RARE RESOURCE 2

Commercialization through collaboration for rare disease medicines
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Overview

The RARE commercialization model

Relate to the community
Collaboration with the care community. Mutually beneficial enduring partnerships. Patient-centric development and commercialization

Adapt to making decisions with limited information
Modelling programmes adept at dealing with risk. Quality of external conversation with the care community. Internal cross-functional collaboration and buy-in

Relevant marketing strategies
Low patient and physician numbers is an opportunity to connect. Leverage clinical programmes. MSL-led network marketing. Education, not promotion. Remain cognizant of access

Entrepreneurial ethos
Collaborative problem-solving approach. Adaptive strategies reflective of trends such as pricing. Creative forms of lifecycle management
**Commercialization the traditional way**

- Commercial
- Quantitative market research
- Analytics
- Forecasting
- R&D lab
- Planning
- Lifecycle management
- Other rare markets
- New geographies
- New indications
- Follow-on drugs

**Internal pre-launch work**

- A linear model: disconnected communities
  - Doctors
  - Pricing
  - Patients
  - Nurses

**Internal post-launch work**

- External communications
  - Payers
  - PAGs
  - Families

**Commercialization through collaboration**

- A connected care community
  - Rare disease medicines commercialization strategies (spanning pre- and post-launch)

- R&D lab
- Scientists
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Introduction

Over the last 30 years, rare disease medicines have undergone a remarkable transformation from being commercially unviable and largely ignored by manufacturers to being a vital engine of growth.

The seeds of this change were sown by the Orphan Drug Act, passed in the USA in 1983, which smoothed the path to market and provided a host of commercial incentives for manufacturers. Similar legislation followed in most major markets, including Singapore in 1991, Japan in 1993, Australia in 1997, and the EU in 2000.

The rise of rare disease medicines is also a case of opportunity meeting circumstance. As companies looked to navigate the patent cliff and ‘end of the blockbuster’ era, opportunities for growth were sought elsewhere. Rare disease medicines became strategically interesting. The co-beneficiaries, of course, were patients, for whom significant unmet medical needs are now being addressed.

The benefits of rare disease medicines for manufacturers include:

• Expedited regulatory review and fee reductions
• Tax incentives and R&D grants
• Shorter duration for clinical trials and greater levels of regulatory success
• Premium pricing and favourable reimbursement
• Faster product uptake, reduced competition and extended marketing exclusivity
• Lower marketing costs and reduced marketing infrastructure

It is no surprise that rare disease medicines have become a major global trend. Such is the level of industry investment that the perception of ‘rare’ is now juxtaposed with the reality of becoming common:

• In the USA over 400 orphan medicines have been approved since 1983 and a third of the medicines approved in the last 5 years were for rare diseases
• Over 55 million people in the EU and USA suffer from rare diseases
• The evolution of the emerging pharmaceutical markets is driving increased interest in rare diseases in Asia and Latin America
• The commercial market for orphan drugs worldwide is anticipated to reach over £100 billion within a couple of years

However, with opportunity comes challenge. Commercialization of rare disease medicines differs markedly from traditional pharmaceuticals and to successfully navigate these challenges, it is imperative that apposite commercialization strategies are employed.
Commercialization begins with the patient

This statement holds true for all pharmaceuticals; however, for rare disease medicines it carries particular significance:

- **Rare disease drug development is by definition patient-centric.** The unmet needs are typically high, whereas the number of patients is low. It is probable that many patients will not have been identified by the healthcare system; you are likely to be developing a new market, not just a new drug. As rare diseases are often genetic, they can also be ethnically and geographically constrained. Therefore, clinical programmes must be designed almost entirely around the patients, with strategies developed to aid identification, diagnosis, education and involvement. Facilitation of trial participation and minimizing logistical barriers such as travel also requires consideration.

- **Choice of trial endpoints** requires attention to ensure accurate and reliable representation of disease progression; there are unlikely to be any precedents to draw upon. Patient outcomes that reflect disease severity and burden are an important consideration for pricing and reimbursement negotiations.

- **Involvement of patient advocacy groups** (PAGs) will be beneficial for bolstering disease and market understanding. The sponsorship of patient registries and compassionate use programmes should be considered. Strong patient/PAG partnerships will continue to be valuable throughout launch.

Investment in these activities will speed up trial recruitment, boost patient adherence and generate vital community advocacy. In turn, development costs will be minimized and time to market (and reimbursement) reduced. A strong trial programme will also generate vital information on unmet needs, care pathways and market structure. Upon launch, it is also commonplace to transfer patients from trial and access programmes to commercial supply. Hence, establishing a genuinely engaged patient populace during development is of clear benefit.

