

Building Relationships and Value with Rare Diseases

- ▶ Aided by the Orphan Drug Act of 1983, biotech and pharma companies have sought development treatments for the approximately 7,000 rare diseases that have been identified.

There is growing commitment across the industry to improve the lives of the 350 million people living with a rare disease across the globe. Since 2013, 60% of the drugs approved by the FDA under the Breakthrough Therapy Designation program have been indicated for rare diseases. Nevertheless, only 5% of rare diseases have an approved treatment, according to Debbie Drell, director of membership services for the National Organization for Rare Disorders (NORD).

As patient organizations around the world prepare for the 11th Rare Disease Day on Feb. 28, 2018, the importance of the relationship between the industry and patients, through advocacy groups, is increasingly apparent. The focus of the 2018 Rare Disease Day is research, with a dual recognition that patients need researchers to develop treatments and cures while researchers need patients to participate in trials and ensure their research is meaningful.

Trends in Rare Diseases

- ▶ Median cost per patient differential is 5.5 times higher for orphan drugs compared with non-orphan drugs
- ▶ Celgene is set to climb to No. 1 position in orphan drug sales by 2022
- ▶ Shire is expected to be largest company by sales in the orphan non-oncology space by 2022
- ▶ AstraZeneca, AbbVie, and Johnson & Johnson set to climb the orphan drug sales ranking table
- ▶ Orphan drugs are forecast to account for 55% of the cumulative value of the European pipeline by 2022

Source: EvaluatePharma, Orphan Drug Report 2017

To continue the advances made to date in bringing breakthrough therapies to treat rare diseases to market, companies must address every aspect of the life cycle: conducting research, working with regulatory authorities, and developing marketing campaigns.

Advancing Research: Recruitment and Retention

Rare diseases add complexity to the clinical trial process. When addressing a disease that affects a small number of patients, companies need to carefully consider site selection, location, and the needs of the patient — from financial, to travel, to emotional support.

To mitigate some of these issues, Thomas

Schall, Ph.D., president and CEO of ChemoCentryx, which is primarily focused on orphan and rare diseases, says the company looks for centers that have experience in treating patients with the rare disease and have had experience with clinical trials.

Companies conducting clinical trials for rare diseases need to consider where patients live, where their healthcare practitioners are, and how a clinical trial will affect their daily lives. Travel support, telemedicine, and other strategies can help to make the trial less burdensome for patients.

Site planning is crucial, to ensure sites selected have patients in the disease population and the investigator is seeing and treating patients with the disease being investigated.

Patient advocacy groups are important

Rare Disease Day

The main objective of Rare Disease Day is to raise awareness among the general public and decision-makers about rare diseases and their impact on patients' lives.

The campaign targets primarily the general public and seeks to raise awareness among policy makers, public authorities, industry representatives, researchers, health professionals, and anyone who has a genuine interest in rare diseases.

Building awareness of rare diseases is so important because 1 in 20 people will live with a rare disease at some point in their life. Despite this, there is no cure for the majority of rare diseases and many go undiagnosed.

Rare Disease Day events are organized by hundreds of patient organizations all



RARE DISEASE DAY®

over the world that work on a local and national level to raise awareness for the rare disease community in their countries.

Since Rare Disease Day was first launched by EURORDIS and its

Council of National Alliances in 2008, thousands of events have taken place throughout the world reaching hundreds of thousands of people and resulting in a great deal of media coverage.

For more information about the thousands of events happening around the world on the last day of February, visit rarediseaseday.org. If you are planning an event, register your event details on the Post Your Event page to get your event listed on the site at rarediseaseday.org.

Big pharma companies are starting to dominate the orphan drug market with seven of the top 10 companies by orphan drug sales being global industry players.

players in clinical trial planning, recruitment, and retention, for example helping to enroll more diverse patient populations, helping to define meaningful clinical endpoints, assisting in the design of patient reported outcomes, and developing study materials that are written to the right level.

Sponsors and trial sites also need to work with patient organizations to better understand the patient's point of view.

Regulatory Hurdles

Experts in the field note that the FDA has been supportive of companies developing drugs for rare diseases and is offering financial support, such as the FDA Orphan Products Clinical Trials Grants Program and waiver of the Prescription Drug User Fee Act (PDUFA) filing fee.

After receiving orphan drug designation, the FDA also offers a variety of regulatory tools to assist orphan drug licensing such as priority review, fast-track, breakthrough, and accelerated approval pathways. In addition, the FDA's Orphan Drug Modernization Plan is a new initiative designed to streamline the FDA's review of Orphan Drug Designation requests, as well as help the agency manage its workload.

