INSIGHTS

Conjoining Six Spokes of 'Orphan Wheel'

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Conjoining Six Spokes of 'Orphan Wheel'

The experience of developing an orphan drug is unique to each pharmaceutical company. In this note, our research experts explain the nuances of developing drugs to treat rare diseases and provide a positive spin on the '6 spokes of the orphan drug development wheel'.

The pharmaceutical industry is moving beyond the conventional and developing drugs for rare diseases (termed 'orphan' drugs), pursuing a significant market opportunity.

According to Evaluate report (2017), orphan drugs are estimated to be the fastest-growing segment in the pharmaceutical industry. Global orphan drug sales is forecasted to reach USD 209bn in 2022 (growing at a CAGR of 11.1% from 2017 to 2022), approximately double growth in the global prescription market (forecasted to grow at a CAGR of 5.3% from 2017 to 2022). Orphan drugs are also forecasted to constitute 21.4% of global prescription drug sales by 2022 (excluding generics).

The population at risk is small for each indication but is exposed to high risk due to the large number of undiagnosed or misdiagnosed cases, and limited treatment options. This 'orphaned', high-risk population comprises about 400m patients globally, who are affected by about 7,000 types of rare diseases and disorders. Statistics indicate that 'rare' diseases are becoming the new normal, with rising incidence.

What has been done so far?

Regulatory frameworks have evolved, with more than 600 orphan drugs approved in the US since 1983, 250+ in Japan since 1994 and 130+ in the EU since 2001. Of course, the evolution of laws has varied by region, the US, EU, and Japan being the more established markets and others that have followed suit.

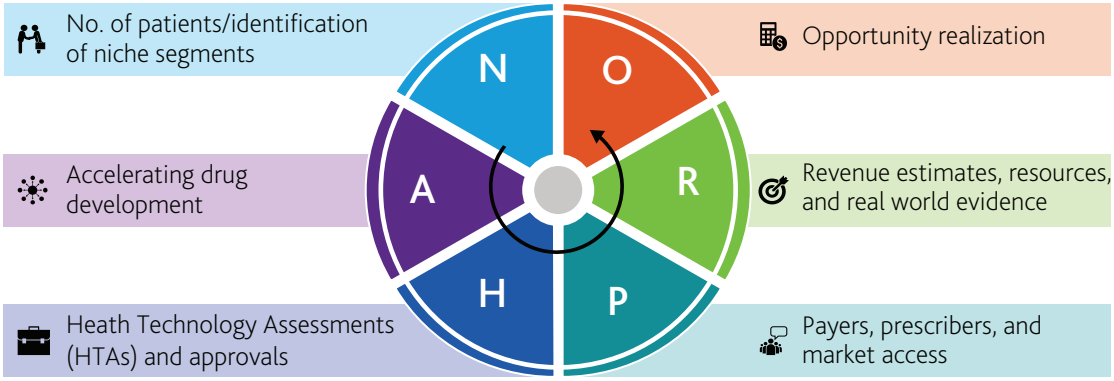
Market dynamics are changing, and researchers are raring to spin the 'Rare Wheel' to develop new orphan drugs, and move from the 'unknown rare' to the 'known rare' space. However, this is only the tip of the iceberg.

Pharmaceutical companies seem to be grappling with many tough questions, the most important being how to ensure an optimal return on investment in small markets, while navigating a complex maze of regulatory and pricing challenges.

What should be the key considerations to keep the 'Rare Wheel' turning?

The drug developers therefore need to consider the importance of each spoke in the orphan drug development wheel. It is also important to note that the orphan drug development experience is unique to a company/product and that the spokes would have to move in the designated order, to steer the wheel in the right direction.

Following are the **6 spokes of the orphan drug development wheel,** in the order of development:



O R P H A N No. of patients/identification of niche segments

Launching drugs for 'niche markets' is challenging because it is difficult to identify the 'right' patient. For example, the number of patients is small, patients are spread across geographies, pediatric trials entail ethical considerations, and there is a lack of sufficient diagnostic advancements. Screening is crucial for identifying the 'right' patient. For instance, drugs that target the ALK gene in patients with non-small-cell lung cancer (NSCLC). The ALK biomarker is present only in 2-8% of patients, but all lung-cancer patients need to be screened. This adds to screening costs and therefore the economic burden of the drug. On an average, it takes 4.8 years and more than seven physician visits for the right diagnosis of a rare disease.

