Therapeutic Update

CTD Holdings supports three clinical trials using its proprietary hydroxypropyl betacyclodextrin product, Trappsol® Cyclo™, via intravenous (IV) administration over an 8 hour period. The phase I trial is nearing completion of enrollment. This is a randomized, double-blind trial to evaluate 2 doses of drug: 1500 mg/kg nd 2500 mg/kg. There is no placebo group. Patients participating in this trial are 18 years and older. They receive 7 doses of the drug over a 14 week treatment period. Outcome measures are safety, pharmacokinetics and pharmacodynamic measures, including markers of cholesterol metabolism. In Europe and Israel, a phase I/II trial is also nearing the completion of enrollment. Trial design is similar to the US study with several notable exceptions: an additional group of 2000 mg/kg is included in this trial; patients participating in this trial are 2 years of age and older; and patients receive 24 doses of the drug over a 48-week treatment period. Outcomes measures are similar to those in the US study, but they also include measures for drug efficacy based on the NPC Severity Scoring tool, SARA, MMSE and other standardized measures.

CTD has reported initial data on these two trials to NPC family conferences, scientific and health care professionals, and to INPDA on 4 occasions during 2019: WORLD (Orlando), INPDA (Lyon), NNPDF (Minneapolis), and NPUK's Interactive Workshop and Family Conference (Wyboston). Initial findings show that the drug has a positive safety profile when administered intravenously, with no permanent losses to hearing. Trappsol ® Cyclo ™ impacts cholesterol synthesis and metabolism, as measured by serum markers following IV dosing, mimicking findings in animal studies. In other words, the drug appears to lift cholesterol from lysosomes, allowing it to cycle through normal cellular processes. Initial examination of liver biopsy tissue with filipin staining shows clearance of cholesterol from the liver, again, in keeping with findings from animal models of the diseases. The drug also crosses the blood-brain-barrier and it persists at least until 12 hours post the start of infusion, the last time point at which cerebrospinal fluid samples were taken. Biomarkers under study in both trials include the neuron-specific molecule, tau, which appears to decrease in the CSF of NPC patients using Trappsol® Cyclo™ intravenously. Early efficacy data from 2 patients who completed the 48-week trial show improvement in NPC Severity Scores by 3 points in total. The company is encouraged by these initial findings and looks forward to unblinding data at the conclusion of both trials.

An extension study for the US trial is underway allowing CTD to continue to collect safety and efficacy data for patients participating in that trial. This study is distinguished from the parent trial in that patients receive IV dosing at home, with periodic visits to the parent site for clinical assessments. An extension study is planned for the Europe/Israel trial participants using the same home infusion paradigm.

CTD is currently designing the pivotal trial for NPC and plans to meet with regulatory authorities in the coming months to discuss key features of the pivotal trial design.

In addition to formal clinical studies of Trappsol® Cyclo™ in NPC, the company supports a limited expanded access program with patients using the drug in countries across Europe, Brazil, Taiwan, and the United States. CTD monitors safety of the patients and works with physicians to collect efficacy information to the greatest extent feasible.

CTD meets with NPC families to understand challenges and needs of the community at every appropriate opportunity. In 2019, CTD hosted an event on the margins of the NNPDF conference to meet with NPC patients, families and caregivers to hear about challenges with daily living as well as to hear how families receive information on trials. CTD participated at the Patient-Focused Drug Development conference held in March 2019 (Silver Spring, MD) along with other industry representatives, using the opportunity to learn about disease features most important from a patient-perspective as drug therapy targets.

CTD supports the International Disease Registry project, INPDR, through its active participation in the Working Group for Industry Partners.

On the Personnel Front: CTD is pleased to have brought on board Michael Lisjak as its Global Head of Regulatory Affairs and Senior Vice President for Business Development. Mike has had a lengthy career managing the regulatory activities and interactions with global health authorities for both large and small companies, most recently at Sanofi Genzyme where he was responsible for regulatory matters in the lysosomal storage disease area as well as in the general medicines and global health therapeutic areas. Join us in welcoming Mike!

In a closing note - We continue to be grateful to all the patients and families who are participants in our current trials. We recognize the enormous time commitment that families make in order to participate in any clinical trial, and we are deeply appreciative. We also thank the physicians at each of our clinical sites who work tirelessly to advance our studies, knowing that clinical trials are an added responsibility on top of all other clinical responsibilities. Thank you all!