Furthermore, the FDA and EMA have been collaborating since 2016 to improve information sharing on various aspects with regard to the development and evaluation of medicines for rare diseases.

Nevertheless, requirements are rigorous, which can present challenges for companies without prior experience in rare diseases, and can lead to delays and added costs.

According to Jay Barth, M.D., chief medical officer at Amicus, the regulatory frameworks for reviewing data and deciding on approvals were not designed specifically for rare diseases. Companies therefore need to consider

having specific pathways or specialized reviewers for rare diseases.

Rare disease companies must also be ready to address reimbursement given the increased costs for payers. This requires companies to emphasize and prioritize proof of clinical and economic value, and provide real-world evidence of successful patient outcomes. With statistics showing the average annual cost per patient for orphan drugs exceeding \$135,000, pricing and reimbursement are critical elements in a rare disease commercialization strategy. Discussions with payers and providers must focus on enhancing understanding of the therapeutic area and highlighting product value, backed by outcomes data.

Product Delivery

Developing a rare disease product and maneuvering the regulatory landscape are two key aspects in bringing a product to market. Equally important is ensuring the therapy gets to geographically dispersed patients in the dose needed and when it is required.

According to Paul Testa of Shire, because rare disease products are typically of much

smaller quantities, it's often necessary to support a make-to-order supply chain model and production approach.

Companies require a flexible approach to managing the supply chain in order to adapt manufacturing capacities to match the supply versus demand.

Cold chain logistics are also crucial to manage temperature-controlled products, especially when transported through climates prone to extreme weather conditions. Given that most rare disease products are manufactured in small quantities and at high cost, spoilage can be a major problem for companies.

A Different Market

When it comes to marketing rare disease products, patient-centricity is key. Patient advocacy groups have typically been involved from the start, often spurring research and development, and building relationships with advocacy groups can help companies to connect with patients.

In addition, patients and their caregivers need to be included in the marketing approach to help them continue to learn about their



Because Rare Is Different

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**Rare Disease
Strategy and Innovation**

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disease. And given that so many patients with rare diseases are children, experts note that caregivers seek out information, so digital campaigns can be highly effective.

Rare diseases companies can expect to have

a direct relationship with patients to help address gaps in care, deal with stress and depression, and ensure a support network.

Some rare disease biopharmaceutical companies have a patient advocate as part of the entire

process — from development through marketing. For example, Amicus has a chief patient advocate who is responsible for advocating on behalf of patients in the community as well as internally.

The role of the physician is just as critical

EXECUTIVE VIEWPOINTS



Laurie Bartolomeo

Executive VP, Creative Director
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DEVELOPMENT PASSION

Often based in groundbreaking scientific discovery, orphan drugs face extensive research and validation challenges, and consist of tiny patient populations — that are difficult to find. Time and financial commitments are massive, with averages of 10 to 20 years and hundreds of millions of dollars required for an orphan drug to make it to market. Most of all, individuals involved in the development and commercialization of orphan drugs require tremendous passion and devotion —and maybe a bit of luck — to successfully journey from discovery to development.

PATIENT GROUP PARTNERS

In the world of rare disease, partnering with patient advocacy groups is a must. Because advocacy groups have similar goals to those of drug companies — finding patients, aiding in earlier diagnosis, facilitating access to treatment, and providing ongoing lifestyle support — an open and trusting relationship can be mutually beneficial for everyone involved, particularly the patients both groups serve.



Cheryl Evans

Senior VP of Clinical & Medical Operations
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RARE DISEASE RESEARCH REQUIRES FLEXIBLE CLINICAL STUDY TEAMS

From an operational perspective, one major challenge of conducting rare disease research is identifying and referring patients to research sites, versus the traditional method of identifying sites when recruiting patients. This requires much more flexibility from sponsor and clinical study teams, since meeting timelines can be challenging in this scenario, especially when working with research-naïve sites.

SHARING EXPERIENCES THROUGH STORYTELLING

Companies can work with rare disease patient advocacy groups by listening to the needs of their members and by helping people impacted by rare diseases share their stories. While research organizations are concerned with good clinical practices, regulations, and protocol specifications, patients and caregivers are motivated by telling their stories and listening to the stories of people who share their experiences.



Wolf Gallwitz, Ph.D.

