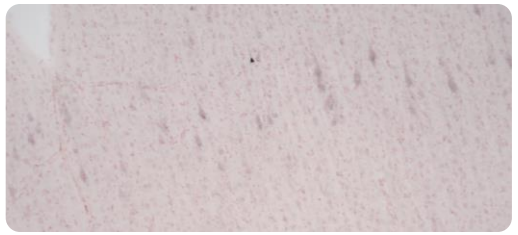
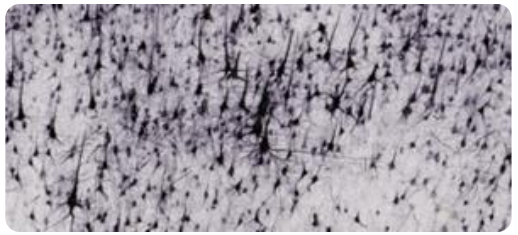
CAPSIDA BIOTHERAPEUTICS

Unlocking the Potential of Gene Therapy for All

September 2024

Capsida is Solving the Challenges of Gen-1 Gene Therapies

Starting in CNS and Ophthalmology, but with IP rights and applicability to all TAs

	CNS Challenges	Capsida Solutions
	Wild Type AAV9	**Capsida Engineered Capsids**
	NHP Cortex 	NHP Cortex 
Crossing the BBB	Limited ability to cross BBB; < 1% neuronal transduction	Cross BBB with >70% of neurons transduced in NHPs
Safety Concerns	Liver and dorsal root ganglia (DRG) toxicity	16x fold liver detargeting and 50x fold DRG detargeting vs WT AAV9
Patient Populations	Narrow therapeutic index limits to ultra-rare/rare diseases	Broader therapeutic index enables more common diseases across all ages
Route of Administration	Direct injection to brain or CSF causes significant risks and inconsistent expression IV delivery increases risk of off-target effects (especially liver) and triggering immune response	Non-invasive IV delivery limits risks and allows consistency across brain regions CNS specificity with no clinical pathology, histopathology, and immunogenicity findings

Wholly-owned Programs Approaching the Clinic and Strong Pharma Validation

3 Wholly Owned Programs Approaching Clinical Stage

IV Administered

IND 1H 2025 - Parkinson's caused by GBA mutations (best in class potential)

IND 1H 2025 - Genetic epilepsy caused by STXBP1 mutations (first in class)

Candidate Declaration– Undisclosed (best in class potential)

Leadership Team

Decades of industry experience, including drug development and manufacturing expertise

World class investors and scientific advisory teams including co-founder Viviana Gradinaru, PhD

Manufacturing Capabilities

In-house capabilities reduce turn-around times and expedite internal process transfer to support clinical studies

Quickly assess manufacturability

Control the process and associated costs

Partnerships

Key partnerships focused on CNS and Ophthalmology provide validation for the platform

Leadership Team and Board of Directors

Decades of Industry Experience and Drug Development Expertise

Leadership

Peter Anastasiou
Chief Executive Officer

Nicholas Flytzanis, PhD
Founder, Chief Research and Innovation Officer

Nick Goeden, PhD
Founder, Chief Technology Officer

Susan Catalano, PhD
Chief Scientific Advisor

Julie Hakim
Chief Financial Officer

Bethany Mancilla
Chief Business Officer

Rob Murphy
Chief Manufacturing and Quality Officer

Swati Tole, MD
Chief Medical Officer

Board Members

Clare Ozawa, PhD

Beth Seidenberg, MD

Viviana Gradinaru, PhD
Founder

Rita Balice-Gordon, PhD
CEO, Muna Tx

Frank Verwiel, MD
Chairman, Intellia

Peter Anastasiou
Chief Executive Officer

Capsida History and Milestones Achieved

2019

Founded upon breakthrough AAV engineering from laboratory of **Viviana Gradinaru, Ph.D.**

$50M Series A co-led by Westlake Village BioPartners and Versant Ventures

2021

AbbVie CNS deal **$90M** upfront including convertible note (CN); future milestones & royalties

2023

Lilly/Prevail CNS deal **$55M** including upfront & equity commitment; future milestones & royalties

AbbVie Ophthalmology deal **$70M** upfront including CN; future milestones, & royalties

Cost sharing manufacturing collaboration

Lead capsids up to 70% neuronal transduction in NHPs; DC for STXBP1

2024

DC for PD-GBA; 3rd internal program; Excellent manufacturing yields and quality specs at or above FDA standards

IND-enabling studies initiated for STXBP1 and PD-GBA

Novel Human receptor identified derisking clinical translation

Pipeline for Rare and Common Diseases Across All Ages

Capsida Wholly Owned Programs

Disease / Target	Cargo	Preclinical	IND-Enabling	Phase 1/2	Next Milestone
Genetic Epilepsy due to STXBP1 mutations	Gene Supplementation	CAP-002			IND Submission 1H 2025
Parkinson's disease associated with GBA mutations	Gene Supplementation	CAP-003			IND Submission 1H 2025
Undisclosed	Gene Supplementation	CAP-004			DC Candidate Selection

Partnered Programs

Partner	Disease Area	Co-Development/Co-Commercialization (Co/Co) Option
abbvie	Neurological & Ophthalmology Diseases	One Program, U.S. Profit Share (Neurological)
Prevail Therapeutics, A Wholly Owned Subsidiary of Eli Lilly and Company; Lilly	Neurological Diseases	One Program, U.S. Margin Share
CRISPR Therapeutics	Neurological Disease	CRISPR owned, Capsida Co/Co Option

Capsida Platform

Capsida – Uniquely Positioned to Lead Gene Therapy

Capsid Engineering Scale

Fully industrialized and roboticized platform

Screening capabilities across cell types in NHPs and human cells

CNS Tropism

>99% specific to neurons at the capsid level

>70% neurons transduced

Broad IP portfolio protecting capsids and capsid/cargo

Peripheral De-targeting

>16x liver detargeted and ~50x DRG detargeting

Superior off-target safety profile

Broad IP portfolio protecting de-targeting

Therapeutic Expression

Expression levels in NHPs with potential to achieve full disease correction

Industry leading expression levels across pipeline programs

Clinical Translatability

Identified and patented novel human receptor with complete homology in NHPs and humans

