

Successful launches in rare diseases

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Patients affected by rare diseases often find there are no treatments for their condition. Of 7,000 known diseases in this category, 95 percent – referred to as orphan diseases – do not have a single FDA-approved drug treatment. Rare diseases by definition affect a small number of patients, and they historically have not attracted significant pharmaceutical investment.¹

Recently, though, large pharmaceutical companies have begun to pay more attention to rare diseases, drawn by government incentives and the greater likelihood that treatments for what are often life-threatening or severely debilitating diseases will be successful. The sidebar “Government incentives” describes some of the measures governments and regulators have introduced to encourage innovation in diseases with low prevalence² and high unmet need.

Government incentives

- **Financial incentives.** Tax credits and R&D grants have been made available, and there are waivers for regulatory fees.
- **A reduction in the number of patients needed for trials.** In the United States, orphan drugs require a median of 538 participants in Phase III trials compared to a median of 1,491 participants for non-orphan drug trials.¹
- **Accelerated development and market access.** On average, clinical review times have been shortened by 18 months in the United States and regulatory review periods by eight months.
- **Extended exclusivity periods.** Orphan drugs are allowed seven years of market exclusivity in the United States, compared to five years for non-orphan drugs.³

The effect has been that, in 2015, 45 novel rare disease therapies were approved by the FDA’s Center for Drug Evaluation and Research, significantly more than the average of 28 approved during each of the previous nine years.⁴ With sales of orphan drugs forecasted to achieve compound annual growth of 10.5 percent a year⁵ to account for 19 percent of worldwide prescription sales at a value of \$176 billion by 2020, and with typically low commercialization costs, rare disease therapies are becoming increasingly attractive and are expected to further bring transformational patient benefits.

How pharmaceutical companies with new rare disease drugs launch their products will be crucial to their success, however. For while all drug launches are complex, launches of rare disease treatments are particularly so. Usually, when a large company introduces such a treatment, it is entering the relevant therapeutic area for the first time. It is therefore likely to lack both expertise in the disease and in-depth understanding of the health ecosystem and of patients’ experience of the disease. Because the condition is rare, the launch team will have few, if any, analogs from which to draw lessons. And because the company is likely to have bought the drug from a small biotech company at a late stage of development, it might allow too little time to prepare for its launch.

1 Source: EvaluatePharma Orphan Drug Report, 2014

2 Defined as occurring in fewer than five people in every 10,000 in the European Union, and in fewer than seven people in every 10,000 – or 200,000 of the total population – in the United States

3 Source: BioMedTracker Orphan Drugs Report, 2013

4 Source: “2015: Another Strong Year for Patients in Need of New Drug Therapies”, FDA Voice, January 4, 2016

5 Almost twice the rate of the overall prescription market, excluding generics

To be successful, the launch of a rare disease treatment needs a different approach from the standard launch framework. This paper explains why, and describes the hallmarks of success.

FOUR STRATEGIC PILLARS FOR A SUCCESSFUL RARE DISEASE DRUG LAUNCH

Our experience suggests that companies that launch rare disease treatments successfully excel in four areas. They show great commitment to the rare disease community, whose support is key. They use innovative methods to identify patients who need treatment. They take a highly tactical approach to patient access. And they help patients and their caregivers navigate a healthcare system not usually geared to supporting those with rare diseases. These pillars might be in place for a few launch archetypes, such as specialized oncology drugs, but the level of commitment and the tactics and capabilities needed to launch a rare disease treatment are of a different order.

Commitment to the rare disease community

Many pharmaceutical companies underestimate how hard it is to generate the insights upon which the successful launch of a drug for a rare disease depends, when so few people suffer from the disease and so few other stakeholders are familiar with it. What is the patient's experience from first noticing symptoms to diagnosis? How many and which types of physicians might they see in search of a treatment? How many treatment centers are there, and where?



This kind of knowledge of the patient ecosystem is crucial, as it will inform every aspect of the launch: the search for patients and prescribers, securing of market access, and ongoing support of patients who ultimately undergo treatment. Those companies that have successfully launched rare disease drugs have discovered the vital role that the rare disease community – patients

and their families,

advocacy groups, and a small number of therapeutic area experts (TAEs) – plays in generating these insights. In addition, it is this community that will help to build awareness of the disease, including among payors. Its members are therefore crucial partners in the launch of a drug, and pharmaceutical companies must be genuinely committed to them to meet their needs.

Launch teams need to invest significant time with patients and caregivers early in the launch process to understand their journey and the barriers they might face in accessing treatment. This in itself can be a sign of commitment, but more can be done. For example, setting up a social media platform can prove valuable to patients who are geographically scattered, enabling them to share experiences and creating a sense of solidarity. Such a site is also a channel for dispersing information about an upcoming launch.

