Dear Canavan community members,

The Aspa Therapeutics team would like to share some preliminary observations from CAN*aspire,* Aspa's clinical trial of intravenous (IV) AAV9 gene therapy for Canavan disease. As a reminder, the aim of Aspa's investigational gene therapy is to provide a healthy copy of the *ASPA* gene in order to restore the function of ASPA protein that is missing or impaired in Canavan disease. The lack of ASPA protein activity in Canavan disease prevents breakdown of a substance called N-acetylaspartic acid (NAA), leading to extremely high levels of NAA in the brain and other parts of the body. After treatment, the measurement of NAA levels in different locations in the body can tell us whether ASPA protein is now present and doing its job to break down NAA --- and if so, where and how much. The hope is that restoring ASPA protein function will ultimately lead to improved brain development and function in children with Canavan disease.

While it is too early to comment on potential clinical or functional effects of our investigational gene therapy, thus far there has been no reported new onset or worsening of epileptic seizures that are a common feature of Canavan disease and tend to intensify over time in most patients.

An initial comparison of CAN*aspire* participants' pre- and post-treatment NAA levels shows a substantial decrease in NAA in the cerebrospinal fluid (CSF, the fluid bathing the brain and spinal cord). These CSF results are consistent with NAA reductions seen in the brain itself as measured by magnetic resonance spectroscopy (MRS), a kind of brain imaging. Reductions in NAA in the urine have also been observed. Taken together, these findings are consistent with the presence of functional ASPA protein in the brain and other parts of the body; however, the results are preliminary and require confirmation based on more participant data and longer follow-up. The treatment also has shown a favorable safety profile to date and has been well tolerated with no serious events either related or unrelated to the treatment.

The Aspa Therapeutics team is encouraged by these initial findings and wanted to share them with the community as we pledged to do at the outset of CAN*aspire*. However, we all must remember that the trial is still in its early days and no conclusions can be drawn from the results thus far. We look forward to updating the community as the trial progresses and as we obtain more data on current and future study participants.

Please feel free to reach out to patientadvocacy@aspatx.com with any questions. More information about Aspa's gene therapy program for Canavan disease and the CAN*aspire* trial can be found at www.treatcanavan.com.

Sincerely,
The team at Aspa Therapeutics, a BridgeBio affiliate company