Validated expression in NHPs and human cells

Manufacturability

In-house process development and GMP manufacturing

Productivity surpassing AAV9

Quality specs exceeding FDA requirements

Only Capsida has created all the capabilities and results needed to deliver on the promise of gene therapy

Capsida Has Developed Best-In-Class Platform

Leverages rigorous drug development principles and high-throughput automation to identify capsids that meet Target Capsid Profile (TCP) for each indication

Engineered Capsids that Meet or Exceed TCP

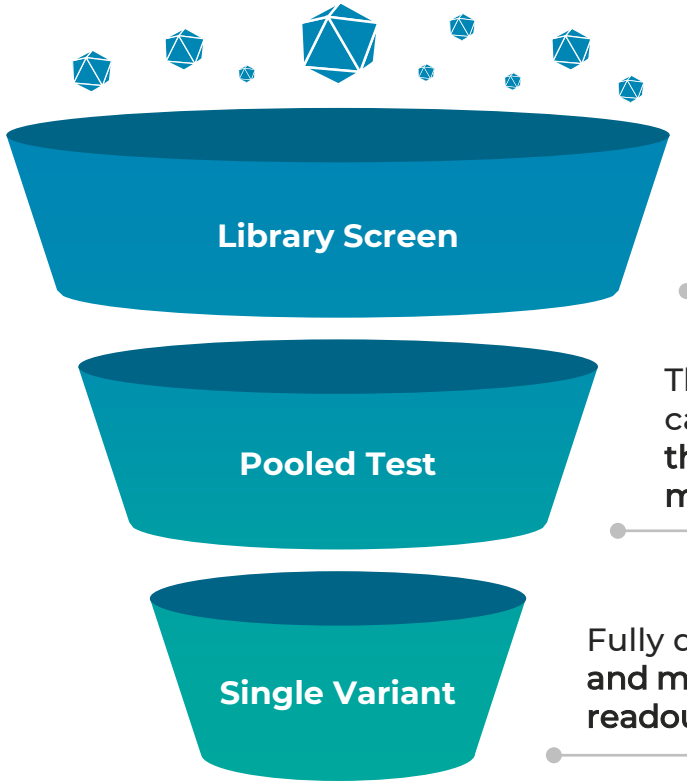
Evolved from engineering in mice to NHPs and screening in human cells to improve human translatability

Industrialized process built around customized robotics platform

Engineer capsids to meet TCP criteria including:

- Targeted tissues and cell type specificity
- High expression levels
- >10x off-target tissue detargeting
- Superior immunogenicity profile
- Superior manufacturability profile

Industrialized Capsid Development



Use directed evolution to create billions of variants screened **directly in NHPs and human cells**

Thousands of Candidate capsids are assessed for **therapeutic expression and manufacturability**

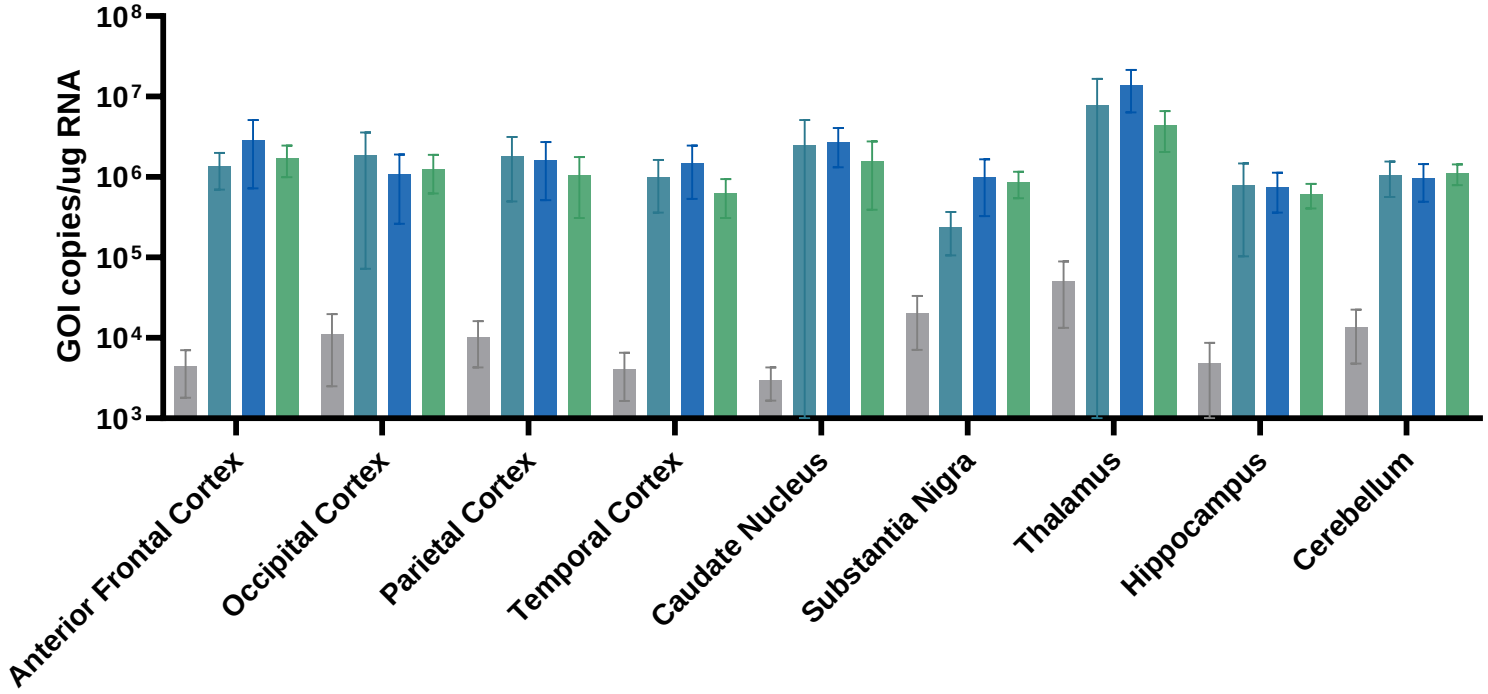
Fully quantitative **efficacy, safety, and manufacturing scalability readouts** for each single variant