Advocacy groups, on which patients often rely as their primary source of clinical information, are equally important partners. In the absence of market research, they can be engaged to help in the development of patient databases and surveys of patients' needs, the design of clinical trials, and in finding and enrolling patients for those trials – a task that can be

extremely challenging even if only a few dozen patients are required. In return, companies can show their commitment to advocacy groups by providing logistical support for fund-raising and awareness-raising activities, or by financing studies that go beyond drug approval requirements – Phase IIIb and IV studies, ISTs, and outcome registries.

TAEs too are valuable, especially in building awareness of a disease. For many physicians, dedicating time and attention to a specific rare disease is a major career choice, and companies can back them, for instance, by involving them as investigators in clinical trials.

Companies will of course need the ability to piece together the various insights they glean in order to formulate a launch plan; there is no launch blueprint. Often, it falls to senior launch leaders to “join the dots,” and this will influence the skills to be embedded in the launch team.



Patient group identification

Identifying the largest possible patient group is a lengthy task. Beyond building relationships with diagnosed individuals, advocacy groups, and TAEs, how should pharmaceutical companies go about it?



Their approach will depend on the disease. For rare diseases with low diagnostic rates, companies can work with advocacy groups to distribute free diagnostic tests. In the case of Fabry’s disease, for example, Sanofi Genzyme partnered with the Muscular Dystrophy Association in the United States to supply laboratories and physicians with testing kits.⁶ Other tactics include hosting events and mounting digital campaigns targeted at educating healthcare providers.

Companies need to learn how to use every piece of information that might help them to identify patients who experience many of the typical symptoms of the disease but have not been diagnosed. Sufferers of rare diseases might by definition leave no digital trace in the form of claims codes, but they do have a medical history. Algorithms can be devised to search for de-identified patients’ claims codes associated with a given disease. For instance, patients suffering from the genetic disorder Gaucher disease might experience fatigue, a distended abdomen, low appetite, bruising, and stunted growth, and hence have accumulated claims codes for splenomegaly, hepatomegaly, anemia, or thrombocytopenia. Armed with this statistical analysis, a company’s field force can focus its visits on physicians with the highest probability of having a patient with the specified rare disease (while those with a lower probability of having a patient suffering from it can be approached through less expensive digital channels). As more and more de-identified patient data is gathered, the algorithm can be refined and improved to target more physicians, more accurately.⁷

6 Source: www.pompe.com/healthcare-professionals/diagnosis-testing/pompe-testing-program.aspx

7 The extent to which pharmaceutical companies can access claims data, even de-identified patient data, varies by country. Launch teams should determine what data they are permitted to access in each country.

Patient access



Navigating patient access to rare disease therapies, key to the success of such drugs, is challenging because of their high cost. In addition to cultivating partnerships with advocacy groups and TAEs, there are three ways in which pharmaceutical companies can work to ensure patient access: by devising early access programs, minimizing the time between a patient's diagnosis and treatment start, and helping to close potential funding gaps.

Devising early access programs to enable commercial use. These programs take various forms. "Experimental access" gives free access to study patients for two to three years prior to a treatment being granted approval in any given country. This can be extended to life even if no commercial access is granted. "Named patient access" offers early access for patients prior to a drug's registration. And "humanitarian access" gives free access for patients in markets where a treatment is not commercially available, which will stop only if commercial access is granted.

Which countries to prioritize for early access will be shaped by the number of patients requiring treatment. But the likelihood of achieving sustainable patient access also counts, influenced by the regulatory system, the availability of alternative funding sources such as private donors, and a program's potential to act as a catalyst to bring about reimbursed access for a broader patient population. Pharmaceutical companies' distribution channels will also be a deciding factor. The particular characteristics of each country will determine which form of early access program is appropriate.

Minimizing the time between diagnosis and treatment start. Preparing the application for coverage of treatment fees can require a considerable effort from the patient, particularly in the United States and some emerging markets. Companies can assist patients with the paperwork and, if coverage is denied, with the follow-up process. In some countries, companies will have a department dedicated to giving this support.

Helping to close potential funding gaps. Patients' access to rare disease therapies can be hindered by high treatment cost or the lack of specialized centers of care. To close funding gaps and facilitate specialized treatment centers' setup and maintenance, companies might partner with third parties such as governments and private donors.



Patient and caregivers' support



Once started on therapy, patients and their caregivers must be given sustained support to ensure adherence to the treatment. Among sufferers of rare diseases we have observed a particularly high rate of discontinuation as a result of both clinical and psychological factors.

