# Aspa Therapeutics' BBP-812 Gene Therapy Program for Canavan Disease

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**02 June 2023**

NTSAD ANNUAL FAMILY CONFERENCE

US—2300056 20230523

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- Overview of Aspa's gene therapy program for Canavan Disease
- Overview of CANinform natural history study
- Background on Aspa's investigational gene therapy, BBP-812
- CANaspire gene therapy clinical trial
  - Study design, eligibility, and requirements
  - Study sites
  - Update on recent results
- Question and answer session

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**BBP-812 has not been approved by the FDA or any other regulatory authority as its efficacy and safety have not been established.**

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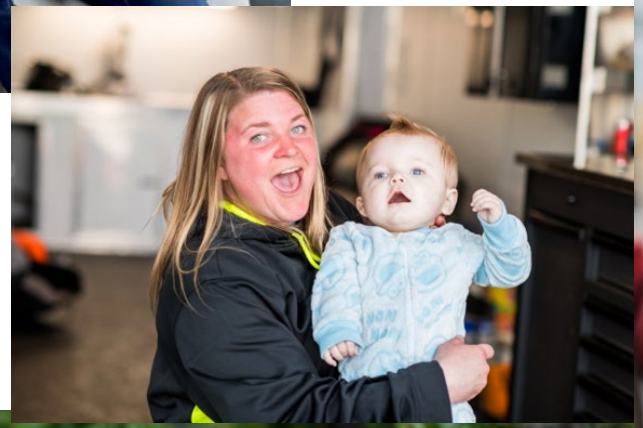
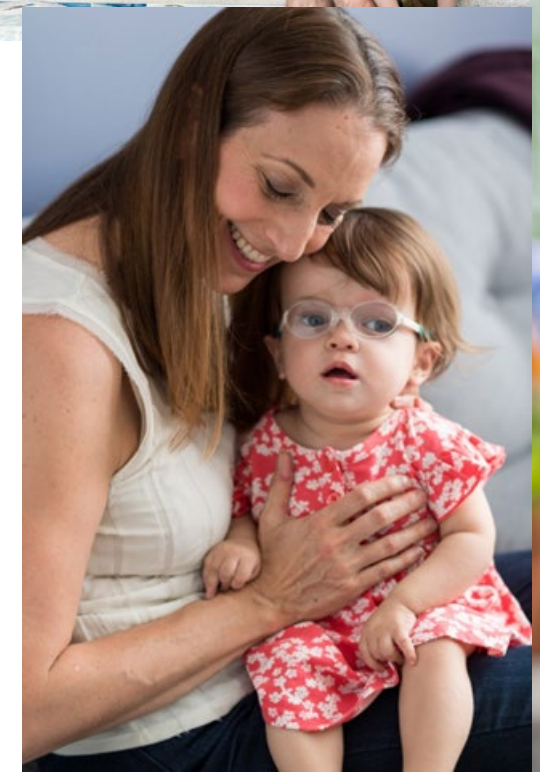

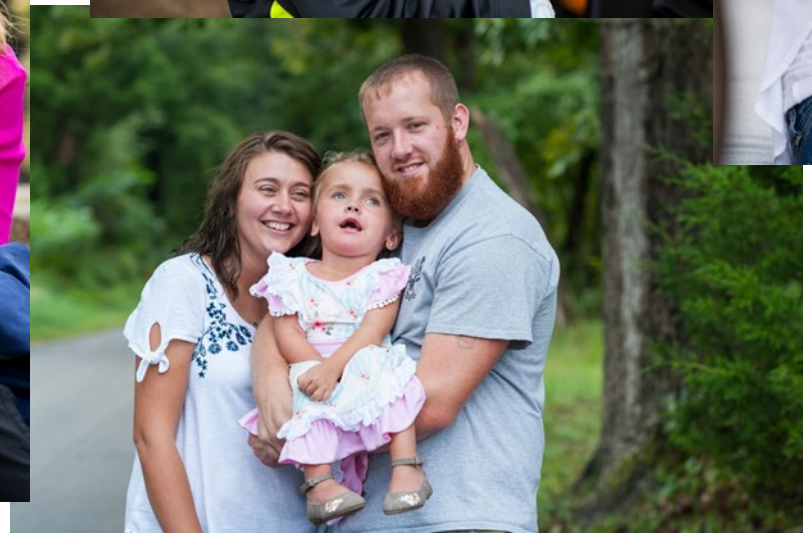










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CANinform

Natural History Study

CANaspire

Gene Therapy Clinical Trial

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# CANinform

## Canavan Disease Natural History Study

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CANinform

Natural History Study

**RETROSPECTIVE**

*Medical Record Review*

**PROSPECTIVE**

*Direct Assessments of Child (optional)*

- Anyone with a diagnosis of Canavan disease, living or deceased, is eligible to participate
- Study consists of medical record collection and data extraction (retrospective – all participants)
- Periodic motor, developmental and neurological assessments of enrolled patients (prospective – opt-in)
  - Most assessments done remotely via video
- No cost to participate

