INSIGHTS INTO WORKING WITH RARE DISEASES

We've asked some of our experts to share insights on the challenges posed by rare diseases in healthcare, particularly in the wake of the ongoing COVID-19 pandemic. Each has given their own take based on their experience of working in the rare disease space, based on the impact on payers, pharmaceutical companies and, most importantly, patients.

OUR EXPERTS

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What is your perspective on the impact of the pandemic on the development of rare disease treatments? Does the COVID-19 pandemic shed any positive light on future rare disease therapeutics?

Michael Rice

From my perspective, the COVID-19 pandemic is having a tempestuous impact on progress in the development of novel treatments for rare disease patients. Older individuals and those with rare diseases suffer disproportionate morbidity and mortality from SARS-CoV-2 infections due to both co-morbidities and immunosuppression related to their disease and the medicines and procedures necessary to manage symptoms or control progression. Furthermore, for those considered at high risk, normal daily living is fraught with continual risks of exposure, particularly when accessing healthcare facilities for clinical management and their lifesaving treatments. In this respect, patients may have received inadequate healthcare or an impaired ability to enroll in clinical trials, which may have worsened their outcomes, and delayed biotech companies' ability to enroll patients for clinical trials of potential new treatments.

At the same time, innovators found the virtual environment and Zoom meetings quite efficient for raising capital to fund translation of early-stage discoveries. Indeed, over the last 2 years, rare disease-focused biotech companies have raised record-level venture capital and private investments to fund investigational new drug (IND)-enabling studies towards first-in-human studies. Another area of progress has been uniquely enabled by the COVID-19 pandemic itself, through the acceleration of the understanding and funding for novel vaccine platforms and mRNA therapeutics. Beneficiaries of windfalls from the COVID-19 vaccines, such as Moderna, Pfizer, BioNTech and others are investing in developing mRNA-based vaccines for SARS-Cov-2 variants and many other infectious diseases.

Beyond vaccines, the learnings from mRNA synthesis and formulation are being applied to individualize cancer immunotherapies and as

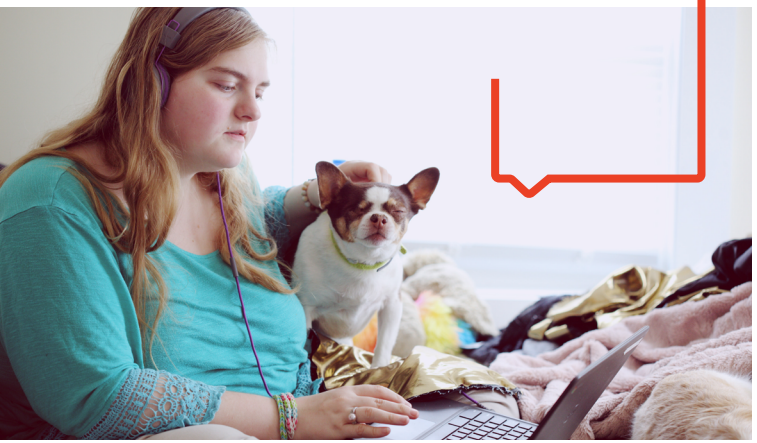
a way to deliver therapeutic proteins for rare monogenetic diseases caused by loss of function mutations and haploinsufficiency. While the promise of creating a greater good from the devastating losses from the last 2 years of the epidemic are in the early stages, we are hopeful that significant unmet needs of rare disease patients will be addressed in the future by such breakthrough innovations.

How has engagement of rare disease communities evolved since the COVID-19 pandemic hit 2 years ago? How can rare disease communities be better engaged in future pandemic events?

Jane Barrett

The COVID-19 pandemic is having a profound but hidden impact on the ability of rare disease patient communities to engage.

Despite the diversity of rare diseases, they share commonalities – they struggle to get a timely diagnosis; they suffer from isolation and the average doctor has little knowledge, which means they gravitate to peers and groups online for information; disengagement from the healthcare



More than ever, rare patients need encouragement to remain engaged with healthcare systems. Being hidden and unheard is a ubiquitous rare disease experience and an event like the COVID-19 pandemic makes it all the more important to demonstrate that the rare voice matters and is being listened to in the face of such high demand on services.

system is always a risk due to difficulty accessing successful treatment and specialized centers.

