BRIDGEBIO

November 17, 2026

Dear Canavan Community,

The team at Aspa Therapeutics, a BridgeBio company, would like to provide you with an update about CAN*aspire*, our clinical trial of the investigational gene therapy BBP-812 in development for the treatment of Canavan disease. Thus far, 18 participants have received the investigational therapy, 10 participants at the high dose and 8 at the low dose. All participants had genetic testing confirming mutations in both copies of the *ASPA* gene. Children whose *ASPA* mutations are known to be associated with a milder form of Canavan disease are not eligible for the trial.

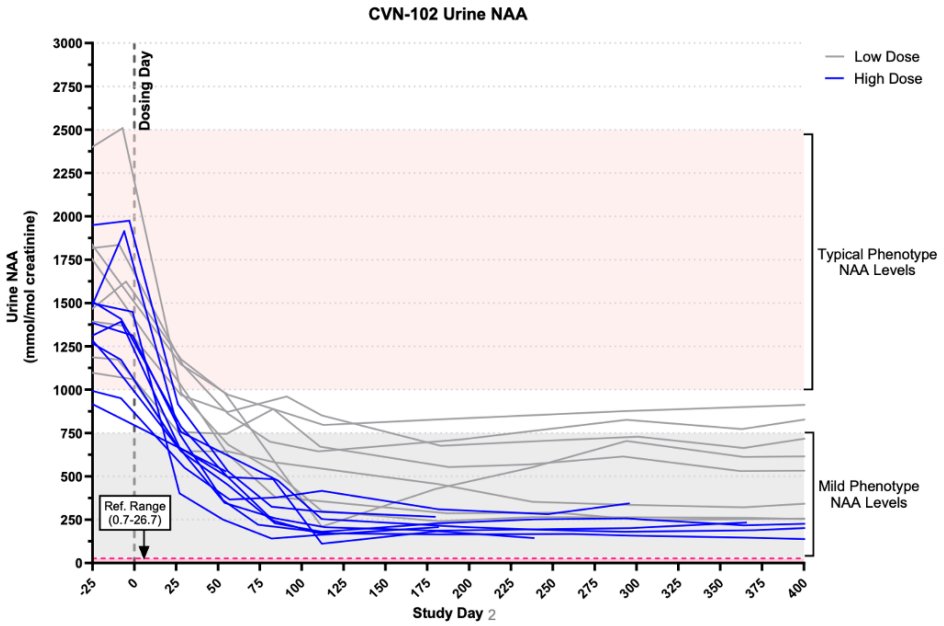
During recent manufacturing of our study drug, the contract vendor that manufactures BBP-812 for us made several mistakes. Because of those mistakes, the material didn't meet our quality standards, so we will not be able to use it for future dosing. These mistakes were not observed in prior manufacturing of BBP-812 and thus there is no impact to previously dosed participants in the study. Manufacturing BBP-812 takes many months, and even more time is required to test against our quality standards. That expected timeline was extended further because of the investigation into determining what went wrong. We are now making a new batch so that dosing in the study can continue and we anticipate that dosing will resume in mid-2027.

We fully understand this is disappointing news and share in the frustration that the manufacturing delays may result in some children no longer meeting the age requirements to participate in the clinical trial. Families who have expressed interest have been notified of the manufacturing delays and the impact on resuming dosing. We are working closely with our manufacturer to produce new material as quickly and as safely as possible, without compromising quality standards. As soon as we have more clarity on timing, we will inform the community.