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# CANinform Natural History Study: Worldwide Participation

55 Participants* Enrolled from 14 Countries

- Australia
- Austria
- Bulgaria
- Egypt
- Germany
- Hungary
- India
- Israel
- Panama
- Poland
- El Salvador
- Switzerland
- Syria
- Turkey
- Ukraine
- USA

*As of 18 May 2023

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# CANaspire

Gene Therapy Clinical Trial

# Overview

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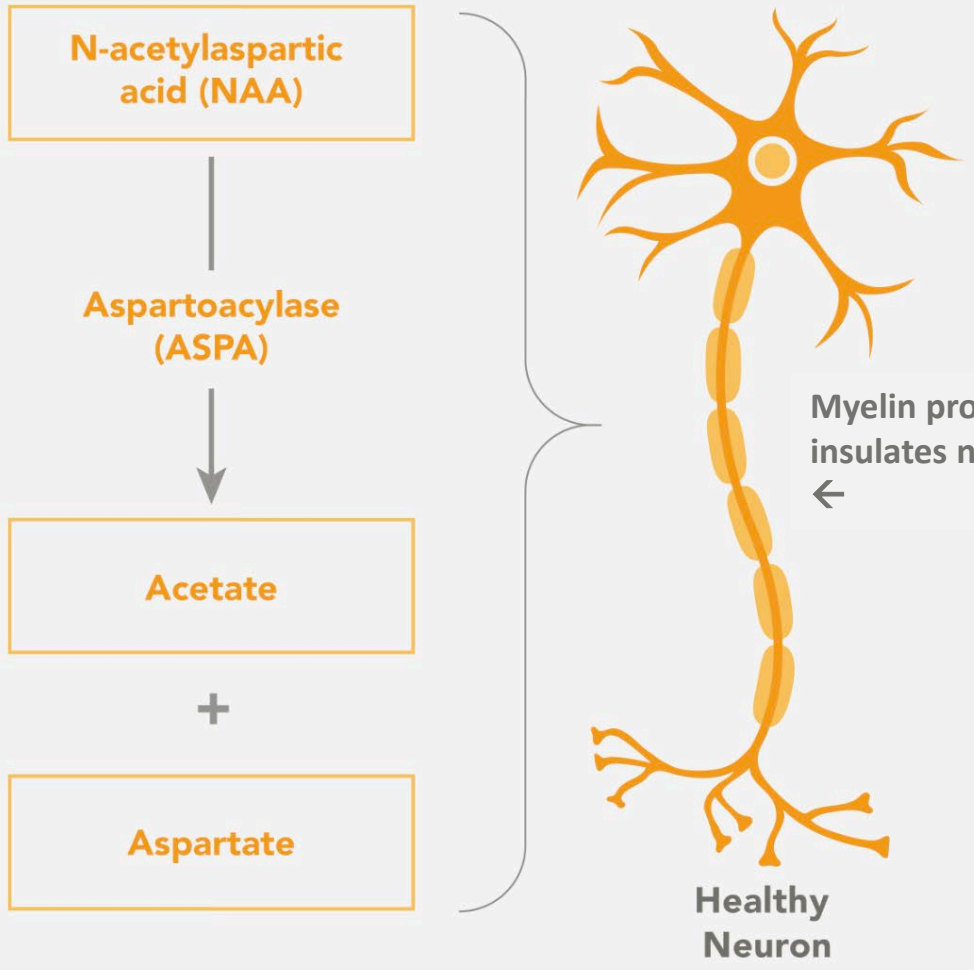
## Without Canavan Disease

