Rare Disease Patients Benefit from Clinical Trial Flexibility

A convergence of trends — including the continuously growing focus on drug development for rare diseases, the rising percentage of biologic drug candidates, and the expansion of decentralized trials — is creating opportunities for more efficient trials that are less burdensome for patients and their families. With a limited number of rare disease patients, clinically relevant data is invaluable. Thanks to innovative and flexible protocols, we are developing new ways to enable us to gather critical trial data to support new drug submissions.

Francis Jones, Ph.D., Tim Rich, and **Meredith McCumbee,** experts in the Thermo Fisher Scientific Research Business supporting PPD Digital and Decentralized Solutions

Growing Interest and Investment in Rare Disease Research

Over the last 20 years, the focus of the pharmaceutical industry has shifted away from blockbuster drugs treating patient populations of hundreds of thousands or millions to more specific treatments that target subtypes and increasingly rare diseases with smaller, more dispersed patient populations (right drug for the right patient at the right time).[1]

Simultaneously, there has been a shift in protocols for clinical trials due to a growing percentage of new drug candidates being biologics, including advanced antibody–drug conjugates, bispecific antibodies, cell and gene therapies, and other novel medicines — a growing proportion of which are focused on treating rare diseases.

The growth of gene therapies coupled with a greater focus on rare

diseases has also coincided with the introduction of remote digital tools that, in part, enable the decentralization of clinical trials.[2] When the pandemic intensified, decentralization became critical for the execution of nearly all clinical trials. As a result, the industry witnessed further adoption and acceleration of hybrid and fully decentralized or virtual study models. This paradigm shift suits the rare disease space well, as patient populations with rare diseases are typically both small and geographically dispersed, making site-based trials for these studies challenging.

As it stands today, digital and decentralized solutions have made it possible for more patients to participate regardless of location. Notably, we are also seeing an uptick in use of decentralized approaches within rare disease pediatric trials, including those with highly vulnerable populations.

Flexibility for Pediatric Patients and Their Loved Ones

Bringing children into a clinic has many challenges, and for children with rare diseases it can be even more difficult. However, with the widespread availability of decentralized options, hybrid approaches are possible which include a mixture of in-clinic and at-home endpoints, supported by bespoke digital platforms and novel trial design solutions.

Patient feedback has indicated that parents prefer to interact with their physicians face-to-face on some occasions, particularly early in treatment, but are amenable to remote interactions outside of milestone visits. Combining home-health nursing visits with periodic on-site physician evaluations can offer a truly patient-centric approach. This gives patients and their families maximum flexibility for clinical trial participation, in that they can opt for what best suits their schedule or lifestyle.

Patient Experience is Paramount to Success

We believe that it is crucial to do everything possible to optimize the patient experience, especially for the rarest of indications. Regardless of how a study is set up — with the patient visiting a local clinic, or the central investigator site or a physician or nurse making an in-home visit — that interaction must occur without delay and with minimal inconvenience to the patient. A white-glove service, such as support of a study concierge, is another way study teams can elevate the research experience while ensuring patients remain engaged and samples are collected on time and handled appropriately, with all critical data collected

Furthermore, the PPD patient concierge service acts as a dedicated resource for patients and their families. These trained individuals serve as a guide through all aspects of trial participation. This single point of contact helps organize everything from travel to reimbursement of expenses and coordination of home health nurse visits. The concierge can also provide reminders about appointments and patient-reported outcomes (PROs) requirements with the goal of making trial participation as easy as possible, while ensuring key data is collected. This is significant because many rare disease patients can spend years before receiving their correct diagnosis. Without steadfast engagement while on a trial, there is a stronger chance of dropout.

A Network to Support All Stages of Research

Significant regulatory expertise and proactive regulatory engagement are essential to the success of modern protocol designs. We help by augmenting the existing expertise of biotechs and pharma organizations to provide more robust knowledge across all regulatory aspects. Our established relationships with regulatory agencies enable us to engage frequently around new

CASE STUDY: Preventing Data Loss for a Critical Rare Disease Study

In a rare disease clinical study in which the primary endpoint was a patient-reported outcome (PRO), it was critical for PPD to ensure no loss of data, particularly owing to missed visits during a global pandemic. Our strategy included building a dynamic protocol and consent process that enabled flexibility. A digital solution to collect the ePRO data was coupled with eConsent, home health care (HHC), home echocardiogram, and PPD Concierge solutions.

When the COVID-19 pandemic emerged during the middle of this clinical study, patients were unable to travel. We quickly expanded the existing digital solutions and added direct-to-patient delivery of investigational medicinal products (IMPs) and, when possible, the transfer of patients within our network to sites not impacted by the SARS-CoV-2 virus.

The dynamic protocol allowed the study team to rapidly offer flexibility for patient care without delays while reducing confusion and uncertainty for trials participants. Overall, non-compliance rates of less than 10% were observed on the primary endpoints, and, rather than the client's expected dropout rate of 30%, the actual rate was below 3%. As a result, the sponsor achieved successful database lock during the COVID-19 pandemic.

Digital and Decentralized Solutions Offer Hope

Meredith McCumbee, Senior Director, Clinical Transformation at PPD, hopes that advances being made by our digital and decentralized solutions team as well as the Rare Disease Center of Excellence will make it possible for her 12-year-old son Aaron to soon benefit from participation in a clinical study.

