CAPSIDA BIOTHERAPEUTICS

CAP-004:
Systemic AAV Gene Therapy with Engineered Capsids for Treatment of CNS and Cardiac Symptoms in Friedreich's Ataxia

March 19th, 2025

Friedreich's Ataxia

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
- Safety demonstrated in NHPs, including liver and DRGs
- Potential for correction of CNS, cardiac, and sensory manifestations
- IND-enabling studies ongoing

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

Next generation capsid enables treatment of CNS and cardiac manifestations of FA through single IV infusion

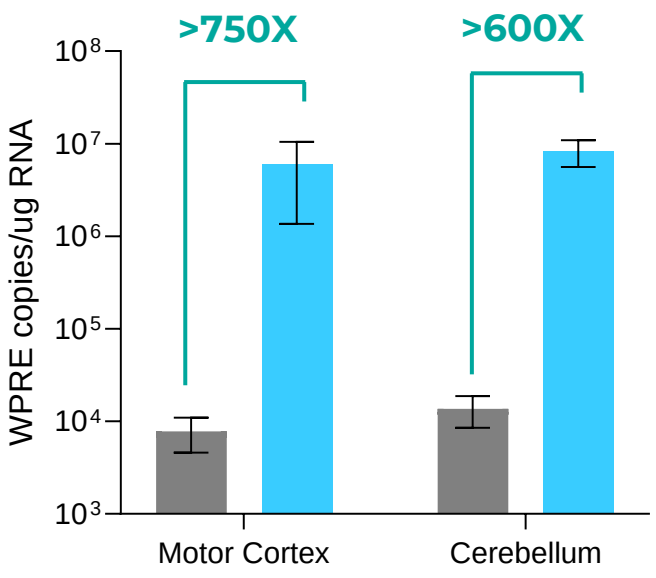
	Gen 1 Capsids	Capsida Solutions
Crossing the BBB	Limited ability to cross BBB; < 1% neuronal transduction	>70% of neurons transduced in NHPs
Safety Concerns	Liver toxicity	>16x liver detargeting; lower dosing
Route of Administration	Direct injection to brain or CSF causes significant risks and inconsistent expression	IV 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
		CNS and Cardiac transduction profile enables multisystem correction

CAP-004 has achieved KOL recommended target capsid profile for Friedreich's Ataxia

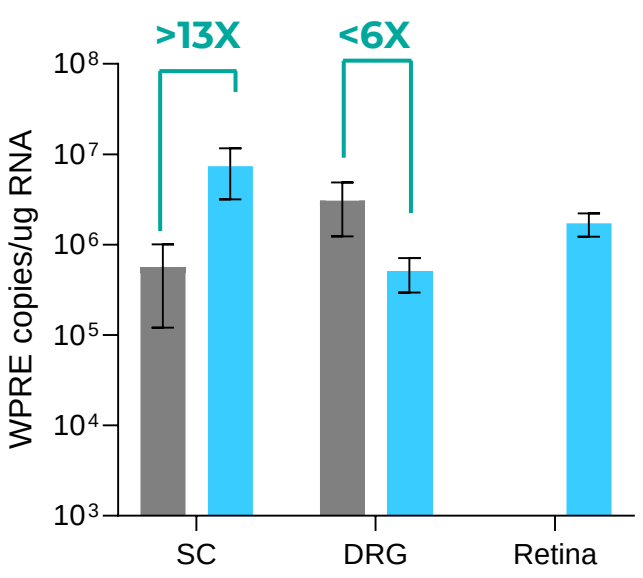
Category	Success Criteria	
Efficacy Surrogates in NHP	>=50% neurons averaged across CNS regions of interest	✓
	Evidence of DRG transduction	✓
	Viral protein levels ~30% endogenous protein levels across CNS regions of interest and left ventricle	✓
Safety Surrogates in NHP	Viral protein levels <5x endogenous 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 de-targeting liver