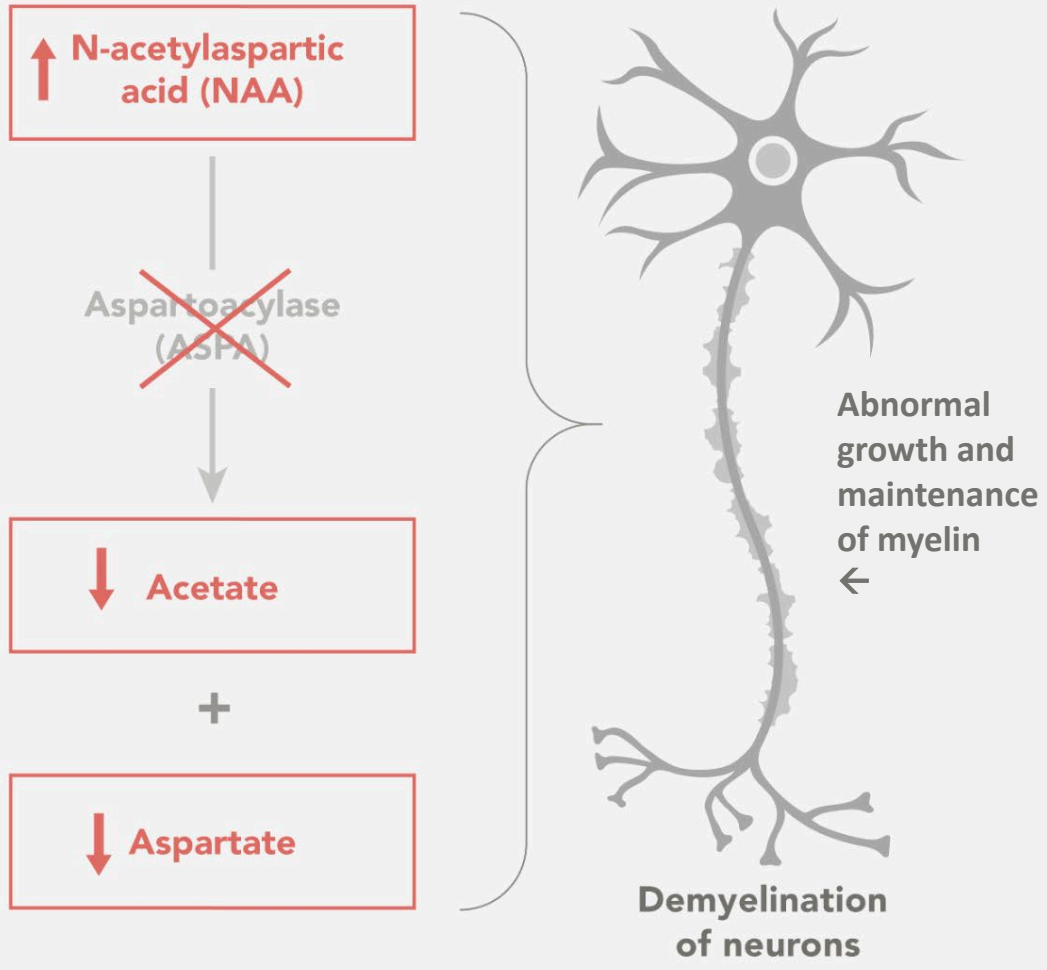
ASPA Enzyme Present




Healthy neuron

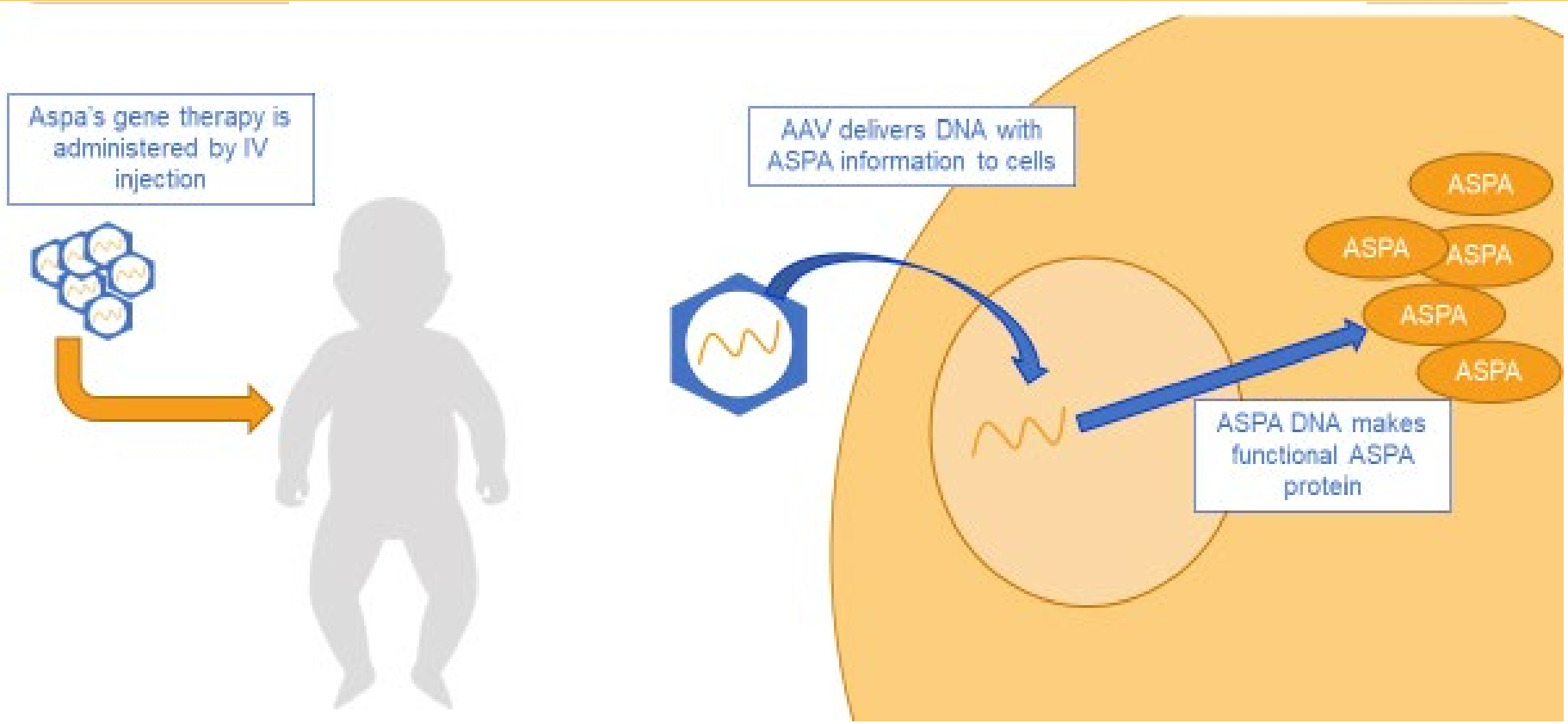
## With Canavan Disease

ASPA Enzyme Absent




Neuron's health and function impaired

# BBP-812, Aspa's Investigational Gene Therapy: Overview


If functional ASPA protein is made, this should result in decreased levels of NAA

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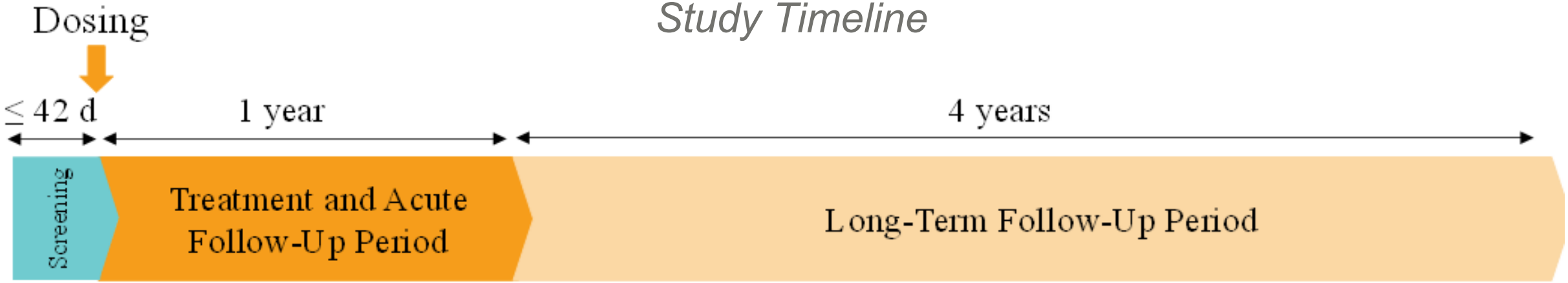
# A Phase 1/2 First-in-Human Study of AAV9 Gene Therapy for Canavan Disease

*Study Timeline*




- **Open-label study**
  - ***All eligible participants receive a single IV infusion of BBP-812***
  - Goal is to use data from untreated patients in CANinform natural history study for comparison
- **Objectives**
  - ***Learn about BBP-812 safety and tolerability:*** adverse events; laboratory tests; physical, neurological and eye examinations; ECGs; spinal taps
  - ***Is it having an impact on the disease?*** NAA levels, motor / developmental assessments, imaging (MRI, MRS), quality of life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# Eligibility and Study Requirements

- **Patient Eligibility**
  - Confirmed diagnosis of Canavan disease including 2 abnormal copies of the *ASPA* gene
  - Otherwise medically healthy with generally normal lab tests
  - Early stage of disease
  - Negative for pre-existing antibodies against AAV9
  - No active viral or bacterial infections
  - Family willing and able to participate in study visits for 5 years

- **Study Requirements**
  - Corticosteroids for at least 3 months before tapering
  - Imaging and spinal taps; require anesthesia & COVID-19 testing
  - Frequent blood draws



https://clinicaltrials.gov/ct2/show/NCT04998396

# Current Study Sites

**Mass. General Brigham**
**Boston, MA, USA**

**Florian Eichler, MD**


**UCSF Benioff Children's Hospital**
**Oakland, CA, USA**

**Alexander Fay, MD**

**Weill Cornell Medicine**
**New York, NY, USA**

**Eric Mallack, MD**

https://clinicaltrials.gov/ct2/show/NCT04998396

CANaspire

Gene Therapy Clinical Trial

# Current Results

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# Important Disclaimers

*The following slides show early data from Aspa's investigational gene therapy BBP-812 which has not been evaluated as safe and effective by the FDA or other regulatory authorities.*