Portfolio planning in rare diseases

Portfolio planning is the process by which decisions are made to optimally meet a company’s business goals. Market research is often a central pillar of this process, with the information gained used to build a picture of the disease (and drug) before forecasting models are built and net present value calculations run. These models then indicate the commercial implications of alternative portfolio decisions and whether or not they meet those business goals. The same holds true for portfolio planning in rare diseases. However, by virtue of low patient numbers and limited previous research, strong market research data are likely to be absent. Making portfolio decisions based on partial or knowingly flawed information is challenging, but this does not undermine its importance. Some key considerations are outlined below:

- **Market research remains vital.** Traditional large-scale quantitative research may not be feasible. Instead, a more consultative qualitative approach can be used whereby knowledge is pooled from across the disease network. For example, strong PAG relationships can help build disease understanding but can also aid identification of patients and physicians in whom to test and hone assumptions. Strong partnerships and quality of conversation is key.

- **The geographical scope of the disease is significant.** Being genetic in origin, many rare diseases are ethnically and geographically constrained and disease dynamics and care pathways can differ markedly by region and by country. Research and modelling programmes should be cognizant of these considerations.
• **Modelling programmes must be adept at dealing with risk.** With fewer patients for input, erroneous modelling assumptions could significantly impact commercial viability and portfolio decisions. Sensitivity analysis, scenario planning, pre-mortems and benchmarking are useful risk management tools. However, involvement, understanding and buy-in from internal stakeholders is essential; effective rare disease modelling is a collaborative cross-functional process.

• **Forecasting methodologies must embrace the available data.** Market sales data will be rare. Epidemiology-based forecasting and patient flow modelling may be more appropriate. Modelling assumptions must be frequently updated as development progresses and disease and drug knowledge evolves. Regular sampling and staying close to customers is advisable.

• **The viability of premium-price expectations** for rare disease drugs is being questioned. Adequate forward-looking pricing and access research should be conducted. Price expectations should reflect the local healthcare environment.

• **Social considerations**, such as disease burden and extent of unmet needs, may hold greater sway in portfolio decisions. The selection of suitable decision criteria for rare disease portfolio decisions requires care.

### Rare disease medicines: a price worth paying?

**Then ...** For traditional pharmaceuticals, cost–benefit analyses and use of quality-adjusted life-year (QALY) calculations are widely accepted tools to encourage pricing clarity and determine whether a new drug offers fair value. For rare disease drugs this model falls short. With limited or no alternative treatment options, the incremental benefit of a new drug to a patient suffering from a rare disease is likely to be substantial. Additionally, with only small trial samples available (often of short duration), it is difficult to gauge long-term benefits at launch – longer follow-up periods are required. Thus, the utility of the traditional QALY thresholds is limited and other pricing factors have been used.

With limited or no benchmark competitors, rare disease drug prices have typically been set at or near the maximum level the market can sustain, with the seriousness of the disease and size of the unmet need used to support the high price. With such low patient numbers, it is also argued that treating a rare disease is unlikely to impact the overall drug budget. The result of this is some of the most expensive drugs in the world and a pricing system that is inconsistent and opaque.

**Now ...** This pricing trend suggests that society affords greater value to treating patients with rare diseases than common diseases. However, the amalgamated budgetary impact of treating many rare diseases is now being noticed and the societal value of paying more based on rarity alone is being questioned.

Manufacturers are also being challenged on certain commercialization strategies, such as creating orphan monopolies by splitting a disease up into sub-diseases that qualify as rare, or using orphan indications as a Trojan horse to obtain fast market access at a high price point prior to submitting marketing applications for subsequent (more prevalent) indications.

**The future ...** Social value-based pricing (assessing the value society holds for different diseases) and innovative risk-sharing price models (whereby if a product does not induce the expected effect, manufacturers receive less money) are two possible routes forward.

As rare disease budgets grow and more data are gained on the societal standpoint on treating rare diseases, this situation will undoubtedly continue to evolve. For the time being, the ‘low-volume high-price’ model remains valid, but pricing strategies must be conscious of this evolving landscape if access is not to suffer.
A rare approach to marketing

Rare disease medicines demand a different launch model to that of traditional drugs, whereby it is feasible to launch an orphan drug without major marketing expenditure and infrastructure. Instead, marketing strategies and tactics can embrace the following:

- **Utilize the power of the Rare Disease Network Model.** Meaningful stakeholder partnerships are nurtured in this model (expanded upon in RARE RESOURCE 1). These partnerships start in drug development and continue beyond product launch; targeted network marketing is key.

- **Focus on education, not promotion.** Knowledge and awareness amongst patients, physicians, PAGs and payers is crucial for obtaining vital advocacy.

