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Fresh Recommendations For Rare Disease Trial Sponsors

by Daniel Chancellor

Best practices to help sponsors design patient-centric studies, build trial awareness among important physician and health care professional groups, leverage advocacy groups to speed up patient recruitment, and ultimately gain a competitive edge in rare disease trial strategies.

Approved drugs are available for just 5% of the approximately 7,000 rare diseases identified, many of which are life threatening or limiting. The pharmaceutical industry is making inroads through R&D, despite the unique challenges facing clinical trials for rare diseases, not to mention often navigating without regulatory precedents and an uncertain commercial outlook. Progress can therefore feel slow despite the priority that many drug companies place on these patients and their unmet needs.

Rare diseases are so-called because of the low number of prevalent patients, with long-standing definitions being fewer than 200,000 people in the US and 1 in 2,000 people in the EU. While rare diseases are individually uncommon, the combined burden is vast. Orphanet estimates a global point prevalence of 300 million patients, equivalent to around 4% of the population.

Trialtrove data shows that clinical activity for rare diseases has consistently grown through the last decade, achieving a minimum 5% growth rate in every year since 2013 (*see Exhibit 1*). In 2010, the biopharmaceutical industry initiated 884 rare disease studies, with the total expanding year-on-year to a peak of 1,609 in 2019. Although there was a slight 4% contraction in the pandemic-affected 2020, similar trends were observed in nearly every other therapy area. Activity through 2021 so far appears robust, although a like-for-like comparison with previous years is not yet possible owing to reporting delays by industry sponsors.

This growth has come from both the oncology and non-oncology rare disease segments. The proportion of oncology studies has remained consistently at 60-65% of the total, indicating the attention on both traditional rare diseases as well as oncology opportunities.

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Industry Trial Activity

Rare disease clinical trials are primarily sponsored by large pharmaceutical companies, as shown in Exhibit 2. The total count is comfortably led by Bristol Myers Squibb with a total of 942 trials since 2010, with a heavy focus within cancer. Novartis, Roche, AstraZeneca, and Merck & Co. complete the top five, both in terms of overall studies (>500 each) but also specifically within rare oncology (>400 each).

Sanofi has sponsored more traditional rare disease trials than any other company since 2010, due to the historical activity of acquisitions as Genzyme and Bioverativ. Takeda is similarly highly ranked through its acquisition of the rare disease specialist Shire, while the remaining leading pharma sponsors have built their presence through a mix of internal R&D and smaller M&A deals. In general, a strong focus on non-oncology rare diseases tends to come at the expense of a leading rare oncology portfolio, although Novartis is the one exception that invests heavily across both areas.

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Strategic Recommendations For Trial Sponsors

Informa Pharma Intelligence's analyst team has designed a series of strategic recommendations for sponsors of rare disease clinical research.

This set of best practices will help sponsors gather insights from clinical experts to design patient-centric studies, build trial awareness among important physician and healthcare professional (HCP) groups, leverage advocacy groups to speed up patient recruitment, and ultimately gain a competitive edge in rare disease trial strategies (*see Exhibit 3*).

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1. Designing Patient-Centric Studies

Informa Pharma Intelligence's survey in collaboration with Rare Patient Voice showed the essential role of physicians in rare disease clinical research. Physician referral is by far and away the most common route to study participation, while physicians also are a common source for trial awareness and information. Physicians can also play a pivotal trial in the study design process, being much closer to the disease in question and patients' unmet needs.

At the trial planning stage, primary research and focus groups allow for the rapid creation of a consensus view, which is not otherwise available for underserved rare diseases. Physicians can offer important on-the-ground information on current standard of care, competitor positioning

and treatment guidelines. Physicians are also a gateway into patient insights and unmet needs. From a strategic point of view, physician and key opinion leader insight can guide the creation of a target product profile, which is a vital document to align multifunctional internal stakeholders around overall development goals, or to conduct due diligence for potential external therapeutic opportunities.

Transitioning into protocol development and study feasibility, physicians and clinical experts remain essential partners. For a clinical trial to produce highly relevant data, physicians are well placed to advise on eligibility criteria, comparator arms and endpoint selection, all designed to reduce burden and increase patient centricity. Study protocols must be critiqued and stress-tested in order to minimize potential costly amendments further down the line.