Advance development candidates that meet or exceed TCP for each indication

Lead Capsids Demonstrate High Expression Across the CNS and Significant Liver De-targeting with IV-dosing

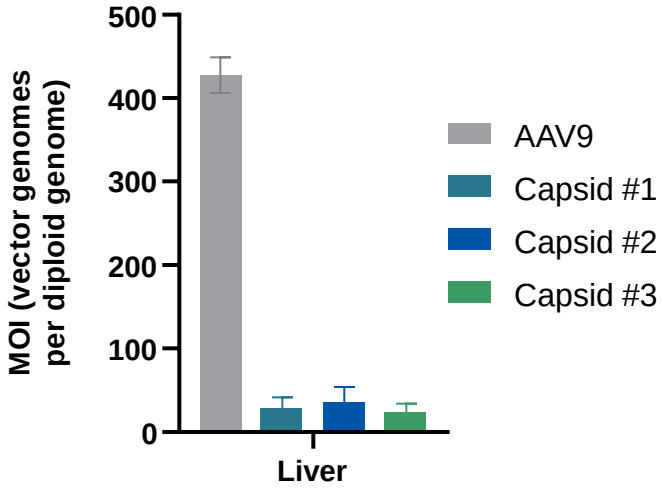
Broad CNS Transduction

Up to ~300x increase in CNS Expression



Liver De-targeting

Up to ~16x decrease in Liver De-targeting



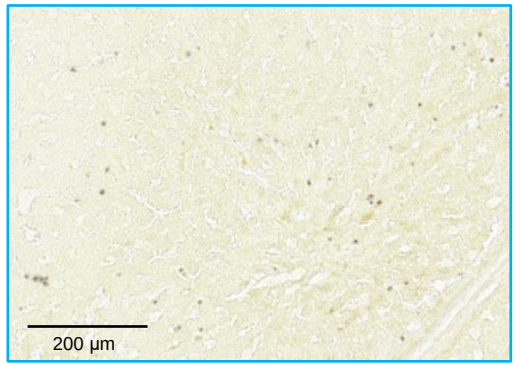
Cargo: HA-GOI | **Dose:** 2.5E13 vg/kg

Species/Age: N = 3 cynomolgus macaques/group, 36-42mo

Capsid selected for CAP-002 and CAP-003 exceeds rigorous criteria for both programs

Significant De-targeting of the Liver and No Histopath Findings, Including in DRGs, After IV Dosing in NHPs

Liver



Dose: 2.5E13 vg/kg
In-life: 6 weeks
Species/Age: N = 3 cynomolgus macaques, ~42mo

16X de-targeted to liver compared to AAV9

Lead capsid is **well tolerated** with no clinical pathology or immunogenicity findings

Unremarkable histopathology across the body, including liver and DRGs

Pipeline Programs

Parkinson's Disease Associated with GBA Mutations

CAP-003 potential to be best-in-class disease modifying therapy

PD-GBA

Mutations in GBA result in decreased GCase activity (25-30% in symptomatic PD-GBA patients) and lysosomal dysfunction

Up to **15%** of PD patients have mutations in the GBA gene[1]

	Limitations of Investigational Therapies	CAP-003 Differentiators
Transduction	— Low neuronal transduction, especially in substantia nigra	+ Up to 70% of neurons transduced (57% in substantia nigra)
Expression	— Don't report GCase activity or haven't seen significant elevations	+ GCase increases exceed levels needed to treat PD-GBA and reach 78% in cortex and 59% in putamen
Delivery	— Invasive delivery	+ Non-Invasive IV delivery
Safety	— DRG toxicity risks	+ Unremarkable histopathology across the body, including liver and DRGs

Disease Manifestations

PD is second most common neurodegenerative disease

Motor Symptoms (e.g., resting tremor, rigidity, slowness of movement) and non-motor symptoms (e.g., cognitive decline, psychiatric)

Unmet Need

No approved disease-modifying therapies

Potential for earlier age of onset, more frequent cognitive impairment, more rapid progression vs idiopathic PD[1]

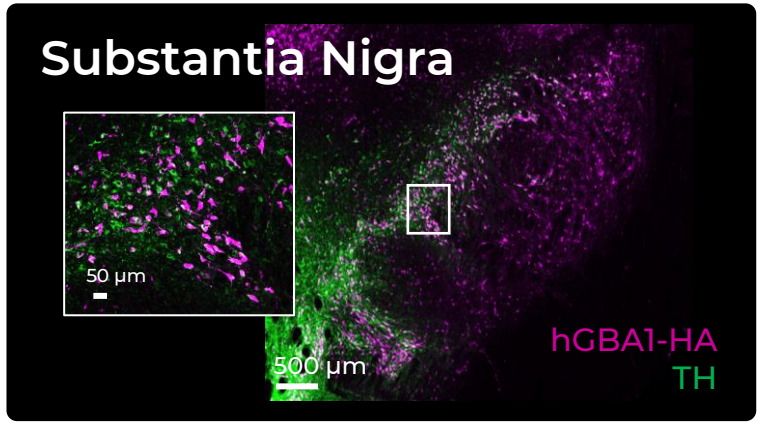
Commercial Opportunity Potential >$1B

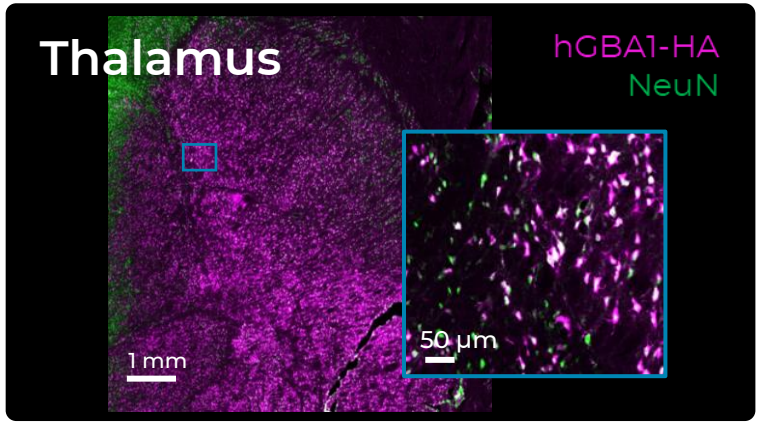
Potential to be first IV delivered gene therapy