*These data are insufficient to determine whether reductions in NAA levels will be associated with clinical benefit to patients.*

*Early data from certain participants in the open-label trial are not necessarily indicative of future or final data from clinical trials.*

# CANaspire Current Safety Understanding

As of May 19, 2023 :

- 6 study participants have received Aspa's investigational gene therapy BBP-812
- Intravenous (IV) infusions of BBP-812 have been well-tolerated (no infusion reactions)
- All participants had at least 1 adverse event (AE); the majority were mild or moderate in severity and considered unlikely or not related to BBP-812
- 5 serious adverse events (SAEs) were reported in 3 participants; all were considered unlikely or not related to BBP-812
- To date, the safety profile of BBP-812 has been consistent with other AAV9 gene therapies given IV

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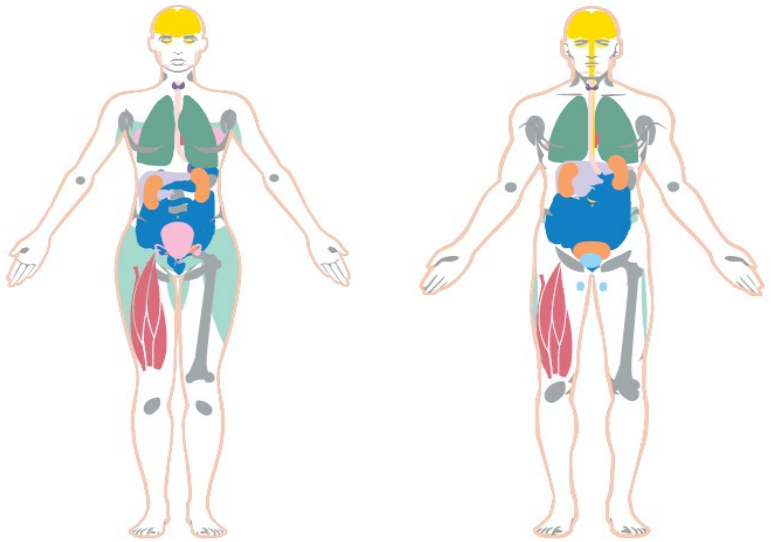
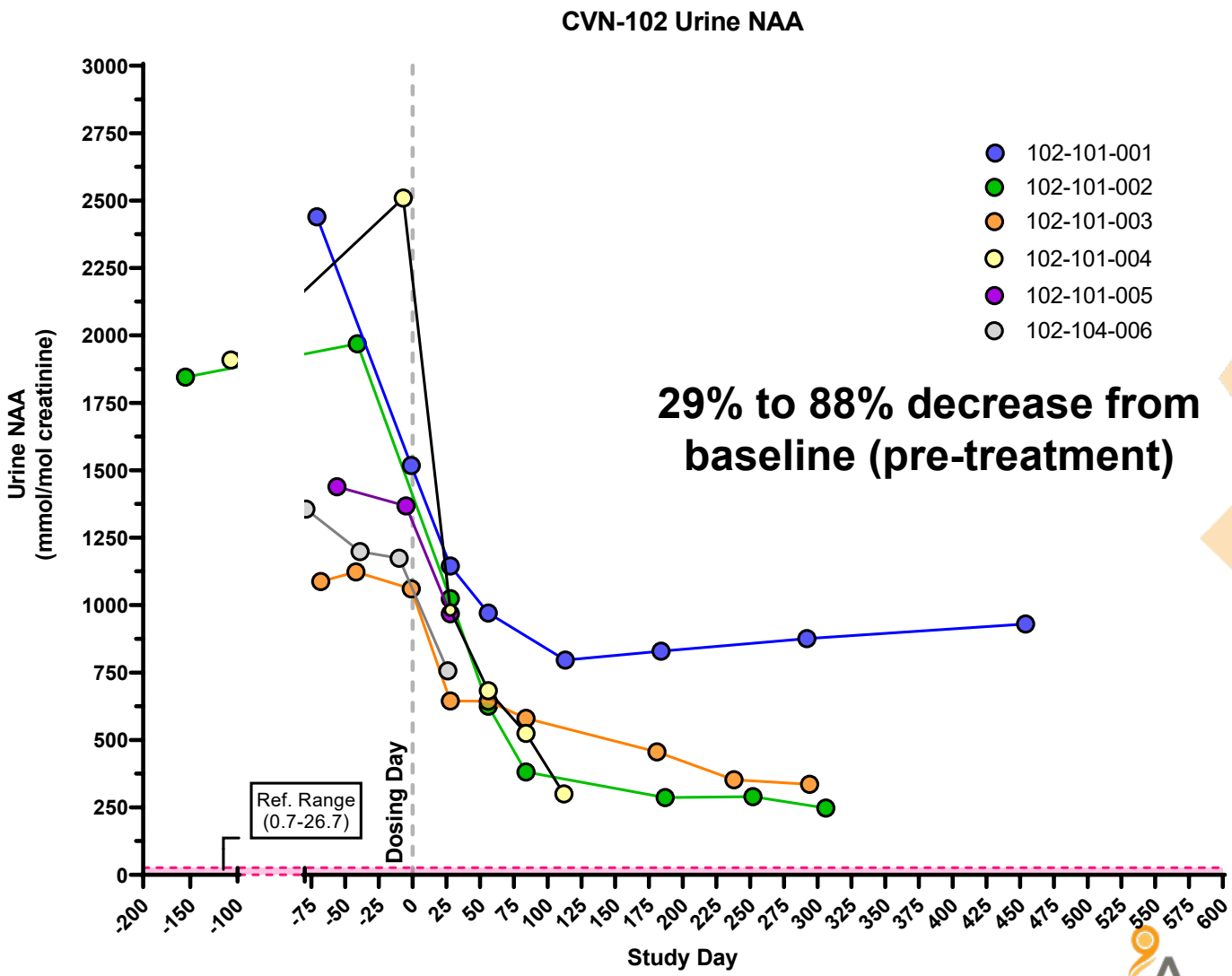
# NAA Levels – Urine

