Evidence-Driven Feasibility Speeds Start-up for Global, Phase III, Gene Therapy Trials for Neuromuscular Disorder

Highlights

- Synteract provided feasibility as a first step for two global, full service, Phase III, rare, gene therapy studies
- The study faced multiple challenges, in age requirements, ancillary drug availability, and varying international requirements
- Synteract's feasibility analysis, regulatory knowledge and experience in gene therapy trials across countries and cultures greatly increases the enrollment success.

Introduction

Synteract is providing full services on two Phase III studies, starting with feasibility and site selection, for a rare, genetic, neuromuscular disorder that affects both children and adults. This disease is one of

the leading genetic causes of infant death, creating urgency for recruitment. Those who survive beyond infancy typically have a lesser form of the disease, with varying levels of disability and a variable rate of progressive decline. The hope is that the gene therapy will completely arrest the disease by fixing the faulty DNA, and the sponsor will gain approval and be able to market it in all the countries where trials took place.

- There are several different types of the disease with varying levels of illness; impacting the age at which death typically occurs.
- A broad age range of individuals are needed for these two studies – ranging in age from 6 months to 65 years old – so the studies will involve differing onset age, disease states and different types of the disease, with varying levels of disability.
- It will include patients who had tried standard treatments that simply delay progression (and who may not have responded well) and those who have never had any treatment at all.

Full-scale Global Feasibility Analysis to Identify Recruitment Challenges

- Global study (North America, Europe, Middle East, Asia Pac)
- Rare pediatric genetic disease study
  - Regulations for gene therapy are very different from standard clinical trials.
  - Gene therapy trials create a greater need for education (in multiple languages) and risk tolerance, especially in countries where acceptance and knowledge are quite varied.
  - Investigators and Study Coordinators must be willing to educate the patients at investigative sites.

- The need to find parents who are willing to put babies/small children on a clinical trial vs. trying the existing standard of care options.
- The long-term study design requires finding patients who are committed to stay with it.
  - Patients must commit to the study for 18 months of active study participation with an additional 7 to 15 years of follow-up.
- The broad age range requires:
  - Investigators who can handle the transitions that will need to be made throughout long-term follow-up, especially from childhood to adolescence and adulthood to seniors.
  - Multiple types of educational and legal materials, in a variety of languages, including assent and consent forms. In consent documents, parents must agree to an autopsy if their child dies.
- The diagnostic odyssey:
  - Variance in diagnosis and access to genetic confirmation of disease on a global and regional level.
    - Routine testing of infants varies globally - whether it's done, socially acceptable, reimbursed, etc.
    - On-label access to required ancillary medication, specifically in pediatric population, and via intrathecal administration route. Confirmed allowance of mixing with or without compatibility data
- Competitive landscape: One drug approved for the disease and potential for another drug to come to market.

Solutions: Evidence-Driven Feasibility Addresses Challenges and Supports Optimal Country and Site Selection

- Identified access to care in each country and at each site to ensure capabilities in place to meet rigor of trials. We identified:
  - Large academic facilities that treat both children and adults up to a certain age where two investigators would work together
  - Pinpointed access to patients by country
    - Disease prevalence and incidence, epidemiology, note the rareness
    - Those that are genetically testing babies in this disease
    - Those that have registries of patients who have this illness as implies an organized effort of opinion leaders, experts and families with disease awareness and care to solve the issue
- Competitive landscape: Understanding the changing marketplace at all stages of the trial is key.
  - We provided a thorough analysis of the competitive landscape, inclusive of, but not limited to, a review of planned and ongoing clinical trials and a list of available therapies per recommended country.
  - Countries with lower levels of competition have been prioritized
- Collaboration among clinical, regulatory and biometrics experts at Synteract to tap into disease experience, understanding of country and pediatric regulations, Genetically Modified Organism (GMO) specific considerations, site level knowledge, assessment of end-point, etc. to prioritize country/site selection.

- Collaboration with key stakeholders, including national and international advocacy groups, to improve access to patients and their families.
- Identified drug administration pitfalls to avoid:
  - The drug requires a highly specialized drug administration procedure coupled with concomitant medications that must be approved locally for pediatric use in order to be used in the clinical trial setting
  - We identified if the contrast media to be used is already available in the country – standard vs off-label
  - Prioritized the countries with sites that can procure and use it without delay
- Deployed communication strategies to enhance collaboration across investigators and sites due to broad age ranges within the trial.

Why Has Synteract Excelled in Helping the Sponsor?

- Deep understanding of this disease and patient community.
  - Understood the standard of care in each country, its approaches to this disease and knew where this treatment paradigm fit in the larger picture
  - Ongoing, real-time monitoring of the approved drug market, competitive trial landscape to proactively manage changes in study conduct if/as needed
- Customized, data and evidence-driven approach derived from variety of tools and subject matter input.

- Validated individual feedback on sites from CRAs through our country managers with local knowledge of sites, resulting in more thorough, strategic and robust country and site selection
- Compiled and prioritized in one tracking system all critical country and site selection metrics to drive decisions, identifying where contingency plans needed
- Many CROs don't do this level of customization; assessments are performed in a step-wise fashion with little deviation from study to study

Results:

- Enabled the sponsor to strategically select appropriate countries for the clinical trial where there were not only patients but a favorable regulatory environment, high likelihood of eligible patients, and logistically feasible drug administration due to access to contrast solution.
  - Detailed data visualization document with country and site-specific metrics that sponsor is using to support decision making
- Feasibility study allowed sponsor to identify potential marketing uptake risks and proactively address concerns regarding need for stability data if Investigational Product and contrast solution must be mixed.
- Positive feedback from expert sites around the globe as they have been able to plan for a successful trial and have had proactive discussions about potential hurdles. Solution-oriented discussions have yielded tailored solutions for each region and each study site.
  - Record engagement and responsiveness from sites globally

- Recommendations of final target country lists already achieved enabling Sponsor to proceed with regulatory submission activities in less than 4 months

About Synteract

Synteract®, a Syneos Health® company, is a leading full-service CRO focused on the emerging biopharma segment. The Company's multidisciplinary teams support biotech and pharmaceutical companies across all phases of drug development, providing deep expertise in oncology, dermatology, general medicine, infectious disease and vaccines, neuroscience, pediatrics, and rare and orphan diseases. Synteract has conducted nearly 4,000 studies on six continents in over 62 countries. To learn more about how Synteract is Bringing Clinical Trials To Life™ by transforming insights to action and making therapies a reality, visit synteract.com and connect on LinkedIn and Twitter.

For more information on how we can support your clinical trial, please visit https://www.synteract.com/Services/Feasibility or ContactUs@synteract.com.