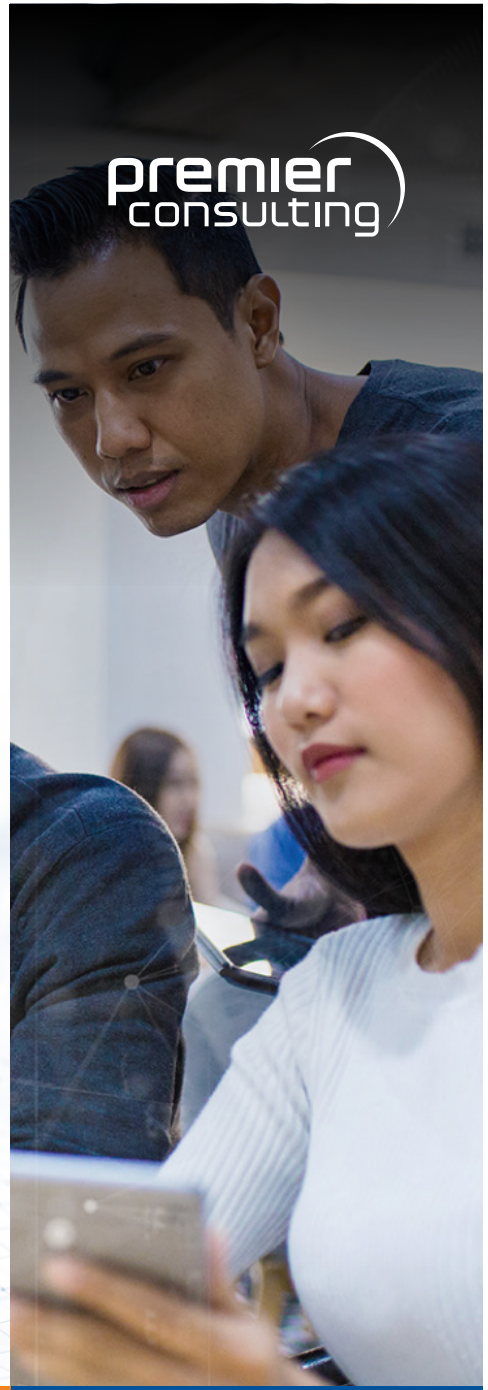
Premier Consulting Insight 201

Using RWD and RWE to Support an Ultra-Rare Orphan Program



Background

Clinical trials for ultra-rare diseases can be particularly challenging to mount. Typically, the patient population is small and geographically diverse. The Food and Drug Administration (FDA) may allow the use of credible real-world data (RWD) and real-word evidence (RWE) in lieu of data collected in a Phase 3 trial – but the acceptance of that data depends on a sponsor's understanding the FDA criteria for historical control groups, study data standards, and clinical meaningfulness. As we see in this case, being able to confidently navigate one or more pre-IND meetings is also a critical asset

Objective

The sponsor had developed a nucleoside treatment for a life-threatening congenital disease. The therapy had received breakthrough therapy designation, but FDA approval would ultimately rest on the sponsor's ability to demonstrate clinically meaningful improvement. To speed this much-needed therapeutic to desperately ill patients, the sponsor approached Premier Consulting to help leverage RWD and RWE and bypass Phase 3 trials.

Types of real-world trials

Observational study

Pragmatic trials

Historical controls

R E G U L A T O R Y

Meeting the Challenges

Challenge #1

Typically, data presented to the FDA is collected within the confines of a clinical trial, in which sponsors set clear protocols of how and when to measure the primary endpoint. RWD is not as neat. Physicians at sites around the world, as part of their normal daily interactions, collect data that is then aggregated into one presentation. They may use different instruments from one another, different calibrations – perhaps even slightly different definitions of each data type. That was particularly true in this case, for which much of the demonstrated clinically meaningful improvement related to patient-specific quality-of-life data.

Our Strategy

At the first pre-IND meeting, we presented the efficacy and safety data the sponsor had collected, organized by specific patient. Then we listened carefully to the FDA's response. Our goal was to understand how the FDA wanted us to present that patient data in a standardized and clinically meaningful way. The FDA requested that the data be organized by primary functional endpoint rather than shown by specific individual improvement over time. Premier Consulting understood this response and asked for permission to present the reformatted data at a second pre-IND meeting. The FDA granted the second meeting, at which, critically, it accepted the now-standardized data.

Challenge #2

When using an historical control group, all patients in that group must be carefully and clearly matched – based on important baseline disease characteristics – to patients in the treatment group *a priori* in order to minimize bias. One of the key opinion leaders had written on the natural history of the disease and been published, but the sponsor didn't feel the data was strong enough to share with the FDA. When compiling the presentation for the initial pre-IND meeting, we honored that preference. But during the meeting we referenced the data – and the FDA expressed interest.

Our Strategy

At the second pre-IND meeting, we presented the natural history data in such a way that the FDA saw its value. The Agency was "reasonably impressed" by the rigor of the published natural history literature. Critically, the FDA agreed that the risk-benefit ratio shown by this data favored the sponsor's product. The sponsor was able to satisfy regulatory requirements without a Phase 3 trial.

Takeaway

The FDA is interested in the totality of the data presented when considering a product. Yet, it is critical to organize that data in a way that clearly meets the Agency's criteria. When leveraging RWE in lieu of a Phase 3 efficacy study, success may depend on partnering with a team with a deep understanding of FDA criteria and long-standing experience in pre-IND meetings.

Project Description

To present real-word evidence (RWE) to the FDA to gain regulatory approval for a breakthrough therapy without the time constraints of mounting a Phase 3 clinical trial.

Therapeutic Area

Rare Disease

Therapeutic

Nucleoside treatment with breakthrough designation

Outcome

After two pre-IND meetings, the therapy received FDA approval based on RWD and RWE.

services@premierconsulting.com | premierconsulting.com