Efficacy and safety of a novel AAV *FXN* gene therapy (AVB-202) for the treatment of Friedreich's ataxia

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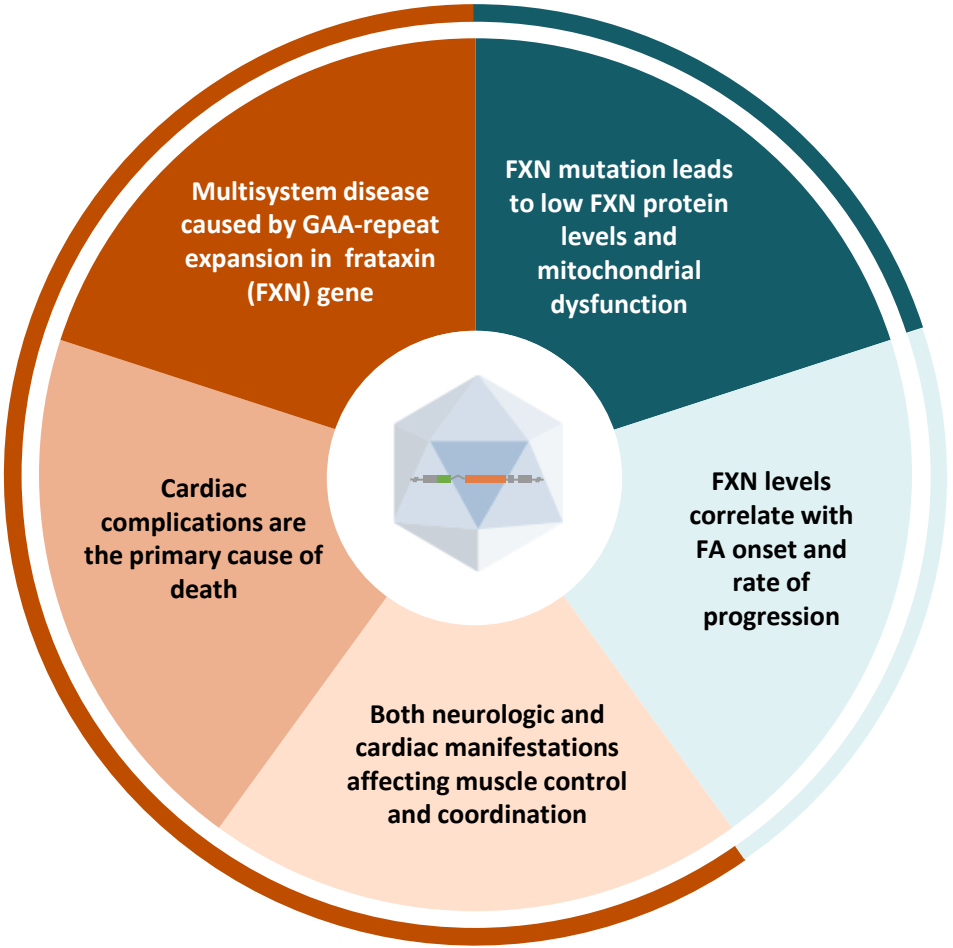
This presentation contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, including statements regarding future expectations, plans and prospects for the company; the ability to successfully achieve and execute on the company’s priorities and achieve key clinical milestones; the benefits of the merger with AavantiBio; the company’s attempt to build an innovation platform enabling the discovery and development of high-value genetic medicines for neuromuscular and cardiac diseases by integrating internal capabilities, including a vector core, validated animal models, optimized expression cassettes, and regulatory elements of target indications, and collaborations with leaders in related clinical and research fields; and other statements containing the words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would,” “working” and similar expressions. Any forward-looking statements are based on management’s current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in, or implied by, such forward-looking statements. These risks and uncertainties include, but are not limited to, risks associated with the ability to recognize the anticipated benefits of Solid’s acquisition of AavantiBio; the company’s ability to advance AVB-202-TT, on the timelines expected or at all; obtain and maintain necessary approvals from the FDA and other regulatory authorities; replicate in clinical trials positive results found in preclinical studies of the company’s product candidates; obtain, maintain or protect intellectual property rights related to its product candidates; compete successfully with other companies that are seeking to develop treatments and gene therapies for Friedreich’s ataxia; manage expenses; and raise the substantial additional capital needed, on the timeline necessary, to continue development of AVB-202-TT,achieve its other business objectives and continue as a going concern. For a discussion of other risks and uncertainties, and other important factors, any of which could cause the company’s actual results to differ from those contained in the forward-looking statements, see the “Risk Factors” section, as well as discussions of potential risks, uncertainties and other important factors, in the company’s most recent filings with the Securities and Exchange Commission. In addition, the forward-looking statements included in this presentation represent the company’s views as of the date hereof and should not be relied upon as representing the company’s views as of any date subsequent to the date hereof. The company anticipates that subsequent events and developments will cause the company's views to change. However, while the company may elect to update these forward-looking statements at some point in the future, the company specifically disclaims any obligation to do so.