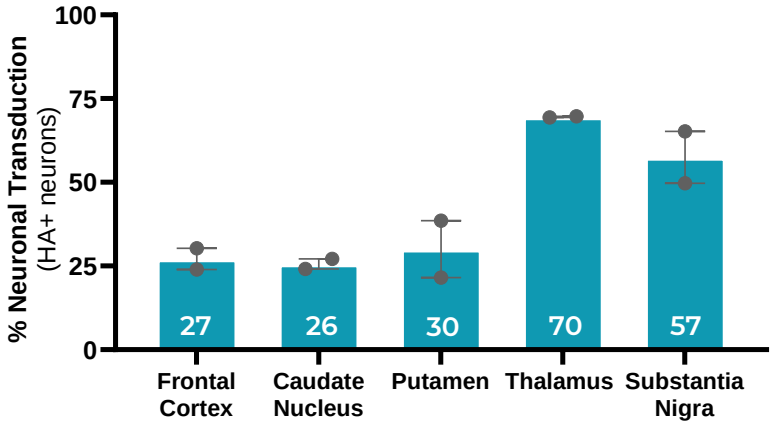
Up to **150K** prevalent PD-GBA population in US[2] and up to **180K** in the EU[3]

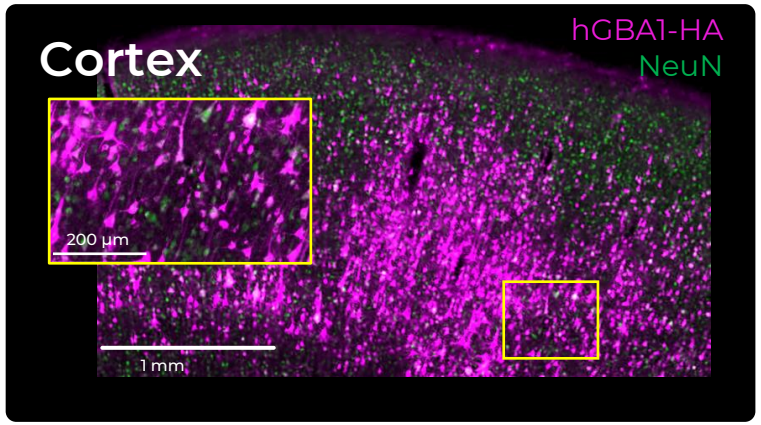
[1]Smith and Schapira 2022; [2]Parkinson's Foundation; [3]Deuschl G The Lancet Public Health 2020

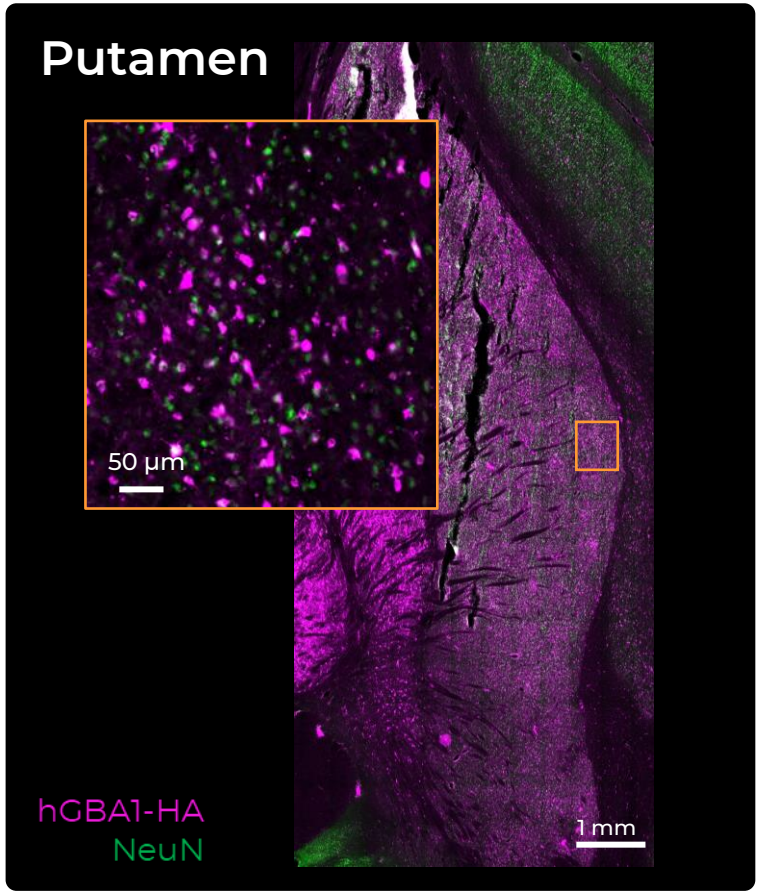
IV Dosing Yields Widespread Expression of hGBA1-HA in Relevant NHP Brain Regions, including Substantia Nigra