About The Data

To gather insights into the clinical trial experience for patients with rare diseases, Informa Pharma Intelligence partnered with the advocacy group Rare Patient Voice. A total of 1,800 people were contacted via email in early 2021 and invited to participate in an online survey that gathered opinions on participation or intent to participate in clinical trials. Over 900 patients participated in the study, providing a base of information on clinical trial behavior attitudes, needs, and demographics.

2. Building Trial Awareness Among Key Stakeholders

Once the protocol is finalized and approved, attention must turn rapidly to raising trial awareness and investigator activation. These external activities must happen in concert with traditional feasibility and site selection processes in order to smoothly transition into patient enrollment. For any rare disease program, successful trial awareness should have a multi-pronged approach that targets the important stakeholders: physicians, investigators, and patients themselves.

A vast majority of patients think it is important that HCPS are aware of studies being conducted in their community, according to a study from the Center for Information and Study on Clinical Research Participation (CISCRP). Rare disease trial sponsors should therefore prioritize outreach strategies to physicians as they are essential allies for raising trial awareness. In spite of the vital role physicians play, current engagement is far from optimal as clinical trial options are rarely discussed during patient visits.

When engaged and consulted, physicians and other HCPs themselves can be more than just advocates for clinical trials, but also potential investigators themselves. For rare diseases, where established investigators with large referral networks may be in short supply, study sponsors should always be nurturing the next generation of investigators with every engagement.

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Expanding clinical trial networks through first-time investigators opens up new pools of patients and referral centers. Just as it is necessary to understand the barriers for patients to participate in trials, it is equally useful to address the hurdles that prevent HCPs from becoming investigators.

Recognizing the growing influence of patient organizations and disease advocacy groups, particularly within the rare disease universe, any trial awareness strategy also needs a patient-focused component. This can be as simple as developing patient-friendly materials and a website presence, rather than relying upon a *ClinicalTrials.gov* entry that may be difficult to understand.

3. Embracing End-To-End Recruitment Models

Recruitment and trial awareness are inextricably linked, such that best practice activities to raise awareness among investigators and patients will support a fast start to enrollment. On the patient side, resources including targeted websites dedicated to ongoing studies can also provide prescreener services, supplying eligible participants that can be triaged towards individual clinical sites. These same resources can be adapted to incorporate HCP-facing components to aid in wider education and discoverability.

There are several benefits to a centralized approach to awareness and enrollment, rather than delegating responsibilities to study partners. A single hub can be used to track patient interest, eligibility and referrals through the system, allowing for real-time monitoring of recruitment channels and site performance. While patients may not meet eligibility criteria for the study in question, analysis of screen-outs can be used to inform future study designs, or indeed introduce protocol amendments if necessary. This hub can also double as a communication portal, encouraging email signup that allows sponsors to reach the right cadence of communication to trial participants. Regular updates with regards to study progress aids patient engagement and retention within the study, supporting an overall positive trial experience.

Lastly, an innovative recruitment model is emerging that is particularly relevant for rare disease studies, owing to the disparate geographic spread of patients and importance of advocacy groups. Citeline Connect is pioneering the patient recruitment collective, bringing together a diverse range of patient-facing organizations from traditional recruitment partners through to disease awareness organizations, patient advocacy groups, pharmacies and even diagnostic service providers. By creating and tapping into a network of validated partners that can steer patients in the direction of clinical trials, study sponsors can cast the net far wider and more equitably. This one-to-many approach has substantial advantages over working with select traditional recruitment partners, which have failed to address the lengthy enrollment period of rare disease trials and reinforce a lack of diverse participation.

Read more: Rare Disease Trial Strategies Whitepaper

About The Author

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Daniel Chancellor has a decade of experience as an analyst in the biopharma industry, spanning roles in drug discovery, market analysis, competitive intelligence and strategic consulting. He now develops and leads Pharma Intelligence's thought leadership program, producing materials that help clients across a range of hot topics in the biopharma industry.