So, what has happened to these recognized dynamics during the pandemic? In non-rare diseases, the collective backlog of delayed diagnoses is monumental, and non-urgent appointments and surgeries are incredibly backed up too. These forces, of course, are affecting the rare disease patients too, though evidence is slower to emerge. However, common sense and anecdote point to COVID-19 having a profound but hidden impact on the ability of rare disease patient communities to engage.

Getting a rare disease diagnosis is challenge enough in normal times, but the overlay of COVID-19 is making this all the harder with the multiple appointments, a prelude to diagnosis, being dragged out over a longer period still. More delays mean more deterioration and, in some rare diseases, this can mean the difference between qualifying for an effective treatment (e.g. gene therapy) or not, because time windows are very small. Many conversations may be needed and the pandemic has sadly squeezed the time for these vital discussions and decisions.

The pandemic has intensified the isolation of rare disease patients and caregivers, making continued engagement harder but more vital. They have had to be even more proactive in their fight for diagnosis, access to an expert and the right treatment, while the availability of such help has shrunk.

Additional stressors and delays have meant that the already important online communities have become even more crucial to meet patient needs – both clinical and emotional. The pandemic has, therefore, increased the influential power of online advocates and patient support groups (formal and informal). This means it is vital that pharma companies make sure rare disease online influencers and patient groups have access to correct information about treatments and to expert centers and specialists. Signposting peer patients to the right treaters will help avoid patients getting clogged up in the waiting lists of those with non-rare conditions in non-specialized hospitals.

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What are the fresh challenges rare disease communities have to expect in a post-pandemic normal?

Michael Parisi

The rare disease community has been defined by their resilience. There is no denying that the

COVID 19 pandemic was the great equalizer. This became abundantly clear in a recent conversation that I had with a young woman living with myelodysplastic syndrome (MDS). When we spoke about the isolation, the fear of getting a life-threatening infection, and the inability to breathe that comes with the pandemic, she said, 'now the world knows what it's like to live with MDS every day of your life.'

As we move into 2022, there are a host of new challenges that the rare disease community will face – some new, and some familiar but with a new complexion. Two things that immediately come to mind-first:

1. **Rare cannot mean forgotten.** Many rare disease communities feel like the urgency around their movements have been overtaken by the needs brought forward by the pandemic – which means they have to shout louder, push harder than ever before to gain the attention and focus on their diseases.
2. **Lost empathy.** A great concern of the community is fear that we have lost empathy, specifically that things they need to do to say safe, such as wearing a mask and gloves, have now become symbols for judgement rather than opportunities to stop and gain knowledge. So, as we move forward, we all need to take a minute to listen and learn so we can better understand and help people living with rare diseases live their best lives.

How can companies developing treatments for rare diseases better serve patient/carer communities?

Ron Akehurst

There are many ways in which companies can and do serve, but I am a member of the Committee

at the National Institute for Health and Care Excellence (NICE) that has responsibility for recommending funding of treatments for ultra-rare diseases in England, and I observe that companies should more effectively demonstrate the **value** of new treatments. In particular, they should make sure they can demonstrate the effects of their treatment on how patients **feel, function and survive** by use of appropriate outcome measurement.

Outcome measures that are commonly used in trials in rare diseases, in particular, biomarkers, are often adequate to achieve marketing approval, but may fail to support the needed price and/or achieve reimbursement from payers, thus preventing the treatment reaching the target patients. Demonstrating in a trial that a biomarker is improved does not demonstrate the effect on patients. Even when registration trials go beyond a biomarker, such as dystrophin for Duchenne Muscular Dystrophy, to measures such as The Six Minute Walk Test, they still only reflect an aspect (albeit an important one) of treatment and miss much. In the latter case, obviously, benefits in the non-ambulant are not captured.

The particular ways in which patients are affected by rare diseases are often unknown, and measures that reflect the improvements that matter to patients have to be created in conjunction with the patient community. In this way, companies will increase the chances of approval from funding bodies and speed the availability of effective treatments to patients.

Can you describe the role of rare disease patients as partners to companies developing treatments for their disease?

Susan Daniels

Rare disease patients, their families and support networks, face a disproportionate struggle for knowledge, advocacy, and options for treatment. This places a heavy personal and financial burden on individuals and families. The rare disease community is actively engaged and uniquely motivated to find valuable solutions to streamline both the clinical trials and approval processes to expedite much needed treatments to market. Given the predicted increase in spending on rare disease innovation in the future, payers

are looking for innovative, multi-stakeholder partnerships to share the risk and investment,

often initiated and driven by rare disease patients themselves.