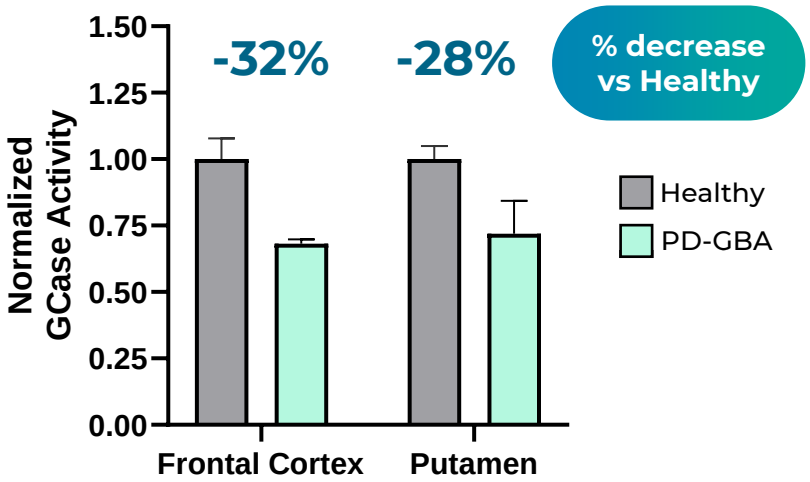




PD-GBA Development Candidate Study
Dose: 2.5E13 vg/kg
Cargo: hGBA1-HA; **In-life:** 6 weeks
Species/Age: N = 3 cynomolgus macaques, ~42mo

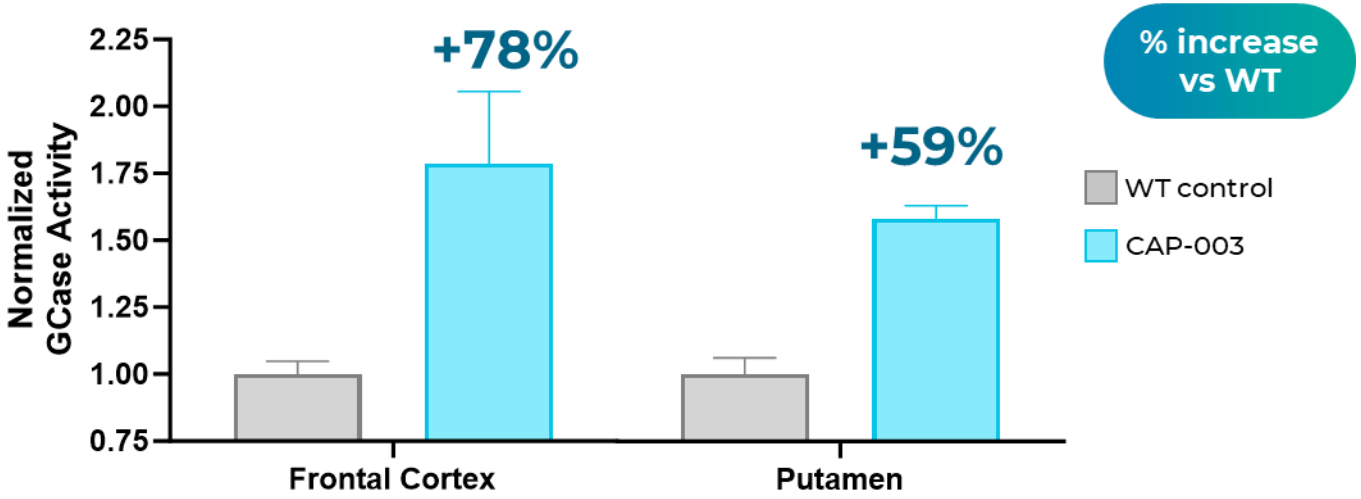
CAP-003 Significantly Exceeds GCase Activity Levels Required for Clinical Efficacy

PD-GBA Patient GCase Deficits



Adapted from Leyns et al., 2023

CAP-003 GCase Increases in NHPs via Mass Spectrometry



GCase increases are expected to **normalize enzyme deficits** and **provide clinically meaningful benefit** for PD-GBA patients

CAP-003 increases brain GCase protein by ~174%

PD-GBA Development Candidate Study
Cargo: hGBA1-HA, **Dose:** 2.5E13 vg/kg, **In-life:** 6 weeks, **Species:** Cynomolgus macaques, **Age:** ~42mo

Syntaxin-binding Protein 1 (STXBP1) Genetic Epilepsy

CAP-002 is first-in-disease and best-in-class disease modifying therapy

STXBP1 Genetic Mutation
Autosomal dominant

STXBP1 is expressed in every neuron and is essential for neurotransmitter release

Reduction in STXBP1 levels results in impaired neurotransmission

	Limitations of Investigational Therapies	CAP-002 Differentiators
Transduction	– Inability to achieve brain wide neuronal transduction	+ Widespread transduction through the brain
Expression	– Insufficient	+ Dose-dependent STXBP1 protein expression throughout the cortex
Delivery	– Invasive delivery	+ Non-Invasive IV delivery
Safety	– DRG toxicity risks	+ Unremarkable histopathology across the body, including liver and DRGs

Disease Manifestations

- Refractory seizures
- Developmental delay, cognitive dysfunction, and intellectual disability
- Motor abnormalities
- Early mortality