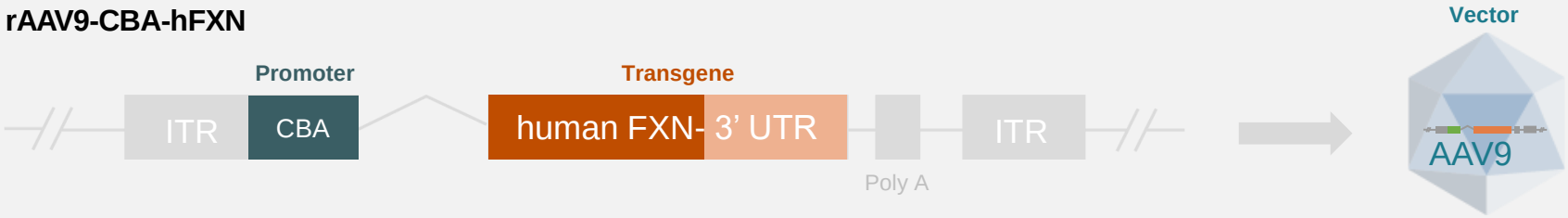
Friedreich's Ataxia (FA): The Most Common Hereditary Ataxia

Solid Biosciences' FA program addresses neurologic and cardiac manifestations of FA via dual IV and IT routes of administration

Data will be presented with AVB-202 using herpes simplex virus (HSV); the program has since moved to a transient transfection (TT) manufacturing process and is known as AVB-202-TT



AVB-202/AVB-202-TT: Designed to Target the Genetic Root Cause of FA



PROMOTER

Enhance transgene expression in multiple, target tissues[1]

Chicken β-Actin (CBA) Promoter

This hybrid promoter, consisting of the CMV enhancer and CBA promoter, directs durable expression of frataxin in target tissues relevant to FA, including the heart, cerebellar neurons, and sensory neurons of the dorsal root ganglia[1-3]

Established regulatory path and history with gene therapies approved and in development[4]

TRANSGENE

Encode full-length FXN protein

Codon-optimized human *frataxin* (*FXN*) gene

The optimized *FXN* gene cassette has regulatory elements in the endogenous 3' UTR to mimic the natural gene and confer post-transcriptional regulation of frataxin levels[5]

The *FXN* sequence is ubiquitously expressed and is synthesized as a 210-amino-acid precursor protein that undergoes maturation within the mitochondria[6]

VECTOR

Deliver the promoter and transgene to disease-affected cells[7]

AAV serotype 9 (AAV9)

AAV serotype 9 transduces all tissues affected in FA, including the heart and the CNS[8,9]

Established regulatory path and history with gene therapies approved and in development[4]

CMV, cytomegalovirus; CNS, central nervous system; ITR, inverted terminal repeat; UTR, untranslated region.

