Systemic AAV Gene Therapy with Next Generation Engineered Capsid Demonstrates Expression Levels Supporting Potential Therapeutic Benefit for CNS, Cardiac, and Sensory Symptoms in Friedreich's Ataxia

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Disclosures

- Celeste Stephany, Ph.D., is an **employee of Capsida Biotherapeutics, Inc.**

- This Presentation contains information regarding the research and development programs of Capsida Biotherapeutics, Inc. that are based on or derived from preclinical data. Clinical trial results may differ. Capsida does not have an approved therapy presently available for Friedreich's ataxia, nor is there any promise or guarantee that Capsida's research and development will produce any potential therapy in the future.

Solving the Challenges of Gen-1 Genetic Medicines

	CNS Challenges	Capsida Solutions*
Crossing the BBB	Limited ability to cross BBB; < 1% neuronal transduction	>70% of neurons transduced in NHPs
Safety Concerns	Liver toxicity	>16x liver detargeting; lower dosing
Patient Populations	Narrow therapeutic index (TI) limits to ultra-rare/rare diseases	Broader TI = more common diseases across ages
Route of Administration	Direct injection to brain or CSF causes significant risks and inconsistent expression	IV delivery limits risks and allows consistent expression
	IV delivery increases risk of off-target effects (esp. liver) and triggering immune response	Well-tolerated safety profile with no adverse histopathological findings

*For more details, see Abstract #93; Wednesday, 2:45-3:00p in NOLA Theater C presented by Nick Goeden

Next-generation Genetic Medicines Company

Unlocking the full potential of gene therapy for all

Wholly-owned Pipeline

Two clinical programs in 2025

CAP-002: STXBP1-DEE[1]
- IND clearance
- ODD granted

CAP-003: PD-GBA[2]
- Human POC in Q4

Third clinical program in 2026

CAP-004: Friedreich's ataxia

Fully-integrated Capabilities

- » **Capsid engineering**
- » **Cargo optimization**
- » **Clinical development**
- » **In-house GMP manufacturing**
- » **Protected by expansive IP portfolio**

External Validation

Strategic partnerships

abbvie » 1st AbbVie opt-in achieved

Lilly Prevail THERAPEUTICS — A Wholly Owned Subsidiary of Eli Lilly and Company

CRISPR THERAPEUTICS®

Contract manufacturing

KATE THERAPEUTICS — A NOVARTIS COMPANY

Capsida is the first genetic medicines company with FDA IND clearance for an engineered IV-delivered gene therapy that crosses the blood-brain-barrier and detargets liver

[1]Abstract #123; Wednesday, 3:45-4:00p in NOLA Theater B presented by Nicholas Flytzanis, Ph.D.
[2]Abstract #1435, Wednesday Poster Session, presented by Kim McDowell, Ph.D.

CAP-004 Enables Treatment of CNS, Cardiac, and Sensory Manifestations of Friedreich's Ataxia Through Single IV Infusion

Disease Background

- Caused by GAA repeat expansion in intron 1 of FXN gene
- ~5000 patients in the US and 15,000 worldwide
- Age of onset: 5-15 years old[1]
  Death: 35-40 years old[1]
- CNS, cardiac, and sensory manifestations
- Existing therapies do not directly address FXN loss

CAP-004

- ✓ Best in class IV-administered program
- ✓ Industry-leading frataxin protein expression in all relevant tissues
- ✓ Potential for correction of CNS, cardiac, and sensory manifestations
- ✓ Safety demonstrated in NHPs, including liver and DRGs
- ✓ IND-enabling studies ongoing, incl. self-regulating cargo
- ○ Q2/Q3 2026 IND Filing

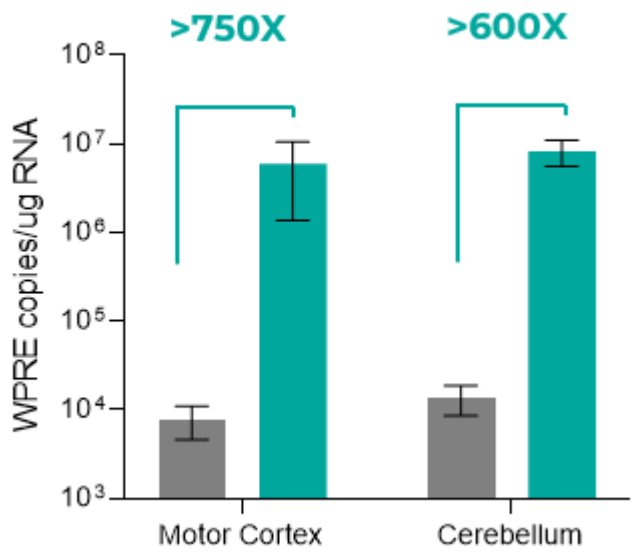
[1] Tsou et al., 2011; Harding et al., 1981

