Success in Rare Diseases — Connections Matter

When it comes to rare diseases, the scarcity of patients requires us to make every connection matter.

In the United States, a rare disease is defined as a condition affecting fewer than 200,000 people, a definition created by the U.S. Congress in the Orphan Drug Act of 1983. Rare diseases then became known as orphan diseases to help entice pharma companies to develop treatments. The Orphan Drug Act created financial incentives to encourage companies to develop new drugs for rare diseases. The rare disease definition was needed to establish which conditions would qualify for the new incentive programs. Other countries have their own official definitions of a rare disease. In the European Union, a rare disease is defined as a condition affecting fewer than one in 2,000 people.

To date, approximately 7,000 rare diseases have been identified worldwide, and an estimated 250 new diseases are discovered annually. Although rare diseases affect a relatively small number of patients, collectively there are roughly 350 million people worldwide affected by one of these rare diseases. A rare disease commonly presents early in life, but can also present in adulthood, with a chronic phase. Rare diseases are often progressive, disabling, and life-threatening. Even worse, approximately 30% of children suffering with a rare disease will die before the age of 5 years.

Most rare diseases, about 95%, still do not have an FDA-approved treatment option, and on average, patients wait five to seven years for an accurate diagnosis. Given this high level of unmet need, the pharmaceutical industry has increasingly focused its attention on the development of treatments for rare diseases.

Rare Diseases Deserve a More Connected Approach With Patients, Caregivers, and HCPs

The difficulties and lag time in diagnosing many rare diseases, combined with a lack of treatments, help fuel the unmet need in these patient populations, which makes the patient community a critical stakeholder from the

Amy Graham
Client Engagement Officer
Ogilvy Health

start. Many patients and caregivers are well informed and highly engaged in their disease and decision-making processes. They often find themselves feeling more knowledgeable than many of the HCPs they face along their journey, driving a thirst for better knowledge, stronger communication, and more connected relationships with HCPs. This patient knowledge also requires HCPs to adjust their approach accordingly when treating empowered patients. Brand communications must recognize and reflect the patient/caregiver depth of knowledge in order to establish credibility and make a connection as a trusted partner.

In traditional therapeutic markets, influence flows from a small number of key opinion leaders (KOLs) to specialists, and sometimes primary care physicians (PCPs), who are the main treaters for most diseases. In rare diseases, the dynamic is quite different. The KOLs are the main treaters while specialists and PCPs are the referring physicians. This results in marketers initially focusing their branded efforts on KOLs, whereas for specialists and PCPs, greater emphasis is placed on unbranded disease and diagnosis efforts. It's important to target the patient community early, often in advance of the product launch. Working with advocacy groups to keep them apprised of brand development can be an important tool to help recruit patients for trials and even work with the FDA to accelerate review.

Brands have an opportunity to serve as a key connector within the rare disease community, delivering more informed conversations and creating a better dynamic among patients, caregivers, and HCPs.

Diagnosis and Treatment Advancements

Science is driving advancements, and knowledge of the human genome has helped to improve both the diagnosis and treatment of rare diseases, given that approximately 85% of these diseases are genetic. Progress in next-generation sequencing has shown that sequencing the whole genomes of large numbers of individuals in a standardized way can improve the diagnosis and treatment of patients with rare diseases. To date, scientists have identified responsible genes for approximately 50% of the estimated 7,000 rare diseases. These genomic developments continue to advance therapeutic research and treatment.

Since the introduction of the Orphan Drug Act, the FDA has approved drugs and biologics for more than 770 rare disease indications. In 2019, the agency approved 22 novel drugs and biologics with orphan drug designation.

Over the past 10 years, the pharma industry has significantly ramped up its investment in this area. Historically, the orphan drug space was overlooked by the large pharmaceutical companies because developing and marketing these drugs was considered not profitable enough. The majority of the research and development activities related to orphan drugs was done by smaller-size biopharma firms, with less than 25% of the orphan drugs being researched and developed by the big firms.

According to the PhRMA, the entry of mid- and large-size pharmaceutical companies to the rare disease market is helping to speed up the clinical research activities related to orphan drugs. The number of clinical trials in rare diseases has increased drastically during the past 10 years, to more than 500 for orphan drugs as compared to a few hundred trials in the beginning of the 21st century. PhRMA reports a promising pipeline in which there are currently more than 560 medicines in development for rare diseases. We've seen incredible advances in the development of medicines to treat rare diseases as researchers uncover the molecular and genomic drivers of

many conditions. Rare diseases are biologically complex, and scientists are working diligently to uncover their underlying causes and clinical courses. Biopharmaceutical companies are following the science to develop orphan drugs and now have more than 800 projects in clinical development.