## Urine



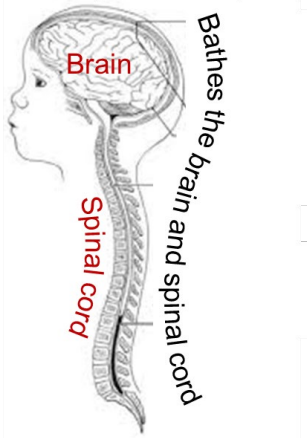
NAA in **entire body**



# NAA Levels – Cerebrospinal Fluid (CSF) and Brain by MR Spectroscopy

## CSF NAA

Cerebrospinal fluid (CSF)

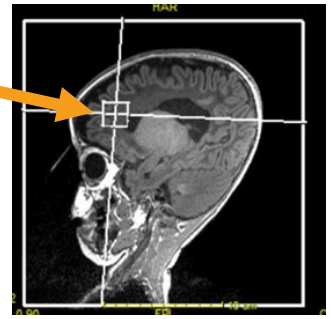






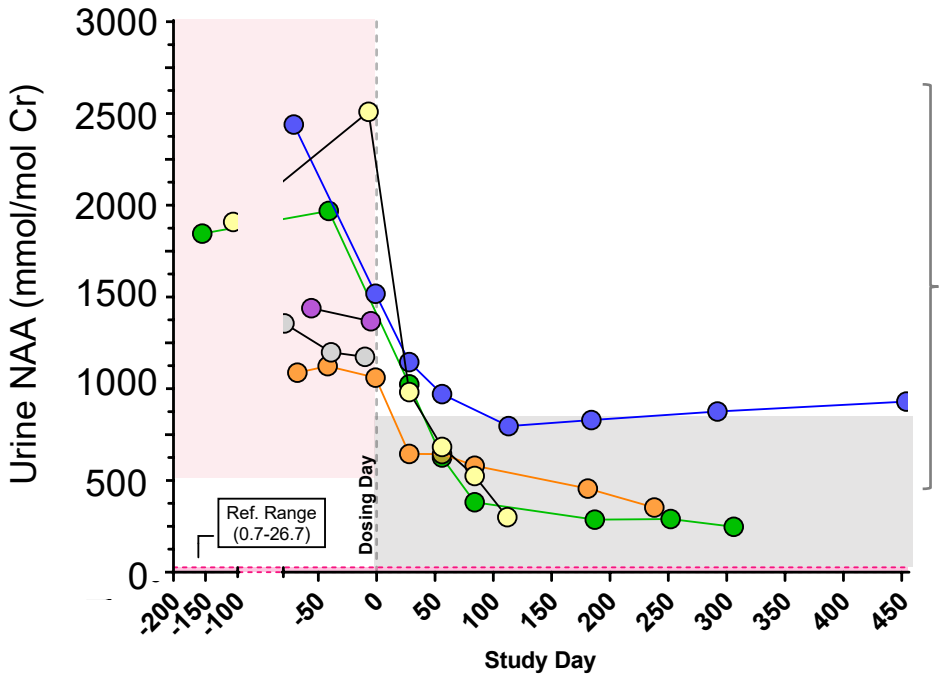
## Brain MRS

*Right Frontal White Matter*



# Lower NAA Levels May Be Associated with Less Severe Disease

***Post-treatment: NAA levels decreased to less severe range***




## NAA Levels for Typical and Less Severe Canavan Disease Obtained from Natural History

- Consolidated NAA data from CANinform natural history study, pre-treatment in CANaspire and review of scientific literature
- Less severe Canavan disease defined as ability to pull to stand
  - ~10% of natural history study participants