CAP-004 Achieves KOL Recommended Target Capsid Profile for Friedreich's Ataxia

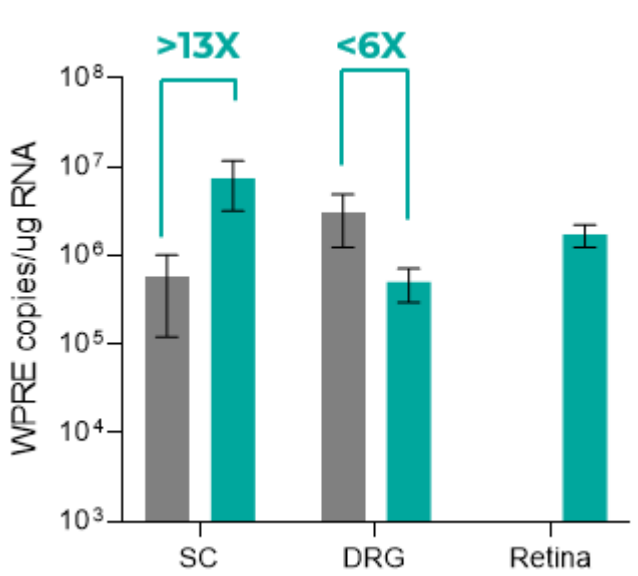
Category	Success Criteria	
Efficacy Surrogates in NHP	>=50% neurons averaged across CNS regions of interest	✓
	Evidence of DRG transduction	✓
	Viral protein levels ~30% endogenous protein levels across CNS regions of interest and left ventricle	✓
Safety Surrogates in NHP	Viral protein levels <5x endogenous levels in left ventricle	✓
	Liver DNA biodistribution lower than AAV9	✓
	No overt findings in CNS, heart, liver, DRGs	✓
Efficacy Surrogates in vitro	Subcellular localization to the mitochondria	✓

IV CAP-004 Achieves Therapeutically Meaningful RNA Expression Levels in Key FA Tissues While Detargeting Liver

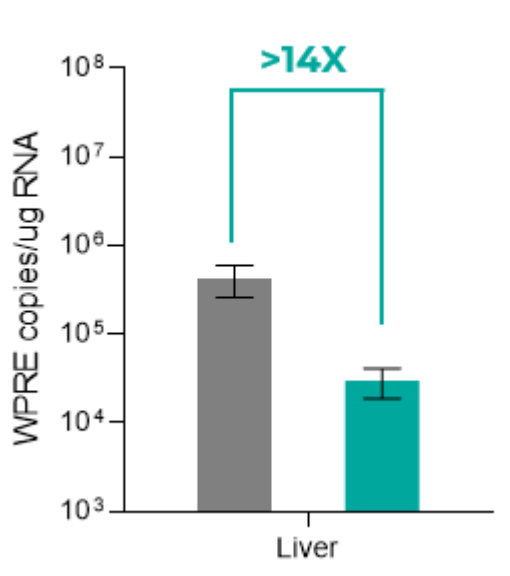
Brain FXN in NHPs



Spinal Cord & Sensory Neuron FXN in NHPs



Liver FXN in NHPs



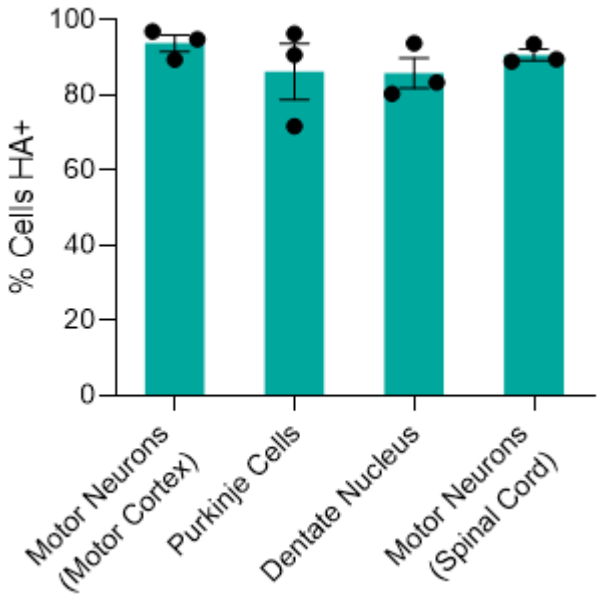
AAV9 2.5E13 vg/kg[1]