1. Klein RL, et al. *Exp Neurol*. 2002;176(1):66-74. 2. Gray SJ, et al. *Hum Gene Ther*. 2011;22(9):1143-1153. 3. AavantiBio, Inc. 2021. Data on file. 4. Zolgensma [Prescribing Information]. Bannockburn, IL: AveXis, Inc; May 2019. 5. Bandiera S, et al. *PLoS One*. 2013;8(1):e54791. 6. Schmucker S, Puccio H. *Hum Mol Genet*. 2010;19(R1):R103-R110. 7. Gao G, et al. *Hum Gene Ther*. 2000;11(15):2079-2091. 8. Gao G, et al. *Curr Gene Ther*. 2005;5(3):285-297. 9. Foust KD, et al. *Nat Biotechnol*. 2009;27(1):59-65.

Study Design in Severe Cardiomyopathy FA Mouse Model

Cre-mediated deletion of *Fxn* in heart and skeletal muscle; severe cardiomyopathy characteristic for late-stage FA

MCK Fxn-cKO

MCK | Cre

4-5 w | 7 w | 11 w

Onset of mitochondrial and cardiac dysfunction

Cardiac hypertrophy

Death

CARDIOMYOPATHY

Study Design

Dose 3 WOA

Echo and survival

Frataxin protein
SDH activity
Histology

9 WOA

Frataxin protein
SDH activity

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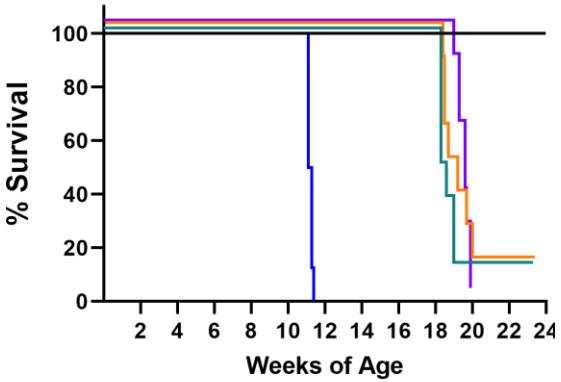
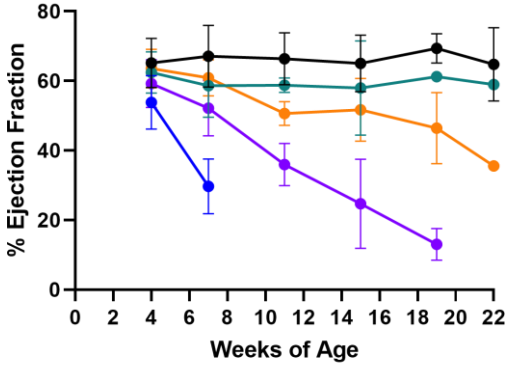
AVB-202 Rescued Cardiac Function and Extended Survival in Cardiac FA Mouse

Robust frataxin expression levels suggest efficacy may be achieved at lower doses

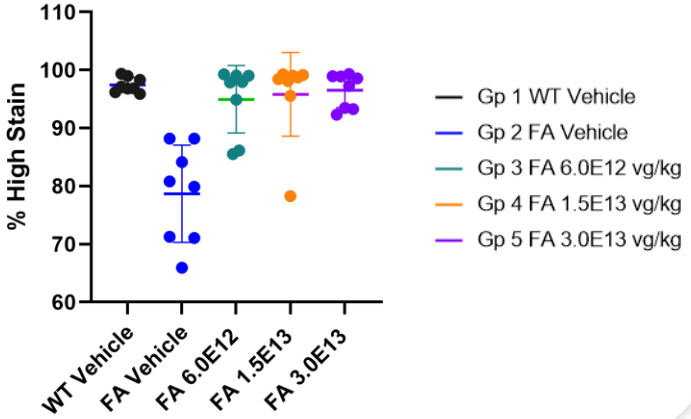
Survival



Ejection Fraction



SDH Activity



Favorable Safety Profile of AVB-202 in 6 Month NHP Safety Study

- Single-dose IV/IT, IV or IT administration
- Vehicle or low, mid, high dose of AVB-202; n=4/group (2M/2F)

