These unique treatments present immense value owing to their one-time, potentially curative profile. They also come with a significant price tag, complex delivery, and an inevitable degree of uncertainty around long-term benefit. In our recent paper for the Alliance for Regenerative Medicines (ARM), we explore these challenges and their implications for P&R, patient access, and the sustainability of ATMP innovation in Europe[6]. In particular, we focus on innovative contracting as an opportunity to mitigate these challenges as well as recent learnings from manufacturers' experience in negotiating these.

P&R frameworks need to evolve with science if they are to fully reflect the value of emerging therapies to patients and health systems alike. Failure to do so will come at the expense of patients and health systems today, and Europe's standing as a global centre for innovation in the longer term.

Requirement #4: Strong community

"Despite the increasing awareness and efforts focusing on rare diseases, people living with ALS and other rare diseases in Europe continue to face significant challenges related to low levels of disease awareness, delays in receiving an accurate diagnosis, suboptimal treatment pathways and a lack of approved treatments"

— Gisela Rovira Tomas and colleagues in 'Amyotrophic Lateral Sclerosis, a rare neurodegenerative disease: European landscape assessment and policy recommendations for improved diagnosis, care, and treatment.' *Publication commissioned by EU ALS Coalition.*

Significant gaps remain in how patients with rare diseases are diagnosed, treated, and supported[7]. For new therapeutic developments to address these gaps requires a strong, multi-stakeholder community that can recognise and communicate patient needs. This is especially true for complex and severe conditions with huge unmet needs and no satisfactory treatment alternatives. Ensuring these patients are properly diagnosed and cared for while waiting for potential new therapies should be seen as a priority. This will contribute to improving their lives, while also strengthening healthcare systems and their preparedness for future innovation.

Dolon was proud to work with the European Amyotrophic Lateral Sclerosis Coalition ('EU ALS Coalition') last year to develop a paper exploring the needs of patients with ALS and policy recommendations to better address these[8]. This work underscores the crucial requirement to make patient needs a focal point in every aspect of their care, including treatment innovation. The EU ALS Coalition is now engaging with policy- and decision-makers to raise awareness and help drive progress.

By establishing a positive rare disease environment in Europe in which all stakeholders, from policymakers to physicians, centre their actions around patient needs, we can ensure that all people living with rare disease can receive better diagnosis and care, while preparing for future innovation.

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