CAP-004 2.5E13 vg/kg

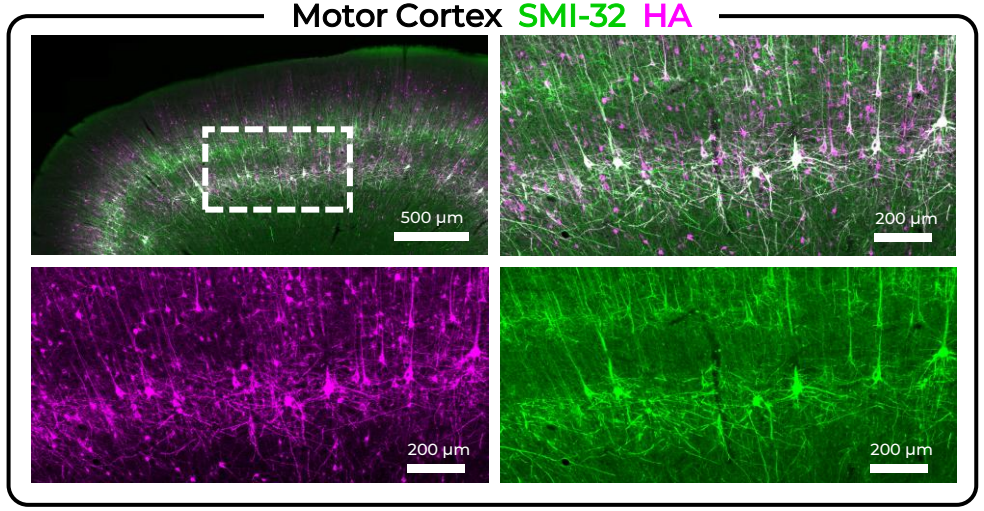
FXN = Frataxin

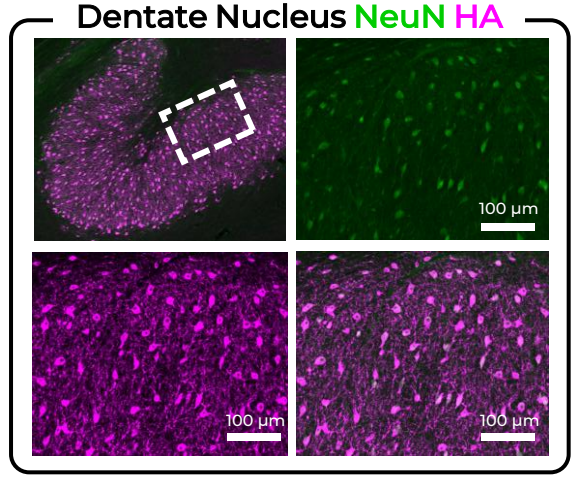
[1] AAV9 data generated from past Capsida study with same expression cassette (promoter, regulatory elements, etc.) but different therapeutic cargo

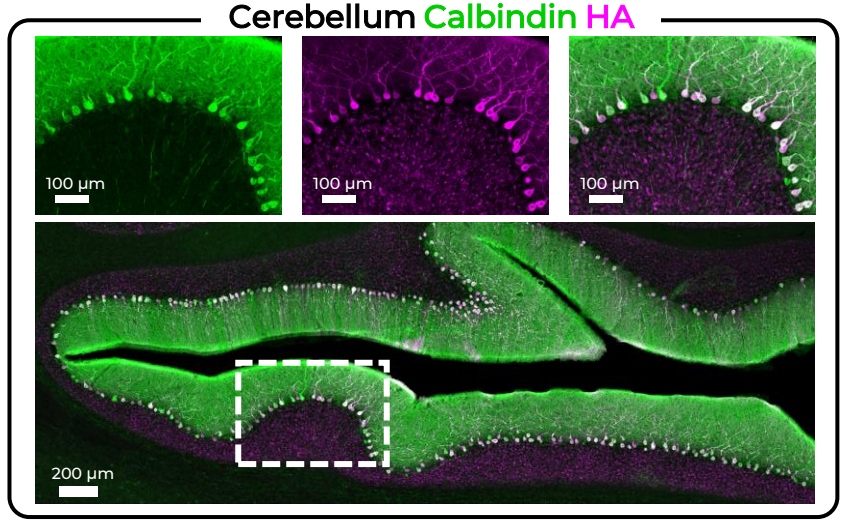
Single IV Administration of CAP-004 in NHPs Demonstrates Potential for Complete Correction Across All CNS Target Tissues