There are several ways pharmaceutical companies can help enhance patient experience and avoid discontinuation. These include providing nursing services to educate patients on how to administer a drug and manage its side-effects, and undertaking to update treating physicians on their patients' condition.

Along with social media groups designed to enable patients to exchange information and share concerns, most successful companies also set up help lines. In addition, they might offer educational resources for patients to learn about their disease and treatment.

A company can provide these support services internally or externally through advocacy groups or other third-party providers, depending on cost considerations and regulatory constraints (a direct interface with the patient is permitted in the United States but usually not in Europe, for example). We found that when permitted, providing these services internally allows for a more consistent patient and provider experience. It is important that companies monitor and refine support services continuously, as once a drug has been launched, much can be learned from patients' experience of their treatment, including whether and why they might consider discontinuing it.

OPERATIONALIZING THE RARE DISEASE TREATMENT LAUNCH TEAM

When it is clear what needs to be done, the question becomes how to deliver it. Much hinges on the launch team, the composition and deployment of which will be quite different from pharmaceutical companies' standard model.

Embed a culture of cross-functional collaboration



An unusually high level of collaboration is required between members of a launch team for a rare disease treatment, for several reasons. First, there are only a small number of TAEs for most rare diseases – in some EU countries there might be only a handful. This means that if the medical, access, and commercial members of the team operate independently, they risk inundating TAEs with multiple approaches and conveying inconsistent messages. A thoughtful, coordinated strategy is required to identify and develop relationships with TAEs and advocacy groups. Cross-functional collaboration is equally important in order to join the dots between the pieces of information accrued by medical and commercial field representatives and thus to generate the patient ecosystem insights required to craft the launch strategy.

One way to achieve the required level of coordination is to put in place a centralized communication system that tracks team members' interactions with the various stakeholders, all the various launch activities, and any key insights. Some companies enforce collaboration and coordination through appropriate incentives.

Another way to avoid a silo mentality and enforce collaboration is to make the team roles themselves cross-functional. Instead of appointing a conventional sales representative, for example, a “field entrepreneur” can be assigned to manage a given territory. He or she will develop and execute a multi-stakeholder plan that includes building and maintaining relationships with physicians and advocacy groups, engaging in discussions with local authorities and payors, and developing patient-finding algorithms. This position requires excellent strategic and commercial capabilities, knowledge of market access and public affairs, and scientific expertise.

Similarly, conventional medical science liaisons can be replaced by “therapeutic area expert developers” who not only build and maintain relationships with TAEs and are able to respond to medical questions raised by prescribers, but also collect insights from the field that are shared with field entrepreneurs and other team members to shape the launch plan. Medical and strategic capabilities are therefore required. The sidebar “Cross-functional roles support a successful launch” describes the operational roles within a high-performing launch team for a rare disease drug.

Cross-functional roles support a successful launch

- **Field entrepreneur.** Field representative with enhanced strategic and commercial capabilities, scientific expertise, as well as knowledge of market access and public affairs; autonomously manages a given territory, develops and executes patient-finding algorithms, and engages physicians (*clinical discussions limited to label and published data*), advocacy groups, payors, and other stakeholders
- **Therapeutic area expert developer.** Field representative with enhanced medical and strategic capabilities, mainly in charge of engaging and supporting TAEs and informing the launch team’s strategic plan with insights gathered from the field
- **Rare disease analytics and marketing expert.** Generates patient insights, devises marketing materials, and suggests improvements to patient-finding and support protocols based on patient data analytics; needs enhanced strategic capabilities as well as analytical skills
- **Policy and access expert.** Sets up market access strategy, prepares negotiations with payors and generates evidence plan and medical or scientific support, ensures payors are well informed about the disease, the drug, and the patient ecosystem, and engages in discussions with authorities about the regulatory framework; needs medical knowledge as well as market access and public affairs capabilities
- **Patient support provider.** Supports patients in preparing insurance coverage application, encourages adherence to the drug regimen, and improves patient-support protocols based on analytics and marketing expert insights; needs strategic and analytical skills as well as patient support capabilities; this role applies mainly in the United States
- **End-to-end third-party manager.** Manages third-party patient support providers in countries where regulators do not permit a direct interface with patients (typically in Europe); needs patient support and compliance knowledge as well as third-party management capabilities

Size launch teams accurately and deploy them early



As a rule, launch teams for rare disease drugs are smaller than those for more conventional treatments, and tend to be allocated fewer resources. Given the challenges associated with finding and supporting patients, developing insights, securing access, and generating real-world evidence, though, they arguably have more to accomplish. To use their resources as efficiently as possible, therefore, successful companies take great care in deciding the size of a team and how it is deployed.