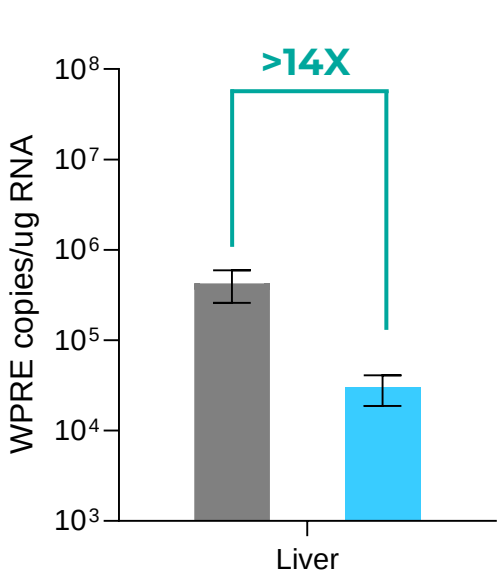
Brain FXN in NHPs



Spinal Cord & Sensory Neuron FXN in NHPs



Liver FXN in NHPs



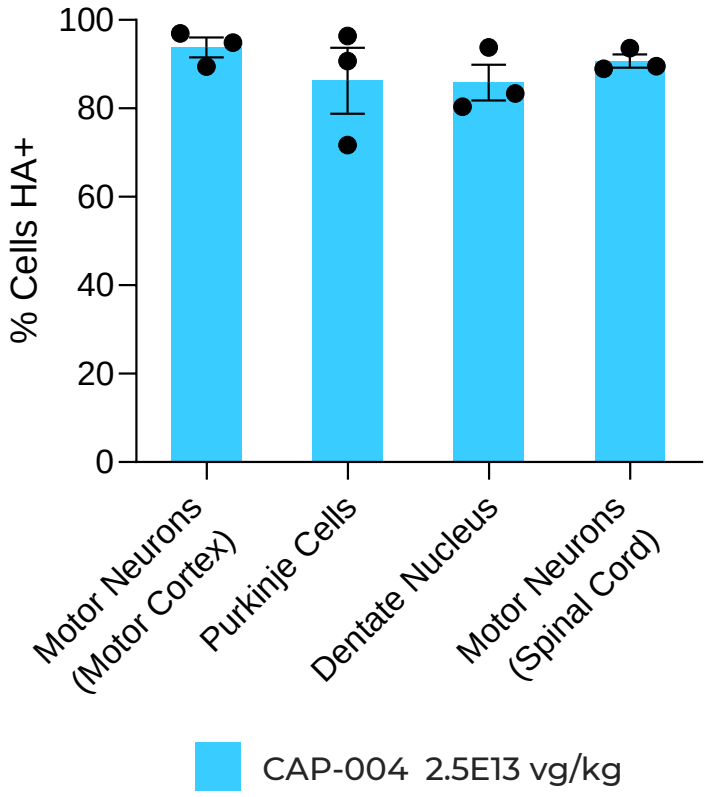
AAV9 2.5E13 vg/kg[1]

