A Challenging Market Dynamic

An estimated **400 million** people worldwide are currently living with **rare diseases**. There are approximately **7,000** different types of **rare diseases** and disorders, with more being discovered every day.

According to the National Institutes of Health Office of Rare Disease Research, approximately 6% of the inquiries made to the Genetic and Rare Diseases Information Center (GARD) are in reference to an undiagnosed disease.

At best, the knowledge base about any individual rare disease is small, fragmented, and often the preserve of a relatively few thought leaders and experts in the field.

Moreover, information that does exist may be spread across a number of language bases and contain markedly different medical, social, and cultural assumptions and judgments.

This extends not only to the nature of the disease, but also to any diagnosis paths, all of which add to the challenges facing any company that is looking to develop a suitable drug or treatment.

Consequently, a far greater emphasis is placed on the role of the individual patient; the patient with a rare disease not only serves as a potential expert in their condition, but also has ongoing involvement and influence in the development of any treatment.

However, the lack of knowledge about a rare disease combined with the sparseness of real-world experience in the field make identifying patients and providing a correct and timely diagnosis of the condition much more difficult. Just as importantly, delayed or repeated misdiagnoses create a separate set of challenges because this not only affects the individual patient in terms of delaying any potential benefits, but it also has a negative impact on those connected to the patient.

An unfortunate reality of the ecosystem of the rare disease patient is that it is characterized by the physical, emotional, and psychological impact that these diseases have, which also influences educational and employment choices made by the family as a whole.

Diagnosis and patient-finding remain the biggest challenge, even after a rare disease drug is approved. Significant effort must be invested to ensure that a sufficient number of patients are identified and diagnosed in order to make use of the treatment; this is complicated by the fact that, for many rare diseases, there is no diagnostic (ICD-10) code that is directly linked to physician reimbursement.

Even when clear patient benefit can be shown and approval has been obtained from relevant health authorities, formulary coverage and patient access present other significant challenges, particularly where current standard of care is the off-label use of generic oral therapies. This is further complicated by yet another challenge for companies in terms of providing patient access.

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Clinical Trials: Big Bets for Uncertain Results

Developing successful rare disease treatments is confounded by difficulties in finding patient samples that are large enough for clinical studies.

Limited disease understanding and complicated pathways to reach clear diagnoses confound the rare disease drug development process. Additionally, defining patient outcomes can be problematic given a lack of comparator benchmarks.

To maximize the chances of success, it is essential to ground the trial design and proof of concept in meaningful terms, not only for the patient but also for all members of the rare disease community. These stakeholders typically include a broad spectrum of physicians, researchers, patient advocacy groups, and governmental organizations.

When it comes to payers, considerable thought needs to be given to generating data that support value in the wider context, where there may be very little known about these patients and their conditions. Because of these challenges, regulatory authorities have adopted a different approach to clinical development, allowing for smaller, nonrandomized studies with endpoints that may not have an evidence base that is as robust as that of more common diseases.

However, this needs to be handled carefully, especially when dealing with payers, as development programs arising from such trials will not have the same extent of data that would be available for other more common conditions, such as diabetes.

To be successful, companies need to be as efficient as possible in the clinical trial participant identification and recruitment process. In practice, reaching and identifying patients can often require individual, country-level resources to help identify participants for clinical trials.

Regional and local “boots on the ground” experts may be the only ones who are able to piece together the puzzle by conducting chart reviews and constructing diagnostic “analogs” for patients who may be suffering from the rare disease, but who are not yet diagnosed.

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While patient registries are starting to become the norm for more well-known diseases, it’s the local thought leaders and patient support organizations that can help companies find potential participants for rare disease clinical studies. This is especially true for ultra-rare conditions that are particularly difficult to diagnose, are currently without viable treatments, and lacking strong advocacy networks.
The Patient Journey: Uncharted Pathways

Understanding the full impact of a **rare disease** on the patient, in its **widest** possible context, is central to developing and implementing a viable strategy that reaches all stakeholders who are **impacted** by the disease.

Gaining a clear picture of the entire patient journey, beginning with characterizing the initial impact of the disease and then mapping the pathway to diagnosis, is essential to identifying the critical challenges that patients and their families face while on the road to discovering and receiving effective treatment and care.

Mapping the rare disease patient journey requires enlisting perspectives from all of the various stakeholders involved, including caregivers, health care providers (HCPs), patient advocacy groups, and payers. It also involves gaining a deeper understanding of how the various stakeholders are connected and how they interact with each other, because each individual stakeholder may potentially hold information that unlocks answers elsewhere.

Most physicians will never see a patient with a rare disease. As a consequence, patients often describe the experience of getting “lost” for many years without access to expert care, going from one HCP to the next, each HCP addressing a single symptom but unable to put the full puzzle together to reach the proper diagnosis.