For its part, the rare disease community is committed to better awareness and knowledge of rare diseases within clinical and research communities. They are advocating for increased and sustained activation of the stakeholder patient communities, for better collaboration to drive support, funding, and experience and, ultimately, better exposure and partnership to the researchers and companies key to the development of solutions. Integrating patient involvement and lived experience in research planning, development pathways and life cycle management is key to this partnership.

As a company, we are firmly engaged with a number of rare disease communities and working in partnerships with pharmaceutical companies who seek to support them. We are continuously dedicated to gaining a better understanding of the unmet needs of patients, with a view to supporting both groups in their quest for better insights and solutions to bring new innovation to these patients sooner.

> **Development of and accelerated access to rare disease treatment has always been key to improving the lives of those with a rare disease. Think what is now possible with the application of these learnings to rare disease!**

What learning should we embrace from the COVID-19 pandemic to better serve those with rare disease?

Angela Wheeler

When imagining a post-pandemic era and its potential impact on rare disease, I was struck by the many learnings we could take from this period to better serve those with rare diseases.

Historically, people living with a rare disease have experienced the isolation and struggle to obtain adequate healthcare that many of us have just experienced for the first time during this pandemic. People with a rare disease have often carried the responsibility for seeking correct diagnosis, educating medical specialists, explaining the burden of disease, amplifying the need for new treatments, creating their own support networks, and making incredible sacrifices to seek specialized care and participate in trials.

What have we learned recently that could better serve the rare disease community? Certainly, the amazing collaboration of pharma companies to share information and develop diagnostic tests, vaccines, treatments, and medical equipment would be welcome. We could continue to examine and expedite drug approval processes to make novel, first-in-class treatments available for emergency use by those at high risk. The acceleration of patient-centric and localized clinical trial design options and the launch of in-home, online and telephone access to medical resources and services could transform the way people with a rare disease participate in the healthcare system.

> **A positive outcome of the pandemic has been broader awareness and emerging efforts on the part of payers to improve access to care and health equity. This positive momentum can be applied to rare disease, where improved outcomes are much needed, and payers are uniquely positioned to help facilitate better access along the patient journey.**

While the scale of the effort required during a pandemic is vastly different, the situational urgency and principal behaviors demonstrated during the COVID-19 pandemic provide a roadmap for how we can better serve the rare disease community in the future. Development of and accelerated access to rare disease treatment has always been key to improving the lives of those with a rare disease. Think what is now possible with the application of these learnings to rare disease!

How can we transform the challenges created by the COVID-19 pandemic into opportunities in the rare disease area?

Amber Gilbert

The COVID-19 pandemic has brought to light both small cracks and major rifts in the healthcare ecosystem. With intention and effort, these challenges can evolve into opportunities to improve care and outcomes for patients overall as well as for patients with rare disease.

One of the most vivid challenges of the pandemic has been the impact of information and misinformation on individual behavior. Payers, health authorities, and other public health stakeholders have experienced the urgency of providing patients with balanced, digestible information that can inform individual decision making. This movement towards more effective sharing of health information can be extended into rare disease where patients can directly benefit from better education to help expedite diagnoses and advocate for treatments.

Another major challenge of the pandemic has been the significant disparities in access to care across vulnerable populations. This challenge is amplified in the rare disease community where under-representation of racial and ethnic minorities in clinical trials is well documented, and treatment is often concentrated into a limited number of centers of excellence. A positive outcome of the pandemic has been broader awareness and emerging efforts on the part of payers to improve access to care and health equity. This positive momentum can be applied to rare disease, where improved outcomes are much needed, and payers are uniquely positioned to help facilitate better access along the patient journey.

Payers often view themselves as a critical part of the care infrastructure for patients. We have the opportunity to help our clients find common ground with payers to better share information and support equitable access to care that can help improve outcomes for patients with rare disease.

What roles do our experts play in solving the challenges that the rare disease community faces during and after the pandemic?

Valarie Leishman

Our in-house experts have worked closely with our rare disease partners to identify their challenges and develop solutions.

One recent example involves the confusing messages and the frequently changing guidance regarding COVID-19 vaccinations and rare disease populations. Patients that are immunocompromised and patients with cancer have requested information regarding the efficacy of the vaccine in their population. Should they receive antibody testing post-vaccination? If they do get tested, how should they interpret the results? Are the third dose and extra boosters safe for these patients?

We have developed patient education to specifically address these questions and to encourage patients to work closely with their healthcare providers to determine the best course of action. We will continue to be there for our rare disease partners to address their ever-changing needs ■