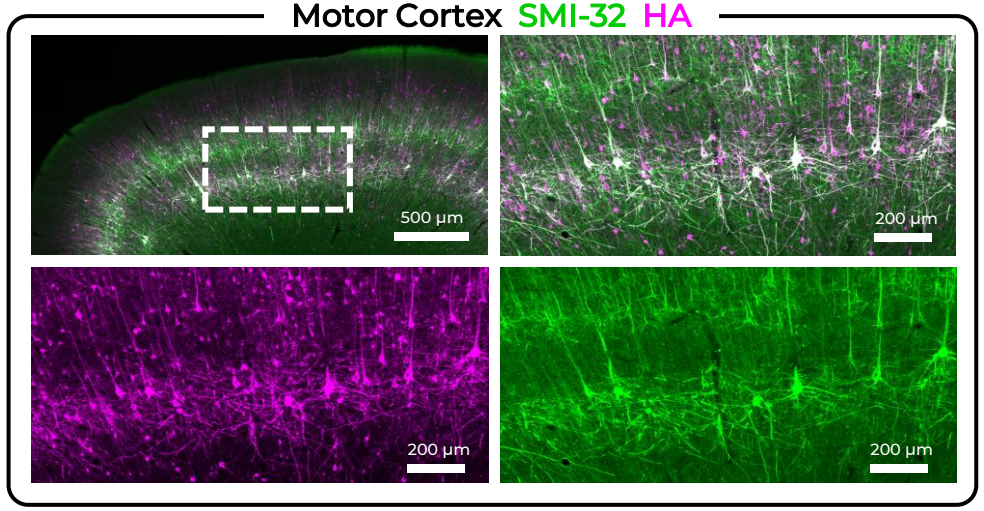
CAP-004 2.5E13 vg/kg

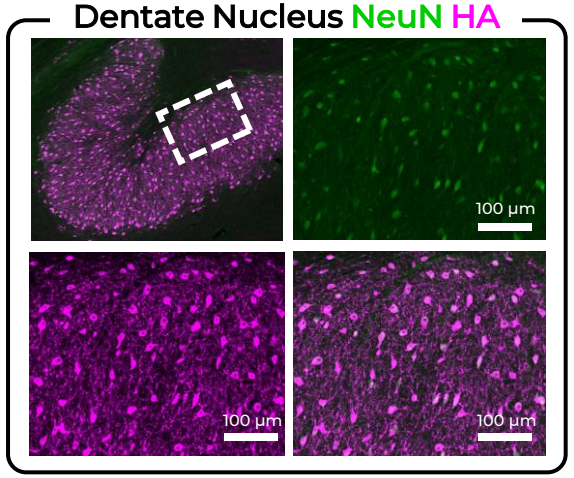
FXN = Frataxin

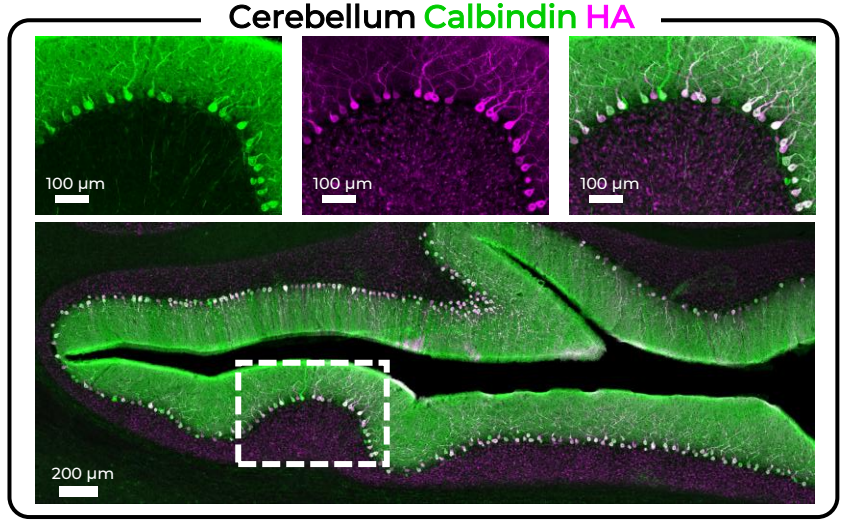
[1] AAV9 data generated from past Capsida study with same expression cassette (promoter, regulatory elements, etc.) but different therapeutic cargo

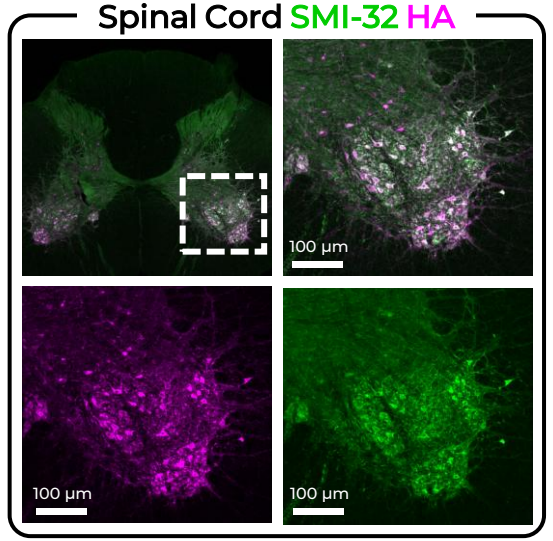
Single IV administration of CAP-004 in NHPs demonstrates potential for complete correction across all CNS target tissues