Inefficiency in getting a diagnosis is obviously a barrier to getting timely treatment. As a rare disease progresses and a patient’s health deteriorates, the condition’s impact multiplies, increasing the burden on patients, caregivers, and health care systems exponentially. Any delays in diagnosis can also mean lost revenue for the company as a result of reduced potential benefits of any treatment.

Before the advent of the internet, patients with rare and undiagnosed diseases were often unable to find any information to explain their symptoms. With the explosion of available health information (both good and bad), patients with a rare disease are now able to educate themselves about their condition, symptoms and pathway to diagnosis, which means that deep insights can be obtained from them to guide the treatment development process.

Recognizing how a rare disease impacts the patient from a holistic sense helps to identify specific pivot-points that are critical to diagnosis, treatment, and care. It also helps to hone strategies in terms of identifying which stakeholders to engage, when to engage them, and how to be most efficient with the limited resources available. This enables companies to leverage the power of their network to maximize perceived and actual value.

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A New Planning Reality

Once clinical trials are underway and the patient journey is defined, the next strategic challenge to overcome is to bring any resulting product to market in a timely fashion. However, when it comes to the world of rare diseases, this invariably involves having to deal with a whole new planning reality.

As with other pharmaceutical products, early market preparation for an orphan drug is essential in order to build a foundation for the real-life impact of the disease; however, given the shorter timelines associated with gaining orphan drug status, the time to market is accelerated, which further confounds the planning process.

Creating a new market or completely reshaping an existing one necessitates a thoughtful, focused, and targeted launch plan scenario. Even the smallest pharma company is likely to be the largest and most financially invested organization involved in the provision of any new rare disease therapy; therefore, it also potentially carries the most responsibility for the degree of success of the outcome. This is especially the case when the impact extends beyond the immediate quality of life for the patient and into the wider patient ecosystem.

The introduction of a new asset can completely change the treatment paradigm, which can lead to a need for higher prices given the small number of patients being treated; this is something that the market may not readily accept.

A successful launch planning scenario for rare disease treatment ultimately depends upon gaining clear, accurate insights and understanding of all stakeholders involved. At a macro level, this involves the implementation of a robust market research initiative to characterize the patient and caregiver burden in its widest sense, and also involves understanding the needs and thought process of the experts, specialists, treaters, HCPs, payers, and patient advocacy/support organizations.

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This approach is essential to guide the development of a compelling story for the entire life cycle of the asset. Each stakeholder has a voice that needs to be heard, not only relating to the introduction of the treatment, but also in terms of helping to guide effective, economic, and efficient tactical planning throughout the entire patient journey.

Alignment of stakeholder perspectives at a micro level involves the creation of educational resources about the disease, its progression, and the impact of any treatment over the entire patient journey.

Comprehensive scientific communications and patient education are especially critical since comorbidities are common in most rare disease patients. With only a very small number of patients recruited per site, sometimes only 1 or 2 patients, there is a further challenge in generating centralized, unified communications materials that are consistent, can be applied globally as well as locally, and are both culturally and linguistically appropriate.
The Power of Teamwork in Building Commercial Success

Partly because of the **significant challenges** highlighted above, rare disease clinical development and commercialization teams are lean. Where teams do exist, individuals are often juggling **multiple responsibilities**.

Launching a rare disease asset necessitates the development of a successful clinical, commercial, and regulatory strategy that can effectively and efficiently find afflicted patients and communicate the evidence to the right stakeholders in a relevant, compelling, and timely way. In order to succeed, this requires a holistic, integrated approach that includes the following:

- Insightful research to characterize the patient journey, define the buying process, identify key pivot-points to inform the strategic planning process and guide the development of a brand-positioning strategy
- High-quality consulting to develop and hone the commercialization strategy, including market opportunity assessment, go-to-market/commercial model design, organization model capability analysis and design, forecasting, potential partnering decisions, detailed rNPV analysis, and deal structuring
- Comprehensive strategic communications and content development support to drive targeted, focused tactical planning and delivery, including core scientific platform/lexicon development, expert engagement, and advisor initiatives
- Disease awareness and patient/caregiver support initiatives, including advocacy groups and communications programming

Developing therapies for rare diseases can be incredibly rewarding because of the strong partnerships that can be built between industry, physicians, and patients. However, the successful development and commercialization of these assets requires greater collaboration, more innovative thinking, and alternative approaches that are not typically needed for other more mainstream diseases.

Therefore, it is imperative that the right partners are engaged to support the process—those who can apply their expertise and innovative thinking to foster effective collaboration among all involved stakeholders, and develop and implement a well-honed and tightly integrated strategy and plan.

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For more information on how to **unlock** the potential of **rare disease assets**, contact the Cello Health team.

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