Horizon
The EU Research & Innovation Magazine

European Commission

The building blocks to make rare disease treatments more common

At present, around 50 new therapies are approved around the world each year. At this rate, it would take more than 100 years to develop a single treatment for every rare disease estimated to exist worldwide. Although such diseases are rare, this situation, outlined in a recent study by members of the International Rare Diseases Research Consortium (IRDiRC), is no minor problem.

28 February 2022 - By GARETH WILLMER

While each rare disease affects less than one person in 2,000 by the EU's definition, the existence of 6,000 to 8,000 such conditions means that a far more alarming one in 17 may be affected overall – or 30 million EU-wide.

Rare diseases have, nevertheless, historically been neglected, even if awareness and action to address them have improved over time. These include measures such as the European Joint Programme co-fund on Rare Diseases (EJP RD) and European Reference Networks (ERNs).

Yet there is a long way to go, said Diego Ardigò, head of research and development for global rare diseases at the pharmaceutical group Chiesi. This is especially the case when you drill down to ultra-rare diseases beyond

some of the ‘more common’ ones like Duchenne muscular dystrophy (DMD) or cystic fibrosis, which affect about one in 3,000 to 4,000 people worldwide.

Some rare diseases can have a prevalence of one in half a million or even less – such as alpha-mannosidosis, for which Chiesi has developed a treatment. Others are not known about at all. ‘You don’t have anything: you don’t have references, and you are navigating without a map and without a compass in an unexplored world,’ said Ardigò.

Indeed, only 5% or fewer of rare diseases are estimated to have at least one approved treatment – known as “orphan” therapies. It can take many years to bring these to market, with the process hindered by limited knowledge, regulatory hurdles, safety and financial risks in developing drugs for small populations, and a lack of systematic application of best practices.

Quantum change

But companies such as Chiesi, public research funders and organisations like non-governmental patient-driven alliance EURORDIS have moved to address this through their membership of the global collaborative initiative IRDiRC, a multinational consortium established by the European Commission and the US National Institutes of Health in 2011.

A key cornerstone of this is IRDiRC’s creation of the Orphan Drug Development Guidebook (ODDG), published in 2020, which sought to draw together all the knowledge we have to date on developing drugs for rare diseases and build a framework for optimal use of existing tools available in Europe, Japan and the US – ultimately inspiring a “quantum change” in the way drugs are developed.

The aspiration is that having such a framework will provide a starting point for reducing costs and accelerating the process, after IRDiRC acknowledged that the pace was too slow to reach its target of approval of 1,000 rare disease therapies by 2027. This also left it off course in its vision to enable all people living with a rare disease to receive accurate diagnoses, care and available therapies within a year of coming to medical attention.

To create the ODDG, IRDiRC brought together a 22-person strong multi-stakeholder task force in 2018, including people from all fields of rare drug development.

‘Diego [Ardigò] is from pharma, I’m a patient representative, but we also had regulators and academics, and really all the possible perspectives,’ said Virginie Hivert, therapeutic development director at EURORDIS, who acted as vice-chair of the committee responsible for the ODDG, alongside Ardigò as chair.

Through workshops and discussions, the task force mapped out 110 building blocks available to orphan-drug developers for taking treatments to market, creating supporting fact sheets for each, including information on how and when to apply them. Though Hivert says this is just a start and it is too early to assess the impact so far, she is hopeful that the ODDG will be sustained and built upon, acting as a platform to accelerate development and awareness.

She also hopes it can act as a guide for new and innovative players in the market, which are particularly crucial in the rare disease sector for developing cutting-edge treatments such as gene therapies. ‘There are more and more non-traditional developers that are operating in the field of rare diseases, so the hope is that this guidebook will also be of great use to them,’ said Hivert.

As part of the ODDG, the task force highlighted that specific clinical development methodologies for small groups and patient-centric approaches to orphan drug development are essential, given that patients are often the people who best understand diseases and have the most experience with diseases that have little knowledge base.

This means involving them every step of the way, from research to clinical trial design, and from regulatory processes to communication with drug developers. ‘You cannot make developments for rare diseases without having the patients as full partners if you want to maximise the chances of success and target the right unmet needs,’ said Hivert.