Dose Group	IV Dose (vg/kg)	IT Dose (vg/brain wt)	Total vg/kg
IV/IT Low	6.00E+12	6.00E+13	1.20E+13
IV/IT Mid	1.50E+13	1.50E+14	3.00E+13
IV/IT High	3.00E+13	3.00E+14	6.00E+13
IV Mid	1.50E+13	-	1.50E+13
IV High	3.00E+13	-	3.00E+13
IT Mid	-	1.50E+14	1.50E+13
IT High	-	3.00E+14	3.00E+13

- Immunomodulation using rituximab and sirolimus; all animals off sirolimus treatment by Day 106
- Endpoints:
  - Clinical pathology and Histopathology
  - ECG, Neurobehavior, Nerve conduction velocity
  - FXN protein and mRNA

- **Dual route of administration well-tolerated**
- **Clinical pathology, nerve conduction and neurobehavior assessments, ECGs, and histopathology indicate favorable safety profile**
  - Microscopic findings confined to DRGs and spinal cord (AAV class effect)
  - Nerve conduction assessments indicate some sensory neuropathies largely limited to IT-only dose groups

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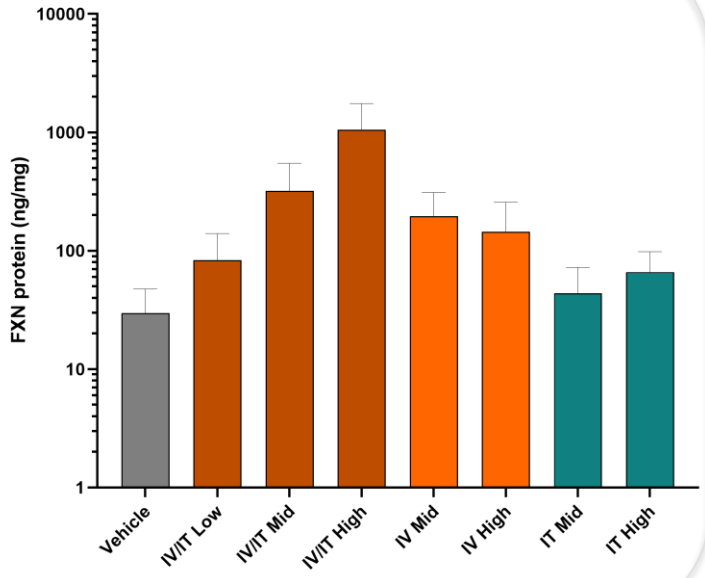
Robust Frataxin Expression in Cardiac Tissue Even at Lowest AVB-202 Dose

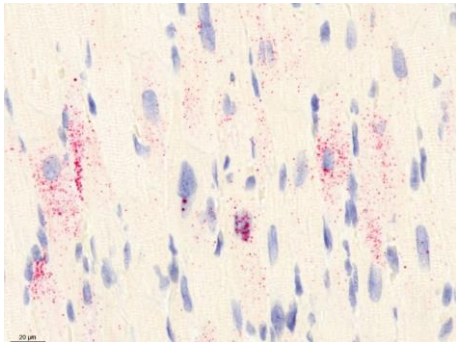
Dual route of administration resulted in increased expression at lower dose vs IT or IV alone

Frataxin Protein



Dose Group	IV Dose (vg/kg)	IT Dose (vg/brain wt)	Total vg/kg
IV/IT Low	6.00E+12	6.00E+13	1.20E+13
IV/IT Mid	1.50E+13	1.50E+14	3.00E+13
IV/IT High	3.00E+13	3.00E+14	6.00E+13
IV Mid	1.50E+13	-	1.50E+13
IV High	3.00E+13	-	3.00E+13
IT Mid	-	1.50E+14	1.50E+13
IT High	-	3.00E+14	3.00E+13

Frataxin mRNA (in situ)