Exactly how many people are needed will depend on certain factors in five areas: the disease, the regulation, the patient journey, the market access situation, and the competition level. For example, finding patients with a particular disease will require fewer resources if there is a straightforward genetic test for it that physicians can conduct. But more resources will be needed if diagnosis is harder and physicians need to be educated on how to make it. Likewise if a disease has especially strong side-effects that require the implementation of a patient support program. In addition, the more treatment centers there are and the more decentralized they are, the bigger the launch team must be. In countries where early access programs are appropriate, dedicated medical capacity will be necessary early in the launch process.

What is certain is that the field entrepreneur for a rare disease will be responsible for a larger sales territory than the sales representative for a drug for a more prevalent disease. Typically, a field entrepreneur for a rare disease treatment in the United States is responsible for a sales territory worth between USD 25 million and USD 30 million. For a specialty drug (not for a rare disease), that figure is USD 5 million to USD 10 million.⁸ In the biggest European countries – Germany, France, the United Kingdom, Spain, and Italy – a launch team of between four and eight people with one or two field entrepreneurs is often sufficient to ensure a successful launch.

In respect of deployment, large pharmaceutical companies typically invest in building field capabilities for a standard drug launch between six and twelve months in advance at country level. Staffing for the launch of a rare disease treatment has to begin earlier, although not everyone has to start at the same time. The medical field force – that is, the therapeutic area expert developers in the cross-functional team – begin first, 15 to 18 months before launch, in order to engage with TAEs and advocacy groups and build awareness of the drug. Policy and access shapers usually start three months later to ensure they have enough time to engage with payors. The rare disease analytics and marketing experts kick off three months after that to generate detailed insights into the local patient ecosystem, while the field entrepreneurs can be deployed three to six months before the launch, just as sales representatives are for a standard launch.

In Europe, companies should take care not to duplicate the entire team in each country. Rather, resources should be shared unless specific, country-related activities need to be undertaken. Field entrepreneurs, for instance, are typically anchored at country level (and accounted for within the country P&L) in large and mid-sized EU affiliates, as they will need to engage with local stakeholders. But other launch roles that do not require specific country

⁸ Source: Expert interviews

knowledge, such as an understanding of local regulation or local language skills, can be shared across countries, even when covering large and mid-sized countries. Small countries are mainly covered through regional hubs, whatever the role.

A further organizational best practice that helps reap economies of scale is the building of regional centers of excellence in areas such as market analytics and supply management. Their role is to build knowledge and share insights, and hence improve capabilities.



Excel at generating real-world evidence



Given the typically high price of a rare disease drug, companies often struggle to win rapid market access, particularly in Europe. Payors frequently wish to see evidence of a drug's value beyond the data packages usually used to achieve market authorizations, often because of the low number of patients available for Phase III studies. Pharmaceutical companies which are successful at launching rare disease treatments therefore put significantly more resources into generating evidence in the real world for several years in order to strengthen the case they put to payors, often securing sustainable patient access in Europe within two or three years of European Medicines Agency approval.

The process for generating evidence is in principle straightforward. Companies first define the value of the treatment, decide what arguments are needed to support their definition of value, determine what data is needed to support the arguments, and design registry protocols, Phase IV studies, observational studies, and other vehicles to generate the data. To achieve this, an exacting level of operational excellence involving fluid and compliant collaboration between the medical, access, and commercial functions is needed.

Studies need to be devised with care if they are to yield high-quality data. Any failings in design might not become apparent for several years, especially if companies decide to delegate studies to contract research organizations. Many practicalities need to be taken into consideration to make the process work. Is the data input interface user-friendly? Are healthcare practitioners able to observe in real life the data the protocol is asking for? Are contracts with third parties structured so that incentives for high-quality data delivery across many years are aligned? And are the third parties charging a competitive rate?



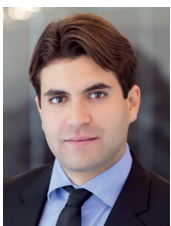
Devising a launch for a rare disease treatment does not necessarily come easily even to a large, efficient pharmaceutical company, as it is likely to challenge the status quo with a new approach and processes in the cause of relatively small patient populations. Companies that have launched rare disease treatments successfully help others to understand where best practice lies. Companies aspiring to emulate this success and help solve hard medical problems for patients should scrutinize their capabilities, their highly tuned medical, access, and commercial operating models, their thinking on organizational structures, and their resource levels – and learn fast.

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