CLINICAL LEADER

Guest Column | October 22, 2020

Ensuring Patient-Friendly Clinical Trials For Complex Disorders — A Small Biopharma's Playbook

By Erin O'Boyle, head of clinical operations, Rezolute, Inc.

Rezolute, a small company based in Redwood City, California, and working in the rare pediatric disease space, is developing a new therapeutic option specifically for patients with congenital hyperinsulinism (HI), an ultra-rare pediatric genetic disorder. For Rezolute, connecting and partnering with advocacy groups and physicians is paramount in clinical trial execution.

Hyperinsulinism's Effects On Patients

Children and adults with congenital HI produce excess, dysregulated insulin from the pancreas, which can leave them vulnerable to frequent, potentially dangerous episodes of low blood sugar if left untreated. During these episodes, infants might exhibit poor feeding, excessive sleepiness, irritability, and seizures; young children may feel tired, shaky, or show sweating or rapid pulse even at rest. When severe, repeated, or sustained, those low blood sugar episodes deprive the brain of essential fuel sources, which can cause serious complications including developmental delays, seizures, coma, or even death. Many patients must monitor their blood sugar on a day-to-day basis and may require a parent or other caretaker to aid with chronic disability. Currently, there is no approved treatment for congenital HI, and better treatment options are needed for the condition in all affected populations.

Rezolute's antibody candidate has a unique mechanism — it binds specifically and reversibly to a site on insulin receptors, dampening insulin's ability to bind and signal through its receptor. As the antibody counteracts insulin only to the extent that insulin is elevated at any given time, it still permits insulin to act at physiological levels without overcorrecting toward harmfully low insulin.

Complex, Rare Disease Presents Protocol Design Challenges

While preparing the drug for clinical trials, the Rezolute team minded the fact that participants with congenital HI would be contending with complications of the condition beyond daily blood sugar challenges: They might need parents or caretakers to transport them to trial site visits; pediatric patients might fear the inevitable blood draws collected for data points; and ensuring compliance with reporting symptoms might prove difficult for those patients with special needs. Additionally, congenital HI is so rare that trial participants must be recruited from around the world, with potentially as many languages spoken as participants enrolled.

By the time Rezolute initiated its latest trial, RIZE—a Phase 2b study—in February, the team had already spent years in close contact with key patient advocacy group Congenital Hyperinsulinism International (CHI) to internalize the personal impact of the disorder on all involved, including patients, their families, and their caregivers. Rezolute has attended family-centered conferences held by CHI to meet and learn from the CHI community. These conferences helped Rezolute explore and address ways the team could improve, to the extent allowed, its trial designs iteratively.

Rezolute collected all this information and worked diligently within the company and with various partners to update a protocol design and build a single data collection platform that would reduce barriers to participation in terms of study education, data collection, travel logistics, language preferences, and overall safety. The team coordinated with study laboratories and pharmacologists to reduce the number and volume of blood draws for data collection as much as possible from each patient population, including toddlers, children, and adults. This reduction helps decrease the overall burden on patients and ensures that collections are meaningful and limited to those that are absolutely necessary for the purpose of the study.

Medical Device Partner Helps Address Patient Needs

As the study requires frequent blood sugar readings as part of its primary endpoint, Rezolute considered ways to reduce stress around the continuous glucose monitoring (CGM) that is being utilized for the daily primary data collection. Of all available CGMs, the team opted to provide participants with the Dexcom G6 due to the fact that a finger stick calibration by blood glucometer was no longer required with the new CGM model, further reducing the burden to the patients and their families or care providers. Early in the study planning, in addition to partnering with Dexcom to source the device and ancillary supplies, Rezolute expanded the partnership with Dexcom to incorporate direct training from Dexcom's medical device experts.

Dexcom is helping train the clinical sites and the trial participants throughout the study, to optimize implementation of CGM for both participants and the company. Direct hands-on training has been critical for setting up the study data collection, maintaining consistency in training across the sites and patients and providing the sites and participants with an experienced resource to answer questions and offer advice when needed during the study. Patients can choose to either use their own glucometer, if they own one they're comfortable using, or a new glucometer provided for their use in the study.

Additional Steps To Minimize Patient And Caregiver Burdens

Rezolute also developed an electronic diary, or e-diary, for participants to use to self-report on important study metrics such as compliance with study procedures, glucose values and related clinical events, lifestyle factors, and medication interventions. Rather than a traditional hard-copy diary that leaves all the responsibility to the patient or care provider to remember to complete each day, the e-diary is prompted with helpful daily reminders and the participant's responses can be submitted instantly, so investigators, monitors, or sponsors can assess patients' well-being and compliance in close to real time. Additionally, the e-diary's prompts are designed with targeted questions soliciting straightforward responses, as opposed to often-seen open-ended questions that are onerous to answer and may not prompt meaningful input.

Participating in clinical trials is always complicated by necessary trial site visits, especially when a patient requires someone to accompany them, as is often the case for children with congenital HI. To offset the time and costs associated with travel, food, and lodging for trial participants and their caretakers, Rezolute offers patient concierge services for assistance to and from trial sites and during the visits themselves to reduce the overall financial and logistical burdens of visits.

Rezolute also considered investigators' perspectives, designing a straightforward, user-friendly pocket guide to simplify study protocol compliance across sites. The guide presents investigators' responsibilities as to-do lists with respect to progressive weeks of the study and offers data collection timelines and which materials are necessary at each collection, as well as best practices for sample shipping. Also included are specific reminders for investigators to send to patients about what to bring to the next visit and directing them to call the site with any questions, ensuring that patient-clinician communication remains open.

Moving Ahead Despite The Pandemic

Additional initiatives aimed at mitigating the risk of spreading COVID-19 have unfortunately become necessary since the trial's initiation. Rezolute now offers home health services for any drug safety evaluations and follow-up visits where it has regulatory approval to do so, for cases where the continuing pandemic prohibits patients from returning to the hospital since beginning their trial regimen.

A principal goal for Rezolute on the RIZE study, even before impacts from the global pandemic, was and still is continually engaging and communicating with all study sites. Due to travel restrictions, the company has had to cancel planned face-to-face time with study investigators and their site staff and replace those meetings with virtual meetings. The Rezolute team aims to ensure that the sites and the patients they will be treating feel important, valued, and protected.

Rezolute remains committed to being a patient- and site-centric company and will continue these efforts with an eye to the needs of the congenital HI community.

About The Author:

Erin O'Boyle serves as head of clinical operations at Rezolute, Inc., before which she accrued nearly 20 years of operational and management experience across all phases of development covering several therapeutic areas, including oncology, anemia, idiopathic pulmonary fibrosis, and rare disease indications. Prior to joining Rezolute, O'Boyle worked at Fibrogen, where she led all clinical outsourcing and governance activities from 2013 to 2018, successfully contracting and managing all vendors for each clinical department. Before transitioning to a clinical lead in both contracting and governance, she was the head of clinical operations at Heron Therapeutics from 2005 to 2013. O'Boyle obtained a bachelor's degree in biology from Stonehill College.