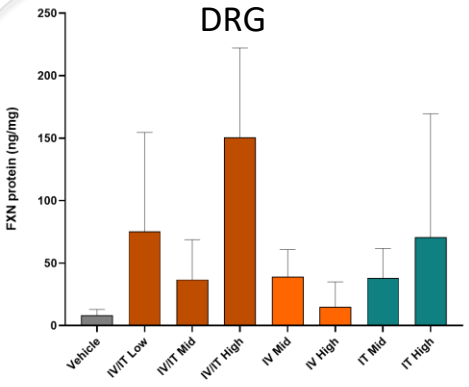


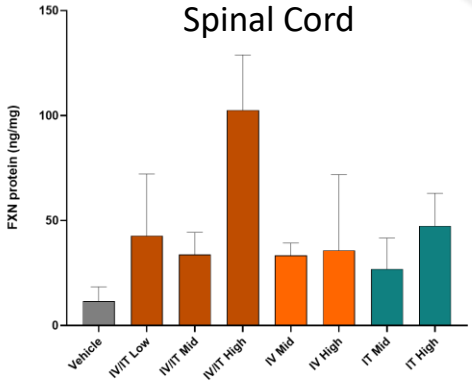
RNAscope

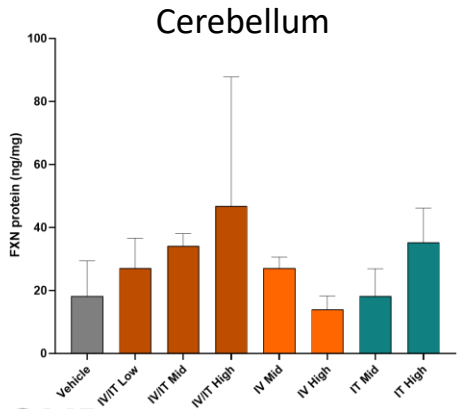
Frataxin mRNA in cardiomyocytes of left ventricle

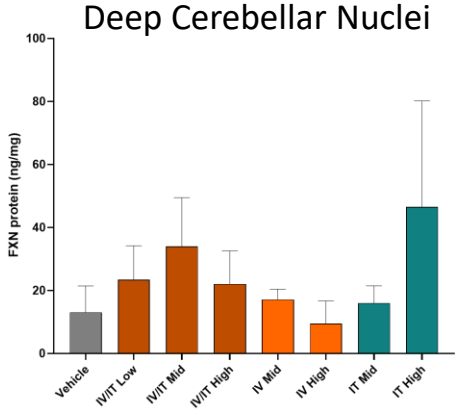
Robust Frataxin Expression in CNS Target Tissues

Frataxin Protein (Bulk)



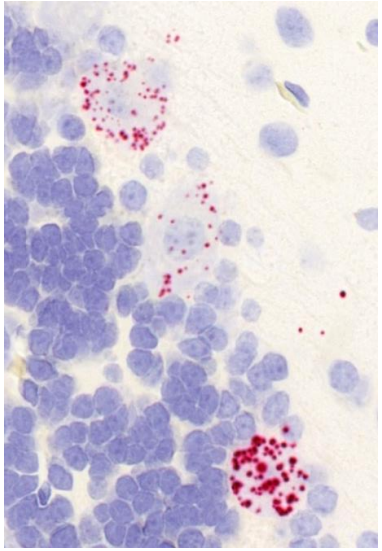






Frataxin mRNA (in situ)

Frataxin mRNA in Purkinje cells of the cerebellum



RNAscope

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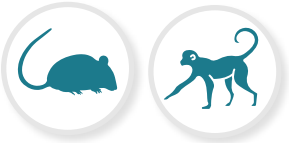
Conclusions



- AVB-202 improved cardiac function and extended lifespan in severe cardiomyopathy FA mouse model
- FXN was expressed in FA target tissues (heart and CNS) in NHPs with a favorable safety profile
- Overall low effective dose range in the mouse and robust expression levels in NHPs suggest that an extensive immunosuppression strategy will not be required
- Studies in neuro FA mouse model ongoing

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