Unmet Need

- No approved therapies
- Anti-seizure medications only partially effective

Commercial Opportunity Potential >$1B

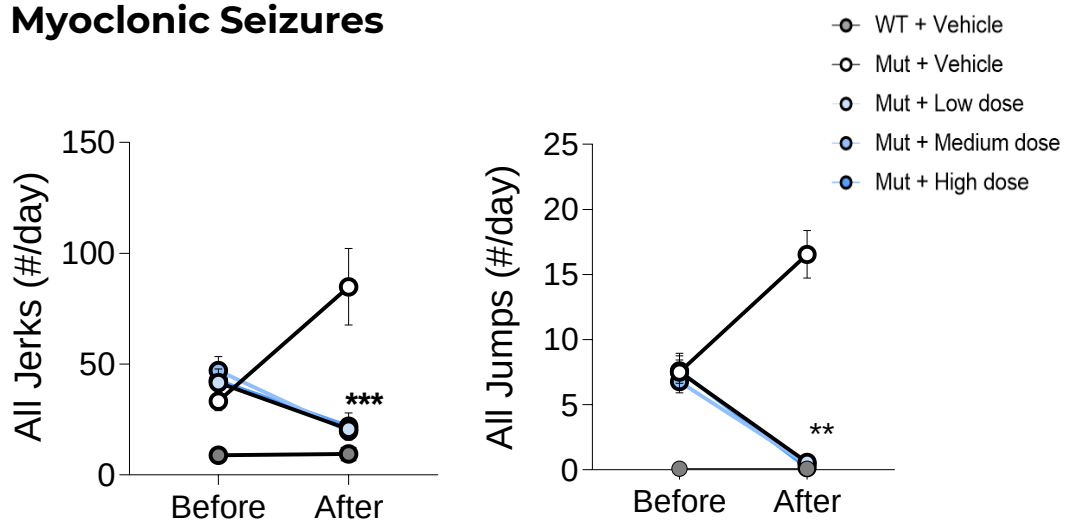
- No disease modifying programs in clinical development
- Potential to be first-in-class and first-in-disease
- 1:30,000 live births[1] (up to 4500 in US and EU) and growing

[1]Lopez-Rivera et al., Brain, 2020

Brain-wide STXBP1 Expression Enables Dose-dependent Efficacy in Epilepsy & Cognitive Dysfunction in Mouse Model

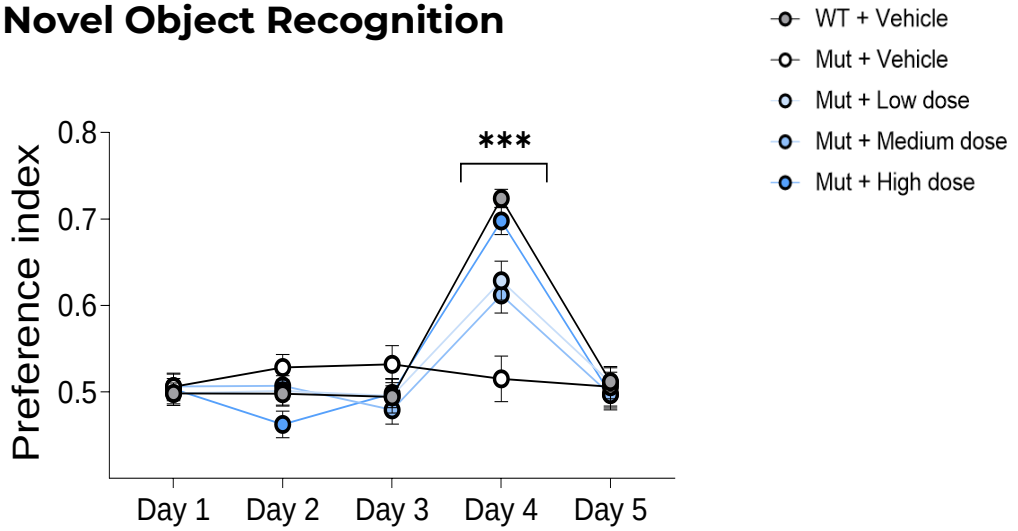
Epilepsy

Myoclonic Seizures



Cognitive Dysfunction

Novel Object Recognition



Difference from Mut + VEH: ns, non-significant, ** $p < 0.01$, *** $p < 0.001$

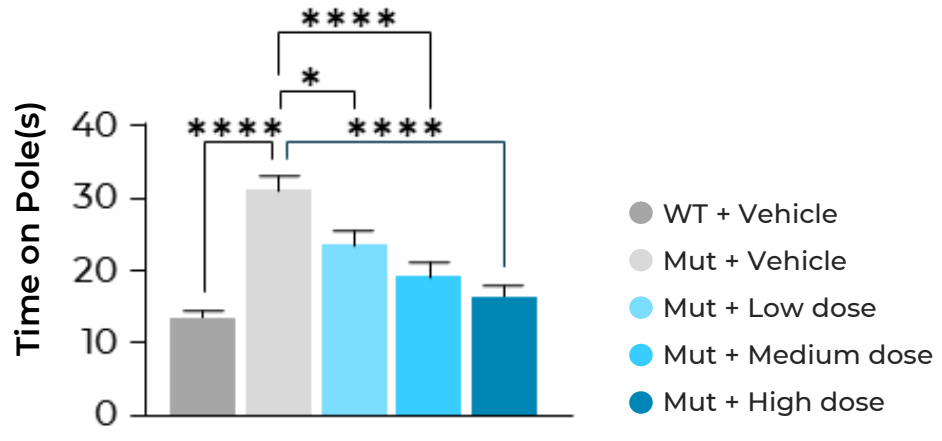
Brain-wide STXBP1 expression achieves significant reduction of seizures and cognitive dysfunction in mice

Murine data generated in collaboration with lab of Mingshan Xue, Baylor College of Medicine

Dose-dependent Efficacy in Motor Deficits in Mouse Model Enabled by Brain-wide STXBP1 Expression