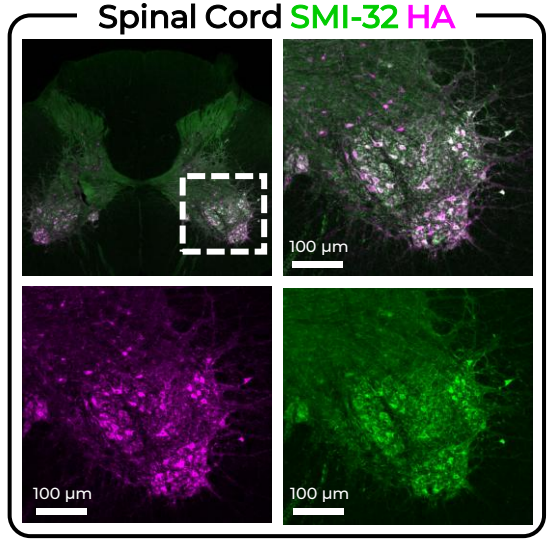


CAP-004 2.5E13 vg/kg





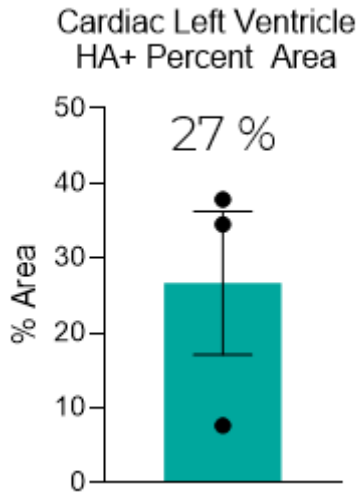




CAP-004 Delivers FXN to ~30% of Cardiac Left Ventricle Tissue Area

Cardiac Left Ventricle % HA Positive Area

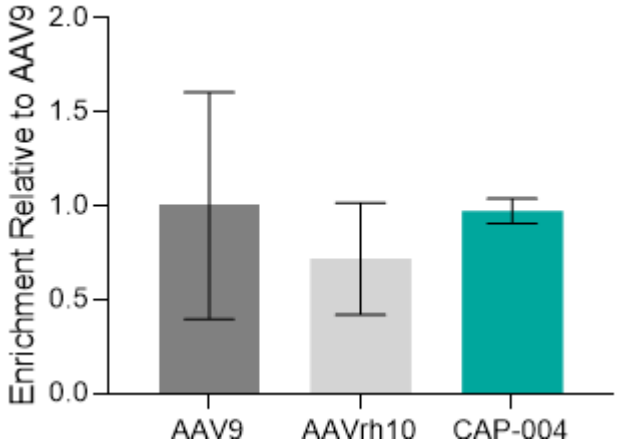
Anti-HA



Cargo: hFXN-HA
In-life: 4 weeks
Species/Age: N = 3 cynomolgus macaques, ~32mo

**Data from single variant CAP-004 study*

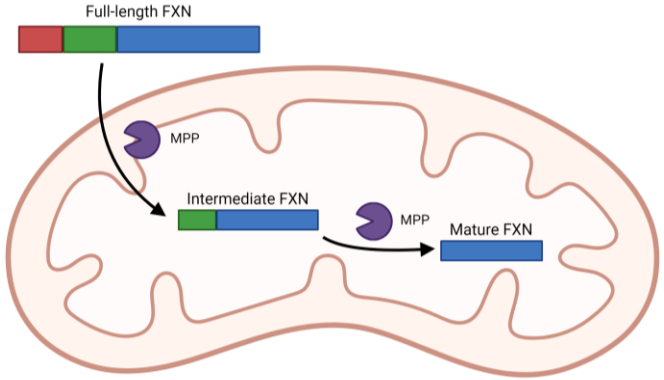
Cardiac FXN enrichment

