ALTASCIENCES

CASE STUDY

Assessing the Safety of Novel Therapeutics for Pediatric Indications

BACKGROUND/OVERVIEW

A biotechnology company focused on developing a novel therapeutic intended for pediatric patients was mandated by the FDA to perform a complex, chronic safety study in 8-to 9-month-old juvenile nonhuman primates (NHPs) to fulfill regulatory requirements and further advance their molecule into the clinic. As pharmaceuticals undergo a technological revolution, and the range of possible therapies for rare diseases grows at a rapid rate, advanced therapy medicinal products (ATMPs) such as gene and cell therapies have shown enormous potential, particularly for inherited diseases. As such, pediatric patients may benefit enormously from these novel therapies which present very specific challenges in terms of nonclinical testing, and often require non-conventional approaches.

THE CHALLENGE

Studies in juvenile animal models bring a host of challenges, such as appropriate species selection and husbandry, along with a clear understanding of the study endpoints. Juvenile toxicity studies usually involve a large number of animals, numerous and diverse study endpoints, and often multiple cohorts of animals to adequately address study endpoints. With the many factors involved, each study must be designed and performed on a case-by-case basis, while ensuring adherence to the principles of the 3Rs (Replacement, Reduction and Refinement).

To meet the sponsor's needs and to comply with regulatory guidelines, Altasciences' experts provided:

- A well-constructed procedure and husbandry plan to support exemplary carefor the young age and size of the test system
- A customized route and duration of administration (IV infusion) given the ageand size of the animals
- Specific sample collection (logistics, numerous markers/parameters and volumerestrictions)

THE SOLUTION

From the onset of our interactions with the sponsor, clear study objectives and defined endpoints were established through continuous communication, including several face-to-face discussions to define and finalize strategies. Study-specific training guides were established for the specialized, age-related procedures required, and our technical staff received training on the procedures for months prior to the start of the study to ensure consistency, quality, and optimal care of test systems. Passive restraining techniques and gear were created (and adjusted with growth) to match the size of the test systems to ensure low levels of stress during study procedures. Specialists in areas such as behavior and enrichment were continuously involved in the development of procedures and husbandry configurations.

Surrogate, adult females were incorporated into the husbandry strategy (a nanny model) to ensure juvenile subjects had sensory awareness and stimulation from adults in their social housing environment, and the same technical team performing procedures was assigned throughout the study to create familiarity, and minimize potential stress caused by change. Enrichment in the form of treats, toys, and positive reinforcement were also incorporated into the study plan to further promote the welfare of the test systems.

RESULTS

Despite the unique study design, age, size, and other complexities presented by the test system, all study objectives were successfully accomplished. The extraordinary steps and measures in husbandry, animal care, and technical precision were clearly reflected in the outcome and results of the study. There was no evidence of stereotypical behaviors by the subjects and the data endpoints obtained indicate that stress was managed exceptionally well during the study due to the strategies and plans established prior to the start of study. Technical deviations were also significantly lower than expected (given the complexity of the study) due to the strategy, planning, and specialized training involved. The results obtained from this study allow the sponsor to confidently address regulatory requirements and potential questions as they continue to advance their molecule into late stage clinical trials.

SUMMARY

Developing cutting-edge therapeutics for rare diseases requires innovation, flexibility and a conviction that every challenge has a solution. Altasciences has a history of collaborating with sponsors to develop solutions to their challenges. The Altasciences team partnered with the sponsor to design and successfully perform a technically complex study in an NHP juvenile test system to advance a novel therapeutic that could one day save children's lives. By cultivating a strong culture of innovation and partnership, Altasciences leveraged its scientific knowledge, animal care, technical expertise to identify gaps and developed solutions with the sponsor to further advance life-saving therapeutics for pediatric patients in the clinic.

ABOUT ALTASCIENCES

Altasciences is a forward-thinking, mid-size contract research organization offering pharmaceutical and biotechnology companies a proven, flexible approach to preclinical and clinical pharmacology studies, including formulation, manufacturing, and analytical services. For over 25 years, Altasciences has been partnering with sponsors to help support educated, faster, and more complete early drug development decisions. Altasciences' integrated, full-service solutions include preclinical safety testing, clinical pharmacology and proof of concept, bioanalysis, program management, medical writing, biostatistics, and data management, all customizable to specific sponsor requirements. Altasciences helps sponsors get better drugs to the people who need them, faster.