Focus areas include the following:

» Careful clinical characterization to identify the 'right' patient (including sub-groups)
» Diagnostic advancements to identify optimal screening tools
» Disease awareness through a multipronged approach

O R P H A N Accelerating drug development

Accelerating drug development in this space poses unique challenges. Retaining the selected patients becomes difficult due to the high mortality rate that accompanies rare diseases and the inconveniences related to travel and lodging. Identifying biomarkers and surrogate end-points given the lack of precedents and limited clinical expertise in this space is also difficult, further aggravated by a lack of knowledge related to treatment initiation and/or sequencing treatment options. The limited number of clinical expert centers adds to issues surrounding drug access, although this is now being addressed.

Several trends have emerged recently, from the development of medically advanced therapies, such as gene therapies, to the launch of advance-in-class therapies, and drugs targeting rare pediatric indications to ultra-rare or multiple rare indications.

Focus areas include the following:

» Third-party management for establishing logistical support, including drug administration centers and patient travel and lodging support across geographies
» Optimal clinical trial design and protocol considerations in consultation with experts
» Timely data monitoring of each case

ORPHAN Heath Technology Assessments (HTAs) and approvals

With rarity being the hallmark of such drugs, regulators are seeking more suitable approaches to evaluating/ scrutinizing the rare characteristics of each orphan drug. Evaluating and generating clinical data to demonstrate clinical benefit versus conventional therapies is an evolving process. Going forward, it will also be imperative to provide additional data if requested by regulators, to ensure approval. The process has transformed from being a basic requirement for pre-market authorization trials to one that requires continued cooperation and coordination with regulators and other stakeholders.

Focus areas include the following:

» Presentation of strong proof of concept with optimal comparators

» Continued cooperation with external stakeholders, including regulators, key opinion leaders, and advocacy groups

ORPHAN Payers, prescribers, and market access

When it comes to payer evaluation, how well drug characteristics are presented is important. It is at this stage that the fine differences in research evidence gathered needs to be presented. Safety and efficacy are important evaluation criteria for regulators, while effectiveness and efficiency are key for payers/insurers. Note that interpretation and acceptability of research evidence differ between settings/regions.

Focus areas include the following:

» Targeted physician and payer segmentation

» Innovative market-access programs

ORPHAN Revenue estimates, resources, and real world evidence

More often than not, revenue estimates for orphan drugs fall short of expectations.
Unforeseen challenges may arise. For example, billing codes not generated by payers, drugs not supplied on time due to significant differences in coverage among regions, and a lack of training of healthcare professionals to administer a new drug have affected adoption of promising therapies in the past.

Focus areas include the following:

» Increasing the number of skilled resources

» Training stakeholders

» Assessing logistical challenges, if any

ORPHAN Opportunity realization

Before an opportunity is realized, it is imperative to understand that approval does not guarantee drug adoption; continued effort is required after approval as well. Having understood the importance of the post-approval phase for orphan drugs, some companies have made a difference by initiating unique programs.

Geographical expansion should be well thought out, considering uncertainties in developed markets. For example, a reduction in the orphan drug tax credit (from the current 50% to 27.5%) to offset the overall reduction in corporate tax (from 35% to 20%) in the US; Brexit in the EU, when the UK's health sector will likely face a dilemma; and Japan's bold policy of repricing expensive drugs (e.g., Opdivo® saw a 50% price cut, a year in advance). Emerging-market conditions should also be carefully assessed. For example, China, where policy is still evolving but the authorities have started to allow foreign data to be used for new drug applications (NDAs).

Focus areas include lifecycle management strategies, such as the following:

» Label expansion, geographical expansion, and repurposing drugs for rare diseases
» Increasing market surveillance studies and building long-term patient registries
» Physician-patient education and awareness

The drug discovery and development companies are willing to tread an unconventional path. **This could offer substantial incentive in terms of the firm being a trailblazer, but could also pose significant risk in terms of it being the first to face the unknown.** What is important is to create the right environment for and approach to developing drugs for rare diseases, with a set of well-researched and rationalized activities before, during and after the clinical development cycle. Companies are innovating at each step, with better and timely understanding of the unmet needs of each stakeholder and enhancing disease management, and not just focusing on drug adoption.

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About MAKS Pharmaceutical and Life Sciences Practice

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Product Management, Sales and Marketing: Market access and pricing research, branding and marketing, supply chain management and research.
Research and Strategy, and Policy: Corporate strategy and research, portfolio management, licensing and acquisition, public policy and regulation.

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