**Pre-treatment: all NAA levels in typical range for Canavan disease**

**Post-treatment: NAA fell to levels associated with less severe Canavan disease**

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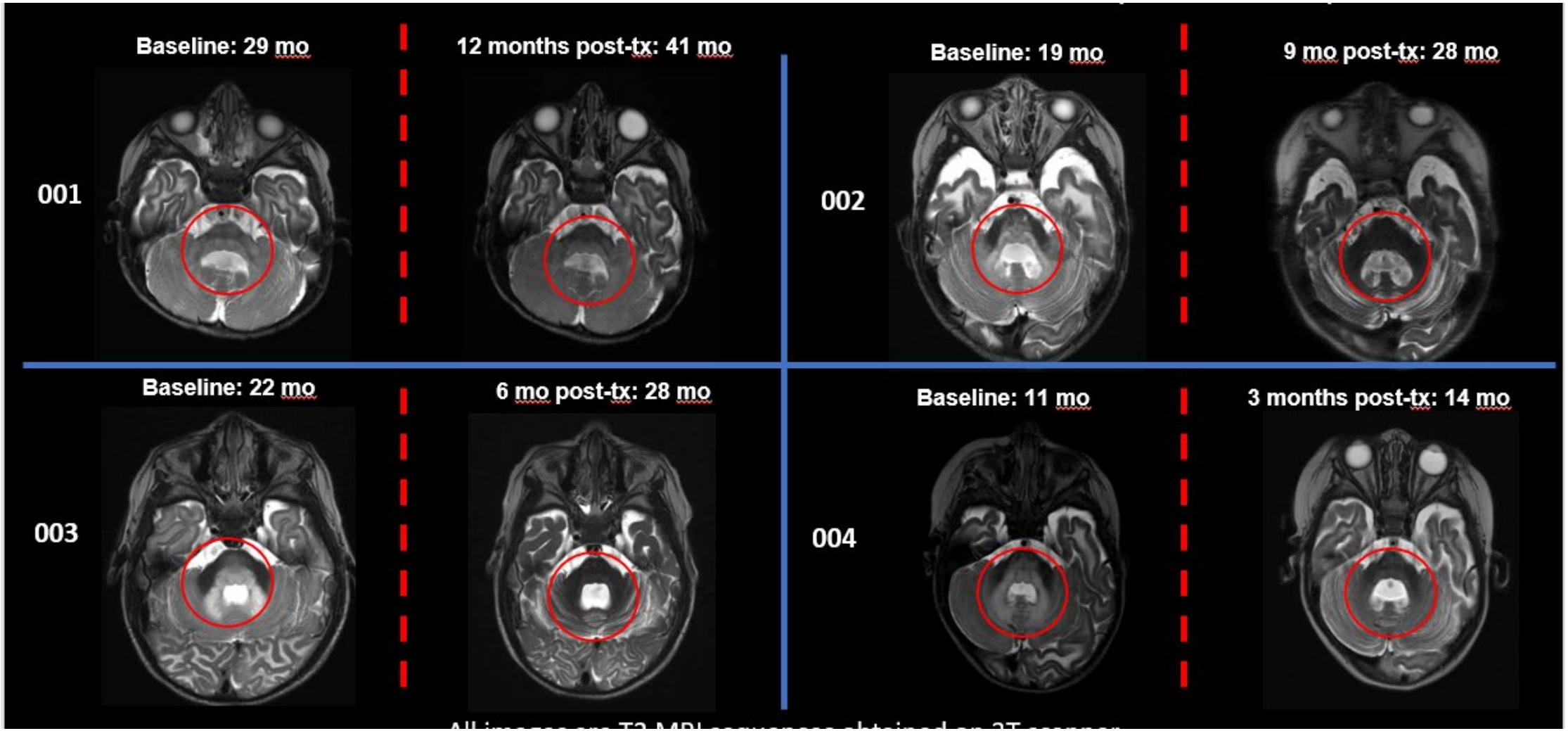
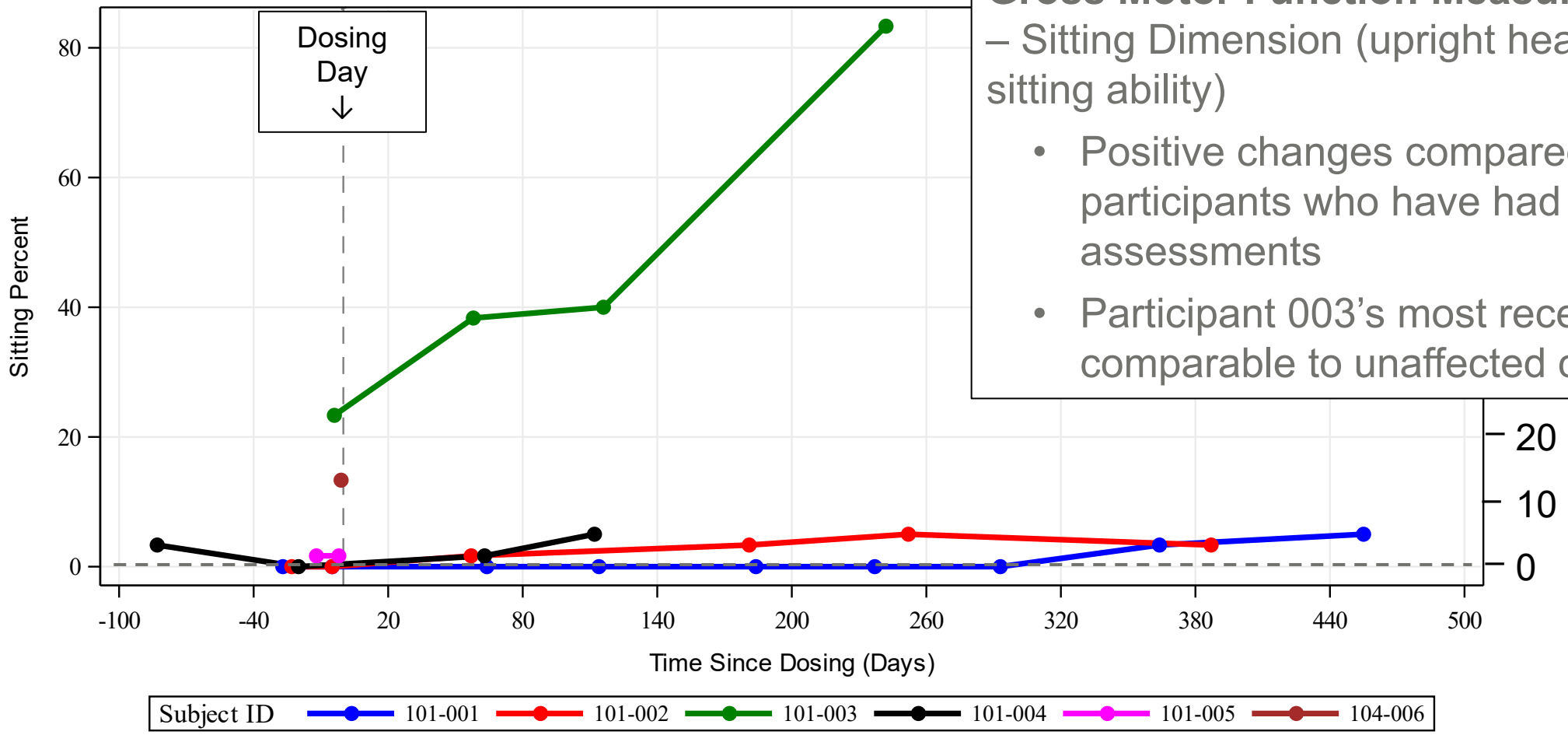
# Early Imaging Data - MRI




