Therapeutic Update

Trappsol® Cyclo™ Development Program

The Cyclo Therapeutics, Inc. team is pleased to provide this update on progress in its drug development program using Trappsol® Cyclo™ for Niemann-Pick Disease type C (NPC). Cyclo Therapeutics is a clinical-stage biotechnology company that develops cyclodextrin-based products for the treatment of Niemann-Pick Disease Type C1 (NPC1) and Alzheimer's Disease. Our drug development programs are based on intravenous infusions of our proprietary hydroxypropyl beta cyclodextrin product, Trappsol® Cyclo™.

We are hard at work readying to launch our global pivotal clinical trial, and we expect to announce inclusion and exclusion criteria and other features of the trial, along with the location of our sites, in the near term. We are aiming to have First Patient In by the end of this year – so the pace of the work is very high!

We were pleased to have two recent opportunities to present on progress in our clinical trials, both at the NNPDF meeting in the US (July) and at the NPUK meeting for the UK (September). While we missed seeing everyone in person, the virtual platforms allowed us to share updates and to hear from many of you.

Our 14-week Phase I study in the US has now been completed. We reported on the positive safety profile and a range of biomarker data showing that Trappsol® Cyclo™ reduces the burden of cholesterol in the liver and that it impacts cholesterol synthesis and metabolism. We shared findings on a biomarker of neurodegeneration in the brain, tau, showing that successive infusions of our drug reduce this marker in the majority of patients who participated. Our 48-week Phase II trial is still ongoing and is expected to be completed in early 2021. For the seven patients who have completed the trial, six met the first efficacy outcome measure, namely improvement in two domains of the 17-domain NPC Severity Scale. In addition, 5 of 7 patients were reported by their clinicians as having improved at some level, and 2 of the 7 were stable. The safety profile in this 48-week trial is favorable, and biomarker data confirm target engagement, including in the central nervous system: in 3 patients who opted to have lumbar punctures at 24 weeks of 48 weeks, the biomarker tau was reduced, similar to that of our Phase I trial. The tau findings suggest that the drug is having a neuroprotective effect. For more information on the Phase I and Phase I/II trials, see NCT02939547 and NCT02912793.

All patients who completed the Phase I study opted to participate in the Extension Protocol (NCT03893071) (US-based patients) or to continue on the drug through Compassionate Use programs in their home countries (non-US patients). We are working with physicians in our

Phase II trial and regulators to allow patients who have completed to remain on the drug. Many are accessing the drug in this fashion and we are working to ensure that all patients have continued access until the drug has market authorization.

We are grateful to the NNPDF for providing us an opportunity to meet with NPC patients and families over the summer and as part of the lead-up to the NNPDF annual meeting. With our colleagues from Worldwide Clinical Trials, we gained new insights into the patient journey. Our gratitude goes out to the NPC patients and families who spent time with us. Because of your efforts, our pivotal trial design was strengthened.

We will continue our tradition of transparency as we launch the pivotal trial and in sharing data from the trials leading to the pivotal. As always, we will keep the NPC advocacy groups informed at every step, and we are ever grateful for the support of so many of these groups in sharing our trial information. We recognize as well the many physicians who support our drug development program, including Dr. Caroline Hastings and Dr. Benny Liu in the US, as well as Dr. Reena Sharma and Dr. Julian Raiman in the UK; Dr. Orna Staretz-Chacham and Dr. Ronen Spiegel in Israel; and Dr. Martin Paucar-Arce in Sweden. We look forward to expanding this network of experts in the pivotal program!

Physicians interested in learning more about our pivotal trial should be in touch with Dr. Sharon Hrynkow, Cyclo Therapeutics' Chief Scientific Officer and Senior Vice President for Medical Affairs at Sharon.Hrynkow@cyclodex.com.

With warm wishes from the team at Cyclo Therapeutics!
