



Dr Thomas Joudinaud
CEO Ceres Brain Therapeutics
ICM, Hôpital La Pitié-Salpêtrière
47 Bd de l'Hôpital, 75013 Paris, France

To the ACD Community

Paris, February 2nd, 2023

Dear Members and Friends of the Association for Creatine Deficiencies (ACD),

We hope that this letter finds you and your families well. We wanted to update you on our program for Creatine Transporter Deficiency.

As you know, Ceres Brain Therapeutics is developing a novel drug that allows the delivery of creatine to brain neurons.

Since our inception in 2019, we have conducted numerous studies demonstrating the potential efficacy of our molecule in Creatine Transporter Deficiency syndrome. Indeed, Ceres' lead compound has demonstrated significant cognitive improvement associated with creatine delivery in brain neurons and improvement of brain plasticity in two different animal models of Creatine Transporter Deficiency (genetically modified mice from Dr Matthew Skelton's lab in Cincinnati and from Dr Laura Baroncelli's lab in Pisa University in Italy). These results have been published in peer-reviewed journals.

Ceres' compound will be delivered by a nasal spray. From the nasal cavity, the compound penetrates the olfactory and trigeminal nerves leveraging the specific anatomy of the nasal cavity to directly reach the brain neurons and diffuse in all brain areas to deliver creatine.

Since mid-2021, Ceres has been focused on ensuring our drug can be safely produced, at scale, in line with all pharmaceutical industry regulations, in Europe and in North America. As of today, we have been able to manufacture more than 60kg of our drug, with all required pharmaceutical key characteristics.

Ceres is now working on the different studies required by the regulatory authorities to obtain the authorization to test its medicine in human patients, mainly safety studies. These studies will also help to predict the right dosage for the future patients.

We are fully focused on these next steps which are essential to protect the patients according to the first rule in medicine "primum non nocere" or "First, do no harm".

We hope that we will be able to begin the clinical studies next year, first in healthy volunteers. Then, our objective will be to conduct the future studies in patients in several centres in Europe and in North America. To prepare these future studies, the works of ACD and Xtraordinaire are an irreplaceable source of insights and connection to the community of patients and their family. Thank you very much Heidi and team! We are also grateful to all the medical doctors and key opinion leaders who are working with us to define the relevant methodology.



We are confident that our drug will bring a significant improvement to the health of children affected by Creatine Deficiency Syndromes, whilst being easy to administer on a daily basis, via nasal spray.

Our historic investors – friends, family, and business angels - have continued to support us this year and we thank them for their trust and help. We look forward to raising funds from venture capital firms in coming years as well.

All Ceres' team remain committed to the patients and their family, and we look forward to seeing you in Paris in September for the next annual meeting.

Sincerely,

Thomas