- **Low patient numbers present an opportunity to connect.** Highly targeted activities to bolster patient identification and diagnosis are both feasible and beneficial, as are holistic care programmes that connect patients and caregivers and embrace the ‘beyond the pill’ concept. Each new patient should be considered a valuable asset.

- **Leverage clinical programmes.** Rapid transfer of patients from clinical and early-access programmes to commercial supply can help establish an active and engaged treatment community. This can aid rapid product uptake as the clinical programme may have already identified a high proportion of available patients. Sponsorship of patient registries will also enhance disease understanding during development and enable tracking of patient progress after launch.

- **The representative-free launch.** As education and community engagement are critical, product rollout may be better served by targeted MSL communications than traditional large-scale sales forces. Target audience assessment is less complex for rare diseases but vital to successful commercialization. With a smaller number of disease experts, micro-targeting and micro-messaging personalized to individual needs is feasible.

The lifecycle of rare disease medicines

Bringing any drug to market is challenging; therefore, once achieved, it is prudent to maximize the opportunity via an astute lifecycle management strategy. This logic is embedded in traditional pharmaceuticals but applies equally to rare disease medicines. There are, however, specific challenges and opportunities that require consideration:

- **Competition will typically be limited or non-existent.** A market monopoly may be advantageous from a pricing perspective, but also means that market development is solely your responsibility, or rather, your opportunity.

- **Pricing strategies** should reflect planned multiple-indication rollout. A Trojan horse approach may be commercially beneficial, whereby a strong price point for a first indication may influence prices for subsequent indications. Equally, geographical rollout should be reflective of reference pricing implications. Criticism of such overt strategies is, however, mounting.

- **Legislative advantages through extended intellectual property coverage** will yield extended return on your initial development and commercialization investment. Astute use of this extra time for developing brand loyalty, follow-up products, line extensions, new indications, or alternative post-genericization tactics would be prudent.
Lifecycle opportunities beyond new indications. By virtue of being of genetic origin, some rare disease drugs will be self-limiting regarding follow-on indications. For other rare diseases, a more traditional pan-indication rollout may be possible. For either scenario, there will be opportunities to apply learnings to follow-on products or other rare disease markets. Sharing of collateral knowledge from an initial launch can constitute a more holistic, more portfolio-based form of lifecycle management that would not be as viable in the oft-siloed field of traditional drug development.

Not all rare diseases are equal

There are currently an estimated 6000–8000 diseases designated as being ‘rare’. In Europe, for example, these range from gastric cancer, with a prevalence of 49.2 per 100,000, to autosomal dominant spastic paraplegia type 29, which has been recorded in only one family (with no numerical prevalence data available). Whilst the term ‘rare’ can be ambiguous, the implications of rarity can be far-reaching.

This paper has discussed how rarity can impact multiple aspects of commercialization; it follows that strategies must be reflective of rarity. The rarer the disease, the more tailored and unique the required commercialization plan. Arguably, a more entrepreneurial problem-solving ethos must be adopted.

For more common rare diseases, it may be tempting to stay on familiar ground and use adapted versions of traditional commercialization models. However, leaning too strongly on such approaches and failing to embrace the concepts raised in this paper, even for the most common of rare diseases, risks missing the opportunity for building enduring and productive partnerships that the rare disease network marketing model offers.

Genuine two-way communication with customers is perhaps the most powerful commercialization opportunity that all rare diseases offer. This opportunity should not be squandered.

Conclusion

Rare disease medicines represent a true embodiment of the ‘patient-centric’ model that many in the pharmaceutical industry are striving for. Fuelled by high unmet needs, legislative advantages, favourable pricing and the evolution of ‘new’ rare disease geographies, rare disease medicines are also providing an attractive source of commercial growth at a challenging time.

It is not surprising that many companies have been swift to move into this space. The industry is adapting rapidly as it learns to operate under the different commercialization models required, whereby collaborative strategies, community engagement and a more entrepreneurial approach focused on problem solving are all-important.

As this trend progresses and ‘rare’ becomes more ‘mainstream’, the market dynamics will undoubtedly evolve – arguably, pricing is already witnessing such a change. However, providing that commercialization strategies remain aware of these developments, rare disease medicines will continue to be of huge potential benefit both for patients and the industry for the foreseeable future. The opportunities provided by this trend should not be overlooked lightly.
Further reading


Simoens S. Pricing and reimbursement of orphan drugs: the need for more transparency. Orphanet J Rare Dis 2011;6:42.


Young D. Market builders: complex, but rewarding work of rare disease R&D. Scrip Intelligence. 17 January 2014.