Aaron has a rare chronic inflammation disorder about which little is known. A combination of genetic and environmental factors that make him more prone and sensitive to allergies and cause his immune system to be constantly challenged and frequently hyperreactive. Over time, the chronic inflammation also leads to esophageal damage that makes it difficult for Aaron to swallow.

In addition to these difficulties, Aaron has been diagnosed with autism and a movement disorder that affects his sleep, leading to other complex behavioral issues. Aaron requires constant supervision, and the family often faces struggles throughout the day as a result.

The family has also watched as a growing number of patients have been diagnosed with this relatively new rare disease, which was first identified about 30 years ago. They wonder if the increasing incidence rate is due to greater awareness and testing or other reasons. The top specialists are, unfortunately, located hundreds of miles away, which limits the family's ability to see many of the key opinion leaders, specialists, and researchers.

From a long-term treatment perspective, Meredith and her husband are constantly searching for possible solutions that will provide Aaron with greater relief and normalcy. As new treatments are being tested and they anxiously await more options, time is spent reading blog posts, articles, and information put out by advocacy groups and posted on Facebook groups.

Owing to Aaron's age and challenges, his parents must make most of his healthcare decisions for him. Each time, they try to not only think about the immediate decision, but also anticipate what the next decisions might be. For them, it is all about education and making sure they have as much information as possible before making any decision for Aaron, with the goal of increasing his quality of life today while preparing for the future.

The family is particularly hopeful that the continued decentralization of trials and follow-up care solutions will make it possible for Aaron to receive more care delivered locally, participate in clinical studies that match his patient profile and needs, and provide more options for his treatment.

concepts and opportunities. We also work proactively with global regulatory bodies on each clinical study we support to ensure that the trial protocols meet their expectations and that the data generated will support product registrations.

Similarly, partnerships with vendors that understand the specific needs of rare disease patients participating in decentralized clinical trials can provide sponsors with a necessary edge and help them select the best solution for their trial. To improve patient recruitment, we also work closely with advocacy groups and others active in the rare disease community.

The Partner of Choice

Rare disease study sponsors are passionate about their programs and extremely knowledgeable about the disease(s) they are hoping to treat or cure. They seek an equally devoted CRO partner that can facilitate other aspects of the study process with the highest level of quality. These clients benefit from PPD custom solutions, particularly when it comes to patient recruitment and engagement in multiple countries (rare disease patients are often difficult to find and must be approached and managed differently from those in a study involving a large cohort of patients with a more common disease) and treatment of patients in non-traditional settings.

More than Just Incremental Changes to Our Offering

In the rare disease space, our therapeutic knowledge, combined with our leading digital and decentralized solutions, supports the seamless design and execution of innovative protocol designs. Our experience allows us to take less of a "bolt on" approach and instead leverage the full spectrum of tools, vendors, systems, and platforms to produce bespoke solutions tailored to patient and research needs, ideally with the PPD team being engaged during protocol development to ensure study design incorporates patient-centric solutions.

For instance, in the United States, we partner with remote clinical staff,

including nurses, nurse practitioners, phlebotomists, and qualified physicians who visit patients' homes to conduct assessments from basic physical exams to evaluations that require highly specialized techniques. For rare disease studies, this solution is another mechanism for taking the trial to the patient.

Our teams have also been instrumental in deploying mobile sites within recreational vehicles. This offering has been used extensively during the COVID-19 pandemic to recruit patients in remote settings or to reach those where an outbreak may be taking place.

Our patient-centered approach to innovation is helping increase the benefits of decentralization in rare disease clinical trials. In partnership with our dedicated centers of excellence, we continue to explore new ways to support this goal by offering a broad range of options for rare disease patients, including those that extend beyond conventional trial approaches. ■

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Francis Jones is a senior director in the consultancy, innovation and strategy group. His role is focused on supporting clients in developing strategies and trial designs focused on reducing patient burden and enhancing trial participation. A key approach to achieving this is incorporating digital and decentralised solutions (DCTs) into the study design and delivery strategy. Francis has more than 21 years' of experience working for pharma and CRO companies in a variety of roles, including operational and strategic leadership roles. He has led trial delivery across all study phases and across multiple indications and therapeutic areas (including rare disease and orphan indications), as well as working on successful new drug submissions and interactions with health authorities.

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Tim Rich serves as vice president and leads the consultancy, innovation and strategy group, which is a driving force behind the adoption of decentralized strategies while bringing forward novel solutions. Prior to his appointment, Rich was a member of PPD's biotech operational leadership group. In this role, he provided strategic direction, leadership, and management across multiple divisions and therapeutic areas by leveraging more than 20 years of experience in project delivery that covers a wide range of indications – including complex rare disease and gene therapy programs. Rich joined PPD in 2006, working in project management and eventually progressing to his current leadership role. In total, his experience spans a variety of areas in the clinical trial space, such as global project management, portfolio management, development operations, and client relationship roles.

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Meredith McCumbee serves as senior director within the clinical transformation group. Meredith joined PPD in 2004, working in various roles across clinical operations, eventually taking on leadership roles supporting business process and system optimization. She has provided leadership and change management strategy across multiple organizational changes, system implementations, and cross-functional process innovations. Meredith and her son, Aaron, are part of the PPD Heroes program, where together they share their family's medical journey in hopes to increase public awareness and encourage education about the crucial role clinical trials play in delivering life-changing therapies to patients.

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