Chief Medical Officer
Razorfish Health

COMPLEXITIES WITH RARE DISEASE DRUG DEVELOPMENT

Three factors stand out that must be addressed to ensure success. Factor No. 1: The Target. Quality, basic medical

research must identify unique and viable targets that have the strong potential to address the unmet need. Factor No. 2: The Patient. We need to identify the right patient population for treatment. Factor No. 3: Regulatory. FDA/EMA and sponsor agreement to the study design, clinical endpoints, inclusion/exclusion criteria, and proper timing of treatment intervention are critical to success.



David Schneider

Senior Director, Strategic Account Management
RxCrossroads

ADVOCACY GROUPS ARE ENGAGEMENT CHANNELS

Manufacturers can provide advocacy groups with disease state information that will help set expectations for patients along their treatment journey. Advocacy groups often serve as an important engagement channel for local activities, disease specific educational forums, as well as fundraisers and each of these serves as a partnering opportunity. Patients can connect with other patients who may be facing similar challenges, gain a better understanding of symptoms, learn tips to manage their symptoms, recognize signs of disease progression, and learn strategies for partnering with their healthcare team. Manufacturers can learn ways to connect with patients, family members, and caregivers and these groups create an opportunity for more targeted connectivity to each of these stakeholders.

in rare diseases but mass marketing fails to resonate in this market, and instead companies need to consider disease awareness initiatives to help specialty healthcare professionals better understand and recognize rare diseases.

As advocacy groups, patients, and companies prepare for the 2018 Rare Disease Day, the development of new therapies and getting them to patients in need will be top of mind. As the organizers of the day have emphasized,

Rare Disease Day 2018 is an opportunity for all stakeholders to be part of a global call on policymakers, researchers, companies, and healthcare professionals to involve patients in rare disease research. 

EXECUTIVE VIEWPOINTS

UTILIZATION MANAGEMENT REQUIREMENTS

Pricing is at the forefront of many discussions for politicians, analysts, and advocacy organizations. With many drugs gaining orphan designation in an attempt to serve a smaller population, it is likely that the price point for these particular therapies will remain high. Payers are likely to implement utilization management requirements in the orphan disease space in order to manage costs. In addition to this, other access barriers in the form of high out-of-pocket costs will create a necessity for patient-support services to provide assistance to patients needing to gain access to therapies treating their rare disease condition.



Matt Silver

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WORKING WITH RARE DISEASE PATIENT ADVOCACY ORGANIZATIONS

Because patient advocacy organizations are most often run by people directly impacted by rare disease and because these people may feel as though they are the ones primarily driving change in their area, companies must honor advocates' expertise and recognize them as equal stakeholders. Strong relationships can emerge when advocacy organizations are offered transparent and dynamic partnerships built around the concept — and spirit —

of co-creation. Pharma is uniquely suited to help drive development of much needed services, education, and tools but must do so in a way that integrates the advocates' expertise throughout the process.



Clareece West

VP and General Manager
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RARE DISEASE DRUG DEVELOPMENT

Rare diseases by definition affect limited patient populations, and historically have struggled to attract significant pharmaceutical investment. The development of any drug is complex, but the task is especially difficult for rare diseases due to the small number of patients available to participate in trials. Resource constraint also can be a significant challenge for smaller companies developing rare disease therapies. Even with positive clinical data, they may struggle to access the regulatory and commercial expertise they need to get their drug approved and successfully launched.

PATIENT ADVOCACY RELATIONSHIPS

Patient advocacy groups, made of up patients and their families, can play a critical role in advancing the objectives of a rare disease drug, including helping with recruitment for clinical trials, generating disease awareness, raising funds for clinical studies, supporting payer discussions, and helping with outcome registries. However, these relationships take time to build. Rare disease developers should reach out to

advocacy groups early in the process, and appoint members of their team to be responsible for nurturing these relationships and building trust with the advocacy groups over time.



Wendy White

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PHARMA'S ROLE IN RARE DISEASE

Companies cannot count on many of the same resources that are readily available in larger disease areas and frequently need to take on an organizing role for patients. Patient participation is critical when there is less existing research data, natural histories, and/or patient support. More than 70% of rare disease areas have no organized patient groups and where there is one, there are frequently many and they don't get along.

PATIENT ADVOCACY PARTNERS

Patient advocacy groups expect to be treated as partners in their own healthcare. As such, companies need to proactively engage with patients as early in the process as possible and communicate on a regular basis, even when there is no new news to share. Patients expect companies to be transparent with issues that matter and to be authentic participants in their communities. They also expect companies to share their sense of urgency.