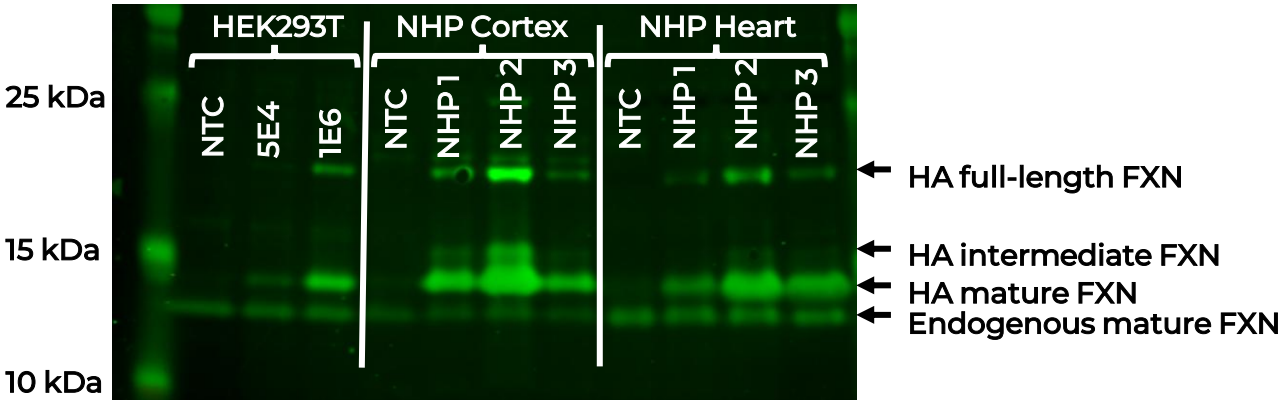


**Data from pooled capsid study*

- CAP-004 delivers therapeutically meaningful cardiac transduction
- CAP-004 Cardiac RNA enrichment is in line with levels achieved by other AAV serotypes that are currently undergoing clinical testing for treatment of FA-related cardiomyopathy

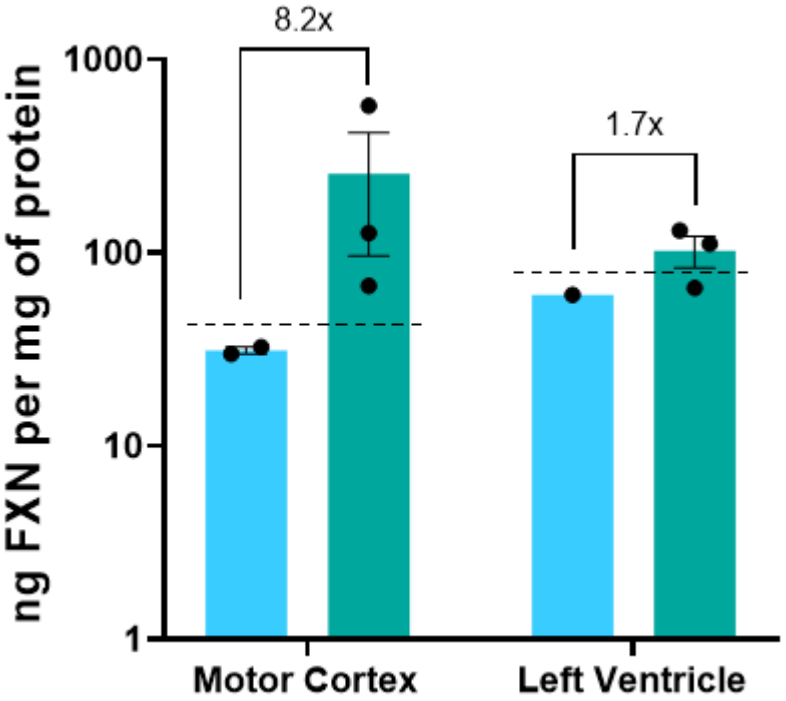
Cardiac and CNS FXN Protein Produced by CAP-004 is Properly Trafficked to Mitochondria and Meets Efficacy Thresholds





