

The value of real-world evidence in rare disease research

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In 2015, the **U.S. Food and Drug Administration** (FDA) approved 21 new drugs to treat rare diseases, which was almost half (47%) of all the novel drugs approved in 2014.^[i] It was also the second consecutive year the FDA approved more rare disease drugs than any previous year in history, highlighting an important trend: After decades of neglecting rare disease research, biopharma companies are increasingly identifying this category as an attractive development pathway. This is great news for the tens of millions of patients suffering from one of more than 6,800 rare diseases recognized worldwide.^[ii]

There are numerous factors fueling this trend, but regulatory incentives have become a primary drive of engagement. With orphan drug designation, sponsors can take advantage of special incentives such as marketing exclusivity, tax credit and waiver of Prescription Drug User Fees and they may qualify for Fast Track, Breakthrough Therapy, Accelerated Approval or Priority Review, all of which cuts the time and cost of bringing these drugs to market.^{[iv][v][vi]}

But carrying out rare disease trials is more complicated than others. These diseases often have no, or few, treatment options, which means there may be little published research, no established development pathway and few endpoints or biomarkers

to guide the trial lifecycle. The patient populations are also very small and dispersed, which makes recruiting a difficult and costly endeavor that increases the risk of failure.

With advances in science, analytics and the advent of “big data,” we have access to more tools than ever to leverage real-world evidence to help overcome these barriers by approaching— orphan product development more efficiently. Registries, for example, provide an important source of data from which to derive evidence and value to support clinical research. In a registry, patients, care-givers and physicians record real-world data about the disease lifecycle, including details about their diagnosis, treatment and long-term quality of life.

These registries can alleviate many of the scientific and communication obstacles rare disease therapy trials face, and are increasingly becoming a relied upon research tool at every phase. A disease registry can also be used to identify patients with the particular characteristics (e.g., a specific genetic mutation) needed for a trial which can speed up recruitment. If it is established early enough—ideally during the early phase of product development—a rare disease registry can provide baseline data about a patient’s care pathway before any treatment is available, which can validate endpoints in the trial design and potentially eliminate the need for placebo arms in later trials. Later on it can provide insights



for epidemiological research highlighting trends in population health that might not otherwise emerge.

Registries, or other real-world studies are vital to support post-authorization evidence generation, particularly for rare disease drugs which may be approved on the basis of relatively few patients. These, and other drugs that are approved via an adaptive or conditional pathway will likely require ongoing benefit-risk evidence to reach full approval.

From a marketing standpoint, registries also give researchers direct access to the patient community, where they can connect with physicians, patients and advocacy groups to share information about their trials, build rapport with the broader patient population, and more efficiently and cost-effectively recruit participants to their studies, all of which is vital to the success of a trial.

To get the most value from rare disease registries, sponsors should set clear goals for the kinds of data they want to collect and start building them as soon as possible. They should also make the most of this opportunity to connect with patients and ad-

vocates by listening to their concerns and providing feedback and updates on their research. In the end, a registry is more than a passive database. It's a place where biopharma companies and the patients they serve can communicate with each other about this disease. If sponsors use this opportunity to create a two-way dialogue they

can engender the trust of patients and demonstrate that they are invested in improving their quality of life.

[i] <http://rarediseases.org/fda-approves-21-orphan-drugs-for-rare-diseases-in-2015/>

[ii] <https://rarediseases.info.nih.gov/about-gard/pages/31/frequently-asked-questions>

[iii] http://ec.europa.eu/health/rare_dis-

[eases/policy/index_en.htm](http://ec.europa.eu/health/rare_diseases/policy/index_en.htm)

[iv] <https://rarediseases.org/assets/files/white-papers/2015-06-17.nord-bio-ey-odtc>

[v] http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000601.jsp

[vi] <http://www.fda.gov/ForPatients/Approvals/Fast/default.htm> 