Brain MRI scans after dosing demonstrate improvements in myelin

# Early Clinical Data - Mobility




**Gross Motor Function Measure 88 (GMFM-88)** – Sitting Dimension (upright head control and sitting ability)

- Positive changes compared to baseline in all participants who have had post-treatment assessments
- Participant 003's most recent score is comparable to unaffected children

# More Understanding to Come

- Although all six participants had rapid and sustained decreases in NAA after dosing, levels were still many times higher than normal

- Despite trending evidence that lower NAA levels are related to less severe Canavan disease, that does not necessarily mean that lowering NAA levels will make existing severe Canavan disease milder

- It is not clear whether restoring ASPA activity and lowering NAA levels will lead to clinical improvement in children with Canavan disease

# Summary

- Aspa's CANaspire gene therapy trial is currently recruiting potential participants from within and outside the US
- Preliminary results from 6 dosed participants are encouraging:
  - Generally well-tolerated to date
  - Reductions of NAA in CSF, brain tissue and urine to levels consistent with less severe Canavan disease
  - Improvement in brain myelination
  - Positive changes in head control and sitting abilities
- **It is too early to determine safety, tolerability and clinical benefit, if any** – more data and longer follow-up are needed

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# Thank you!

www.treatcanavan.com

https://clinicaltrials.gov/ct2/show/NCT04126005

https://www.facebook.com/AspaTherapeutics

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