



Dear Angelman Syndrome Community,

We are writing this letter to share with you an update on our progress towards initiating our clinical trial in people living with Angelman syndrome. Last year was incredibly difficult on so many levels, and while 2021 will continue to have its challenges, we remain hopeful that our lives will begin to return to normal, and that there will be many great advancements towards a treatment for those living Angelman syndrome in the year ahead.

As we announced in December 2020, we anticipate starting our clinical trial in the latter half of 2021, and we remain on track to meet that goal. We are completing the necessary preclinical studies with our lead compound and we are confident that we have selected best compound to take forward as a potential treatment for the broadest Angelman syndrome population. We have also begun preparing for the operational activities to launch our clinical trial. Some of those activities include discussions with local regulatory authorities in the US and other countries, site identification, as well as the development of Angelman syndrome specific tools, to create optimal opportunities to capture and measure potential participant changes that may be seen in the clinical trial.

We are on track to initiate the global Phase 1-2a study later this year. The study will enroll up to 50 participants, and it will include a broad age range from young kids to adults. The primary goal of this first study is to determine the safety and tolerability of our drug. The study will include several clinical assessments completed at the clinic visits, as well as questionnaires that the parents or caregivers will complete at home.

We understand that it's vitally important to communicate often with the community and we are committed to providing regular updates on our progress. Our goal is to keep you informed on the clinical trial process, the activities related to the study start up, and the expected timelines.

We are very grateful to all families who volunteer to take part in research and drug development efforts. Only with your support can we advance potential therapies towards clinical trials. We look forward to continuing our remarkable partnership with the community as we advance towards a treatment for Angelman syndrome.

Sincerely,
Ionis Angelman Syndrome Team