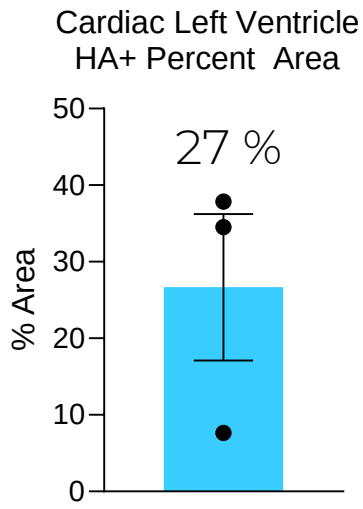


CAP-004 delivers FXN to ~30% of cardiac left ventricle tissue area

Cardiac Left Ventricle % HA Positive Area

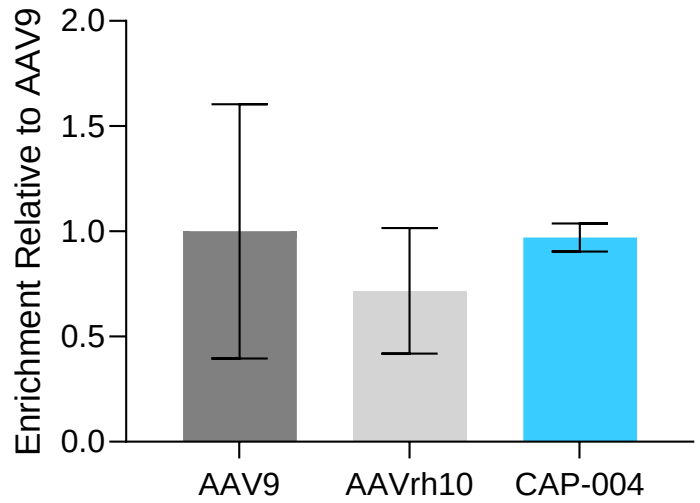
Anti-HA

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



**Data from single variant CAP-004 study*

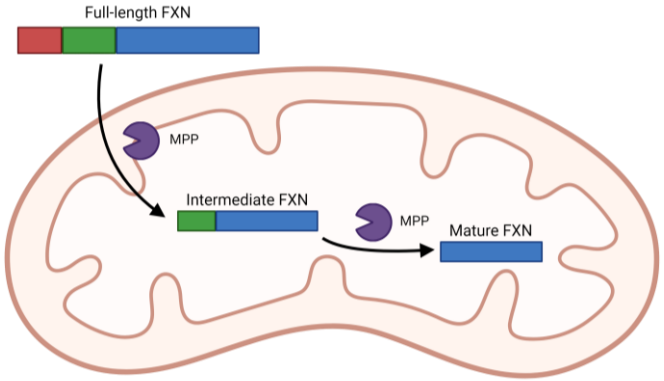
Cardiac FXN enrichment

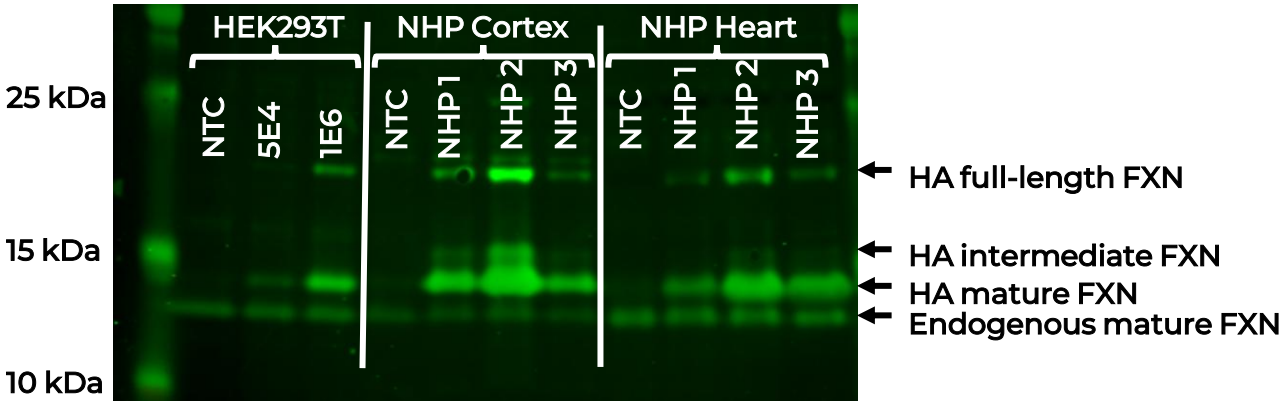


**Data from pooled capsid study*

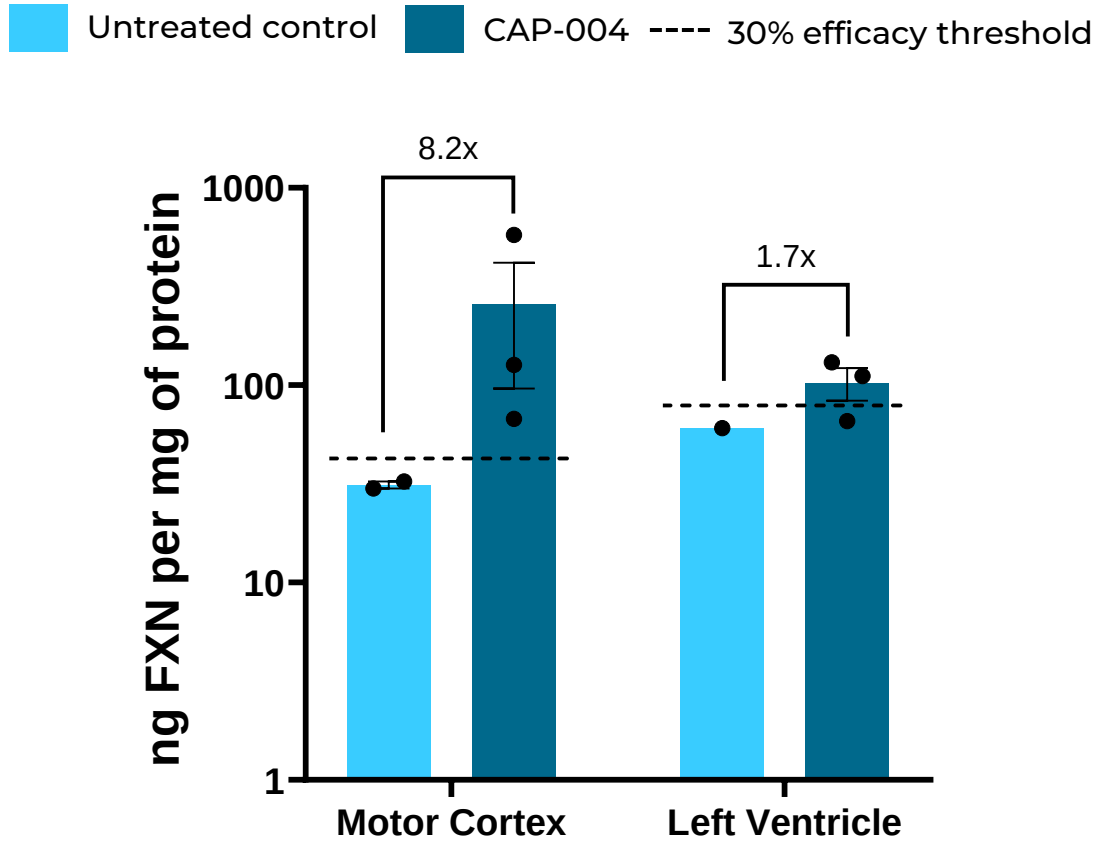
- CAP-004 delivers therapeutically meaningful cardiac transduction.
- CAP-004 Cardiac RNA enrichment is in line with levels achieved by other AAV serotypes currently undergoing clinical testing for treatment of FA-related cardiomyopathy

Cardiac and CNS FXN protein produced by CAP-004 is properly trafficked to mitochondria and meets efficacy thresholds





hFXN ELISA



Best in class systemic AAV for treatment of FA

» Near complete coverage of key sites of CNS pathology

» Cardiac transduction profile exceeds efficacy thresholds

» Potential for sensory system correction with retina and DRG exposure

» Well tolerated safety profile over 4 weeks in-life