Raising the profile

Nick Sireau, CEO and chairman of the Alkaptonuria (AKU) Society in the UK, agrees that this type of patient engagement is essential. He says things have improved in the 20 years he has been involved in the society – which started after his two sons were diagnosed with the rare genetic disease AKU, which affects 1 in 250,000 to one in a million people.

This has been aided by patient groups such as EURORDIS, of which the AKU Society is a member. 'EURORDIS has managed to significantly raise awareness on rare diseases in policy and funding areas,' said Sireau. 'Patient groups are increasingly involved now in the development of research and medications for new diseases.'

Yet Sireau thinks there is still much to do, particularly around funding. 'One of the things I've been saying a lot recently is there needs to be much more funding to help rare disease patient groups really build their capacity, and their work with industry and universities.' He suggests measures such as an independent foundation into which big pharma can donate a percentage of profits for subsequent redistribution to patient groups.

From his own experience, Sireau also highlights the huge amount of time it can take to get treatments to market. This comes after the AKU Society saw a breakthrough via its involvement in the EU-funded DEVELOPAKURE project, in which a drug called nitisinone – repurposed from treatment for another disease called HT-1 – was approved in 2020 after it was found to also ease the symptoms of AKU.

'This was a drug that was already approved for another condition, and yet it still took us 15 years to get it all through the clinical trials and approved,' said Sireau. Despite this, he is optimistic about the success and the potential for new technologies such as mRNA therapies, which the AKU Society is looking into.

Long-term view

Ardigò hopes the collective work that has gone into forming the ODDG over the last 20 years will provide the basis for advances in the sector.

'I think the help that the guidebook can give is to provide clarity to a confused, complex and complicated field,' he said. 'You also have a quick reference to making tools usable.'

One of the big hurdles to overcome in drug development is still the limited perceived profit in rare diseases, but Ardigò points out that it is possible to generate value for developers and society, given Chiesi's own experience in the past. He says doing this requires collaboration between all stakeholders in forging a long-term view and shared understanding of what patients really need, keeping alert for drug repurposing opportunities, and treating rare drugs as a collective issue rather than each one as a single, isolated problem. He believes organisations that can do this can put themselves at the forefront of future drug development.

'The area of rare diseases is a field of learning for future medicine. It has been a playfield for highly innovative technologies,' he said. 'There is a really big opportunity if we are able to figure out how to move into the lower scales [by tackling ultra-rare diseases].'

Despite the setbacks caused by COVID-19 to research and resources for tackling rare diseases, he sees reasons for positivity after what the pandemic has shown about the potential for collaboration and acceleration of drug development. 'With COVID, in less than a year we got the first vaccines,' said Ardigò. 'We have to push for that level of collaboration – for sharing of data, for sharing of information and for working together as a community.'

Though he thinks IRDiRC's target for 1,000 treatments by 2027 will be challenging in the present climate, he points out that the organisation already set a high goal of 200 new drugs in the decade from 2011, and this was reached in just six years. 'So maybe we'll be able to do much more than we think,' he said.

Whatever the case, there is a need to act now, said Ardigò, backed by knowledge accrued from initiatives like the ODDG. 'There are patients there who have these diseases today… they cannot wait, so we cannot wait.'

EU research on rare diseases

The area of rare diseases has long been a priority area for the EU, and is recognised as a field where EU and international collaboration is an indispensable condition to progress.

The European Commission, through its funding via successive framework programmes for research and innovation and its Health research policy, supports the development of new treatments and diagnostics for rare diseases across Europe.

Under Horizon Europe (2021-2027), the new research and innovation funding programme, a proposed European Partnership on rare diseases is expected to catalyse a systemic transformation in the area. It will coordinate national, local and European research and innovation programmes with the goal of developing diagnostics and treatments to improve the quality of life for people living with rare diseases.

The research in this article was funded by the EU. If you liked this article, please consider sharing it on social media.

More info

This article is part of our Monthly Focus on rare diseases.

IRDiRC

European Joint Programme on Rare Diseases

European Reference Networks

EURORDIS

DEVELOPAKURE

EU research on rare diseases