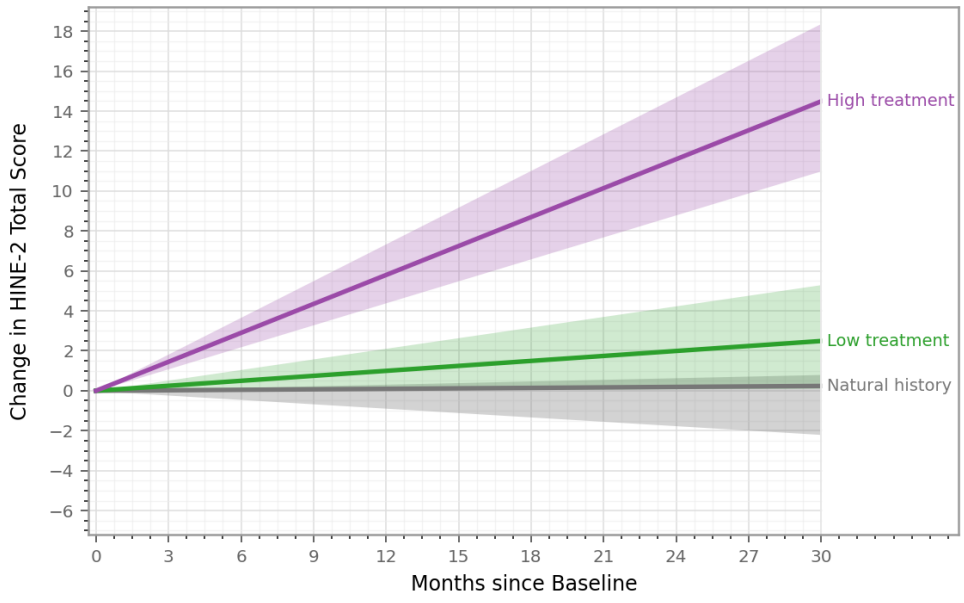
While the manufacturing delay is disappointing news, participants in the clinical trial continue to have their planned follow-up visits and are demonstrating evidence of efficacy in a number of different dimensions. A summary of the learnings, most recently presented at the 48th Annual National Tay-Sachs & Allied Diseases Association (NTSAD) Family Conference is below:

- **Biomarker Changes: N-acetylaspartate (NAA)**
    - The CAN*aspire* clinical trial measures NAA levels in the urine, and in the brain using magnetic resonance spectroscopy (MRS). Elevated NAA levels are a key chemical marker in children with Canavan disease.

- All participants experienced a rapid and lasting reduction in NAA levels in both urine and brain MRS measurements. Urine NAA levels for the high dose participants are lower than those of low-dose participants and nearly all participants' NAA levels decreased to a range consistent with what the literature classifies as mild Canavan disease (Nagy et al., *Human Gene Therapy* 2024).



- **Functional Impact: Hammersmith Infant Neurological Examination, Section 2 (HINE-2)**
  - The HINE-2 is a motor function assessment tool that assesses eight different motor skills: voluntary grasp, head control, kicking, rolling, sitting, crawling, standing, and walking.
  - Preliminary data show that children dosed with BBP-812 have improved motor function over time (green line = low dose, purple line = high dose) compared to natural history (gray line).



- **Safety Findings:**
    - Gene replacement therapies come with risks. Safety findings experienced in the investigational gene therapy trial are consistent with known safety risks with other IV administered AAV gene replacement therapies.
        - All participants had at least one adverse event, most mild or moderate and unlikely or not related.
        - As of our most recent data cut, 30 serious adverse events (SAEs) had been reported in 16 of the 18 participants:
            - 9 were considered likely related to BBP-812, including: elevated liver function tests (LFTs), low platelets (thrombocytopenia) and thrombotic microangiopathy (TMA), involving damage to small blood vessels.
            - 1 was considered possibly related to BBP-812.
            - 20 were considered unrelated to BBP-812. One participant passed away which was determined to be unrelated to BBP-812.
    - All serious adverse events thought to be related to the investigational therapy have been resolved.

Aspa Therapeutics remains committed to the Canavan community and is dedicated to making BBP-812 available to families. We are grateful for the continued partnerships with advocacy organizations and families as we continue to work together to create a potentially transformative therapy for people living with Canavan disease. For more information on common manufacturing questions, please see the article "Manufacturing Matters" by the American Society of Gene & Cell Therapy available here: https://patienteducation.asgct.org/research-clinical-trials/community-quick-takes/manufacturing-matters. Questions and comments are welcome. Please write to patientadvocacy@aspatx.com.

Sincerely,

The Aspa Therapeutics Team