Motor Deficits

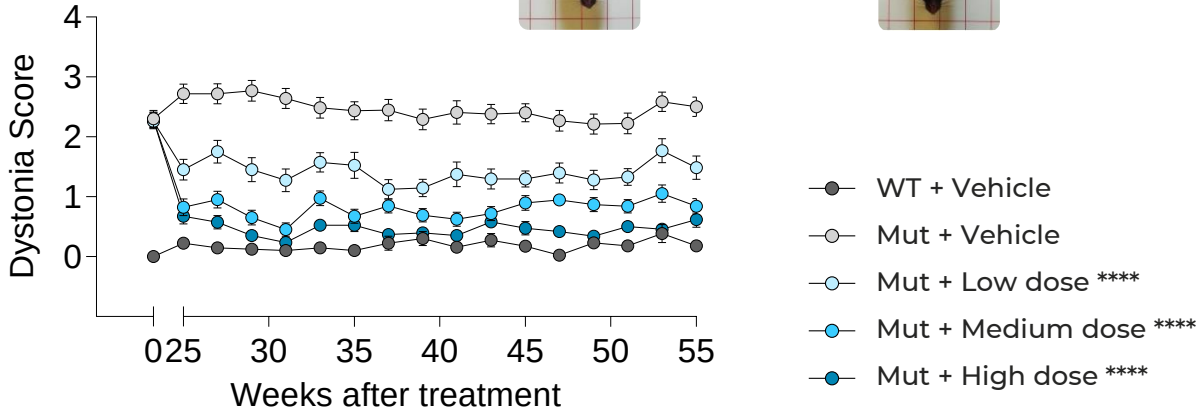
Vertical Pole



Dystonia

Before AAV injection

After AAV injection



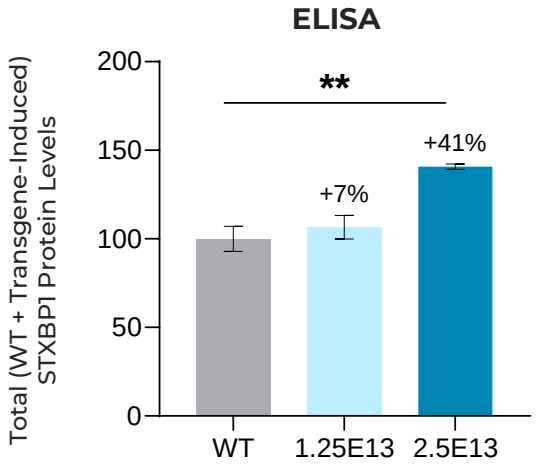
Difference from Mut + VEH: ns, non-significant, * $p < 0.05$, **** $p < 0.0001$

Brain-wide STXBP1 expression achieves rapid and long-lasting efficacy in motor deficits in mice

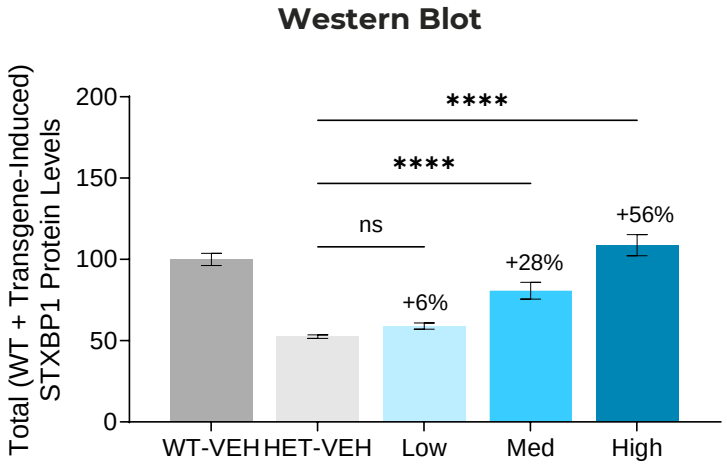
Murine data generated in collaboration with lab of Mingshan Xue, Baylor College of Medicine

CAP-002 Achieves Significant STXBP1 Increases Throughout NHP Brain Following IV Delivery

NHP with WT STXBP1 background



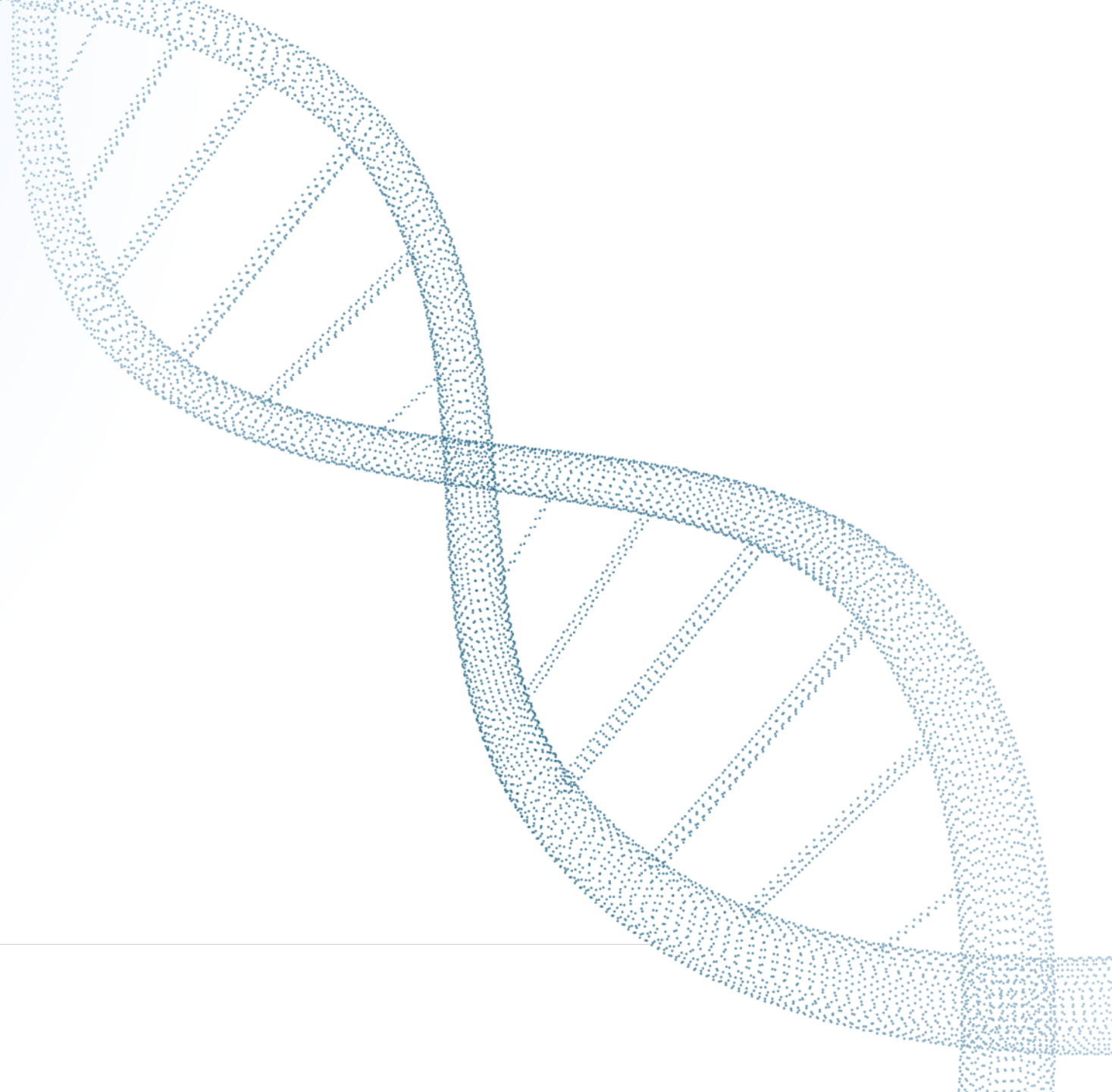
Mice with haploinsufficient STXBP1 background