hFXN ELISA

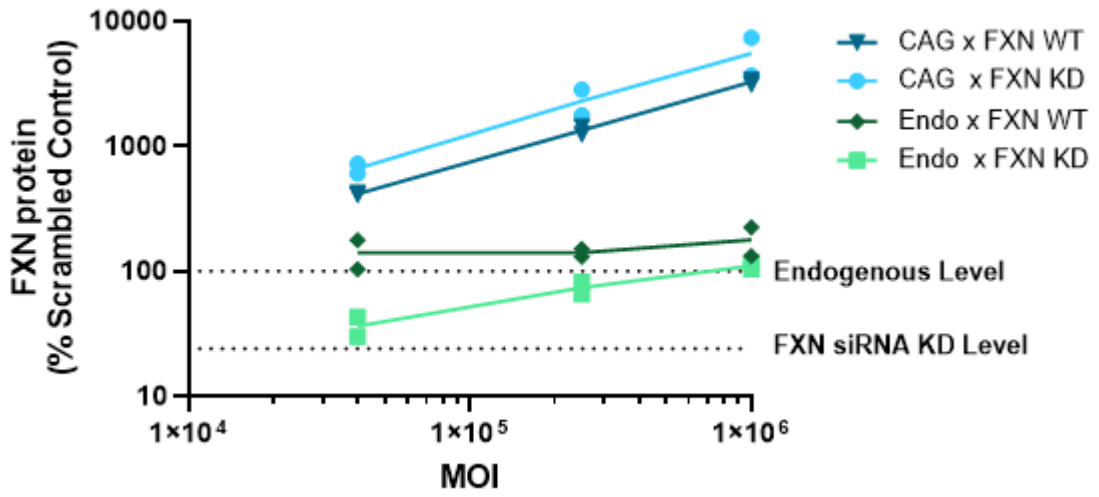
Untreated control CAP-004 ---- 30% efficacy threshold



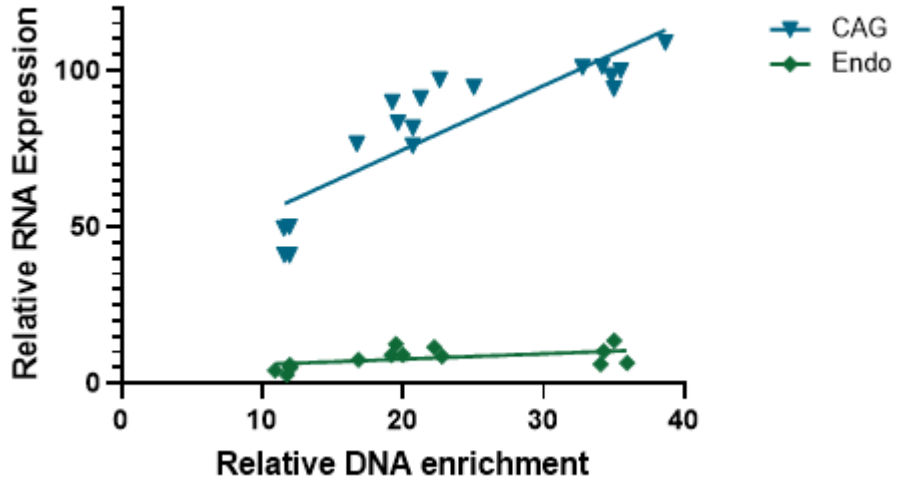
CAP-004 safely meets or exceeds all CNS efficacy criteria at moderate dose suggesting broad therapeutic index

Self-Regulating Cargo Has the Potential to Expand the Therapeutic Window for CAP-004

Endo promoter limits FXN expression to ~100% endogenous levels in human cell lines across doses



Endo promoter keeps relative RNA expression stable with increasing DNA in NHP pool



- Proprietary endogenous promoter (Endo) efficiently drives FXN expression while limiting overexpression
- Endo promoter is being tested in CAP-004 DRF and may be selected to advance to GLP tox

Best-in-class engineered AAV for treatment of FA

- A single-IV infusion has potential to deliver:
  - Near complete coverage of key sites of CNS pathology
  - Cardiac transduction profile exceeds efficacy thresholds
  - Potential for sensory system correction with retina exposure and therapeutically-relevant levels of DRG expression
- Well tolerated safety profile over 4 weeks in-life
- Potential to limit cytotoxicity with proprietary endogenous gene regulatory elements
- Characterization of a human receptor that binds engineered capsids with complete homology between humans and macaques in the predicted binding pocket*

*For more details, see Abstract #93; Wednesday, 2:45-3:00p in NOLA Theater C presented by Nick Goeden

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