Rare Disease Research: Q&A with Dr. Murphy on the Current State of R&D Activity in Orphan Disease Trials

WORLDWIDE CLINICAL TRIALS

Q. What are the most common challenges in rare disease clinical trials for Clinical Research Organisations (CROs)?

A name can carry a lot of meaning, and in the case of "rare diseases," this means difficult-to-find and difficult-to-treat patients that push the envelope in both trial design and study operations. By definition a rare disease is a one that effects fewer than 200,000 per FDA guidelines and 1 in 2000 by European standards. In addition, many rare diseases occur in children and require specialized care and additional regulatory oversight for interventional studies, which can make assessment and data collection techniques challenging. Insightful study design and operational methods must be developed during study planning to enable brisk and efficient execution. For example, a mosaic of "outside-the-box" concepts demand scrutiny: use of placebo; contributions of historical data; the sensitivity and specificity of measures; or the utility of adaptable risk mitigation monitoring strategies that "target" sites and patients, and certain key data fields are part of this mix. Every functional group touching an orphan disease program within a CRO will need to be at the top of their game to be contributory to this discussion.

Potentially more so than in any other clinical program, engagement of diverse stakeholders is critical. These include the patients (and caregivers), and specialized doctors, nurses, and rehabilitation staff given the multiple organ systems frequently affected by many rare diseases. Additionally, CRO services that are differentiated will facilitate regulatory/sponsor interactions for program design and anticipate data requirements for those organizations responsible for formulary placement and reimbursement. These are opportunities, and not impediments. This is where focus, uncompromising commitment, and experience in trial design and operations in general and rare disease research in particular is critical. Knowing the challenges, and the staffing and project organization required for rare disease trials, permits seamless transition from design, to operations, to successful product authorization.

Q. Would you say CROs are not inclined to conduct rare disease clinical trials because of the aforementioned operational and regulatory challenges?

These challenges may discourage some CROs from entering the space. Yet, with each challenge, there is an opportunity to demonstrate innovation in the trial design and operations that are the hallmarks of 21st century clinical trialists – the "Jedi Masters" of the art. Because of these challenges, not in spite of them, a CRO with staff who are grounded in medicine, science, clinical care, and study methodology can be an excellent partner in development of rare disease therapeutics. Additionally, because of the operational runway required to evaluate and commercialize innovative products, strategic rather than transactional relationships across a program benefit both the sponsor and the CRO. At Worldwide, we welcome the challenge of rare disease trials as they in many respects reflect the raison d'etre of the company – medical and scientific expertise coupled with operational acumen. Helping sponsors achieve a successful trial is our commitment; creating opportunities for innovative therapy where none have previously existed is our passion. Worldwide's organizational philosophy of "standing with the sponsor and speaking for the patient" achieves its full potential within orphan disease research and development.

Q. What role do drug companies play in the mix? What is the current level of investment into orphan disease drug research?

Development of any treatment for a rare disease indication demands extraordinarily intellectual capital and vision as well as investment in both time and money from a sponsoring drug development company. Many of the emerging therapies in fact are transformative, and reflect an astoundingly sophisticated understanding of disease processes and the spectrum of drug discovery capabilities characteristic of modern R&D efforts. For the basic scientist, or translational clinical researcher, rarely have there been a more opportune moment for career development. The potential financial incentives involved with the development of rare indications brought about by the Orphan Drug Act and the new 21st Century Cures Act has increased the levels of interest in product development in this arena, although orphan disease R&D has developed independently of these incentives. Indeed, increasingly nuanced understanding of disease pathophysiology has been accompanied by equally impressive innovation in clinical trial methodology, permitting treatments to be rapidly and efficiently evaluated.

An increasingly supportive regulatory climate, combined with a maturation of clinical trial methodology, facilitates brisk product approval and commercialization based upon financial commitments that are only a fraction of those required in many traditional indications. Indeed, it is important to note that not only has there been increased investment in rare disease indications, but there have been record high FDA approval rates for drugs treating rare disease indications in recent years – reinforcing the vision prompting investments and other development commitments.

Q. What is Worldwide Clinical Trials approach to orphan disease research?

The approach to clinical research is strategic, and not transactional. At Worldwide, we believe that whether it is recruitment of patients and sites, or engagement of regulatory and payer stakeholders, strategic planning is critical to successful programs in rare disease clinical research. Service differentiation is demanded across the continuum of clinical development. We begin by understanding the corporate objective of the sponsors (development to inflection point? development to commercialization?), the potential attributes and liabilities associated with a platform of therapy, a range of clinical trial methodologies that might facilitate product evaluation, and particularly the perspectives of patients and families at a clinical care level. This last point of emphasis reflects our commitment to understand the "illness," and not only the "disease" as a mechanism to enhance trial design and conduct.

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Dr. Murphy's professional career within the pharmaceutical industry has spanned more than 25 years, serving in positions that emphasize the integration of medical and scientific acumen with operational excellence. He is board-certified in psychiatry and has a doctorate in pharmacology, with training at Tulane University, Stanford University and the Mt. Sinai School of Medicine.

He has been a consultant for the Duke Clinical Research Institute and is Research and Development Editor for American Health and Drug Benefits™, a publication that focuses upon cost, quality and access in the transition of novel diagnostics and therapeutics from discovery to commercialization.

As a faculty member within the Center for Experimental Pharmacology and Therapeutics at Harvard-MIT Division of Health Sciences and Technology, he has been a lecturer for 15 years within a competitive and credentialed clinical investigator training program.

Our strategic orientation allows us to identify and address challenges preemptively. Our geographical footprint facilitates a process in which key success factors at both a regional and global level are identified. And since operational solutions commonly are fungible across therapeutic areas, having an international presence in many different therapeutic areas which demand tools, process, infrastructure, and scalability facilitates global studies for the difficult-to-find, and difficult-to-treat patients. So, strategic planning, geographical locations populated by staff that are linguistically and culturally competent, and "borrowing from Peter to pay Paul" in trial management techniques can promote successful trials and facilitate the development of therapy for patients with rare diseases.