CAP-002 **achieves dose-dependent STXBP1 expression in NHPs that correlates with correction of epilepsy, cognitive, and motor phenotypes** in mice

CAP-002 increases STXBP1 in NHPs beyond levels needed to demonstrate a direct benefit and is expected to correct deficits in all phenotypes in patients

Murine data generated in collaboration with lab of Mingshan Xue, Baylor College of Medicine



Manufacturing

Integrated Process & Analytical Development and cGMP Capabilities

In house capabilities reduce turn-around times and expedite process transfer to support clinical studies

Vector Production		Rapid production of engineered capsids for preclinical studies
Process & Analytical Development		Conduct manufacturability assessment in HEK293 suspension process
		Up to 50 L bioreactor scale
		Develop and optimize key analytical assays
cGMP Manufacturing		15,000 ft^2 cGMP Manufacturing Facility
		Leverages single use systems
		Up to 200L bioreactor scale
		Finish – fill operations
		Unidirectional flow
		In-house QC capabilities for product release
		Modular clean rooms

Excellent yields and quality specifications at or above FDA standards

Capsida Summary

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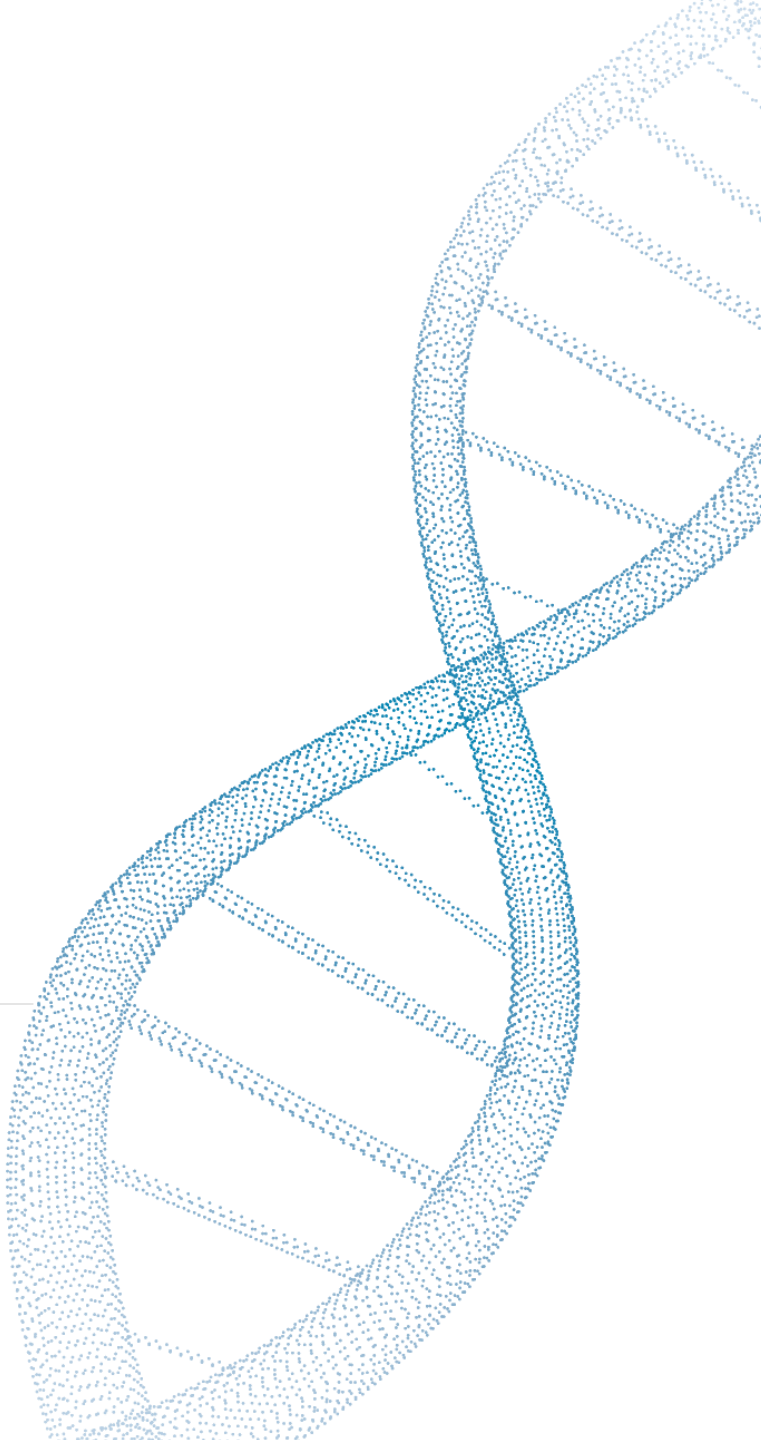
Our Pipeline is Making the Impossible Possible



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