In December 2020, PharmaVOICE published an excellent article: Therapeutic Digest: Rare Disease Progress and Challenges. It was reported that while the industry has traditionally focused on small-molecule drugs, "advances in molecular biology and understanding of the human genome have enlarged the drug discovery toolbox, first to protein-based therapeutics (proteins, peptides, and antibodies) and more recently to antisense oligonucleotides (ASOs), small interfering RNAs (siRNAs) and gene and cell therapies. These therapeutic modalities differ in their ability to target molecular disease mechanisms and/or to effectively reach certain cellular compartments. Together, these therapeutic modalities allow a broad coverage of targets and mechanisms, which can be expanded by combining modalities, such as small-molecule conjugation with an antibody.

PhRMA acknowledges that developing medicines to treat rare diseases presents scientific and operational challenges. The complex biology of many of these diseases poses unique hurdles for scientists, making it difficult to design and implement a drug development program. Within each disease there can be many variations or subtypes, resulting in different clinical manifestations and disease progressions. Additionally, due to the inherently small population of patients with a rare disease, recruiting for and conducting clinical trials can be arduous.

Connections Are Helping to Drive Advancements

The very nature of rare diseases, where a limited patient pool is available, creates a number of hurdles for drug development. To help overcome several of these obstacles, connections are key. Closer partnership between the many stakeholders in the development of therapies is imperative. Together, the biopharma industry, academia, government agencies, and patient advocacy organizations (PAGs) are working to drive progress in the quest for new treatments.

A few examples of collaborative programs driving success in the field include:

- **Patient Advocacy Group Registries:** Independent disease registries for pre- and post-approval of novel treatments for rare diseases are increasingly important for healthcare professionals, patients, regulators, and the pharmaceutical industry. PAGs are playing a critical role in partnering to share data, while allowing patients to maintain ownership of their data and how it's used. PAGs have taken actions to help advance treatments, including: creating national registries, understanding the barriers to identifying patients with certain rare disease subtypes to participate in clinical trials, partnering with the biopharmaceutical industry, collaborating with the regulators, and incorporating market access and using insights early in clinical development.
- **Telehealth:** A key factor contributing to initial misdiagnoses is the shortage of clinical geneticists. Despite an estimated 85% of rare diseases being genetic in origin, there are significant barriers in accessing appropriate genetic counseling. Telehealth has helped break down these barriers. The broad acceptance of telehealth has the potential to change the diagnostic journey for patients through the adoption of telegenetic consultations. A pilot program at Children's National Hospital in Washington, D.C., worked with Microsoft to pioneer the use of telegenetic consultations for patients and, more specifically, for those who are searching for a diagnosis, potentially for a rare disease. Since the program's inception in 2019, the average time a patient would wait to see a clinical geneticist decreased from three to four months to just six to eight days.
- **Regulatory programs:** The FDA is establishing a "Rare Disease Cures Accelerator" program to help support innovation and quality in the drug development pipeline for rare diseases. Through the Accelerator, the FDA is looking to facilitate a cooperative approach and common standardized platforms to better characterize rare diseases, incorporate the patient's perspective in clinical outcome assessment measures, and build clinical trial readiness in the pre-competitive space.

Connections to Support Patients and HCPs

Pharmaceutical companies have an opportunity to embrace new ways of thinking to better meet the most important needs of patients with rare diseases, care givers, and their families.

Their journeys have been exhaustive and fraught with misdiagnoses. They've not been taken seriously, have been bounced through the system, and left struggling for answers.

The rare disease community has earned the right to demand better connections, knowledge, informed communication, and more meaningful relationships with their healthcare providers.

- **When overcoming biases through behavioral sciences,** old habits beat new intentions almost every time; unseating these habits takes disruption. Marketers need to leverage behavioral science strategies to make prescribers more self-aware of their cognitive biases, create better communications, and ultimately drive better results for the brand.
- **Shared decision-making** is a process, one in which clinicians and patients work together to select tests, treatments, management, or support packages, based on clinical evidence and the patient's informed preferences. This process can help drive better choices, alignment, and treatment understanding — a critical set of tools, especially when faced with therapeutic decisions that are life-impacting or life-changing (ie, gene therapy).
- **Enhanced brand storytelling** — the real value of the brand has to be at the heart of all storytelling; in rare diseases, the patient voice and value of what the brand affords them is central to all communications. The goal is to create an emotional connection between the brand science, the HCPs, and the patients in their care. Facts matter, but the "why" behind those facts is the real brand value.

The rare disease patient's journey will continue to face hurdles, but the connection that the collective "we" brings to the table — advocacy, industry, government, academia, and communications agencies — is vital to alleviating some of these obstacles and can be key to helping drive meaningful advancements in the rare disease space. PV