



Delivering the Future of Genomic Medicines

May 2025

Forward-Looking Statements and Legal Disclaimers

This presentation, and accompanying oral commentary, contains forward-looking statements regarding our current expectations. These forward-looking statements include, without limitation, statements relating to: the therapeutic and commercial potential and value of our product candidates and engineered capsids, including the ability of our zinc finger epigenetic regulators to address various neurological diseases and our capsid engineering platform to expand delivery beyond currently available methods; potential STACTM-BBB partnerships and its manufacturability at commercial scale; the potential to develop, obtain regulatory approvals for and commercialize durable, safe and effective therapies to treat certain diseases and the timing, availability and costs of such therapies; the potential to use ZF, SIFTER and other technologies to develop durable, safe and effective therapies and capsids; the potential for us to benefit and earn development and commercial milestone and royalty payments and additional licensed target fees from our collaborations and the timing of any such benefits and payments; plans for the near-term execution of a Fabry commercialization license agreement; anticipated revenues from existing and new collaborations and the timing thereof; plans and expectations to seek partners or collaborators for certain of our programs; the potential for isaralgagene civaparovec to qualify for the FDA's Accelerated Approval program, including the adequacy of data generated in the Phase 1/2 STAAR study to support any such approval; expectations concerning the availability of additional data to support a potential BLA submission for isaralgagene civaparovec, and the timing of such submission; the potential to accelerate the expected timeline to approval and bring isaralgagene civaparovec to patients sooner than previously expected; the anticipated advancement of isaralgagene civaparovec to registration; the advancement of our preclinical neurology programs, including the potential of ST-503 to transform the chronic neuropathic pain landscape, plans to initiate patient enrollment and dosing for ST-503 and announcement and timing of such preliminary proof of efficacy data, and anticipated prion disease CTA submission and announcement and timing of related preliminary clinical data; plans regarding our financial resources, including the impact of a potential Fabry commercialization license agreement to provide cash runway through clinical data readouts for lead neurology programs, iSFN and prion disease; plans to reduce our operating expenses; the impact of our streamlined structure and future potential cost reductions, anticipated plans and timelines for us and our collaborators conducting our ongoing and potential future clinical trials and presenting data from our clinical trials and those of our partners and making regulatory submissions; the anticipated advancement of our product candidates to late-stage development, including potential future registrational trials, execution of our corporate strategy, our pipeline, the identification of additional targets, and the advancement of preclinical programs to the clinic, key milestones and catalysts, and other statements that are not historical fact. These statements are not guarantees of future performance and are subject to certain risks and uncertainties that are difficult to predict. Our actual results may differ materially and adversely from those expressed. Factors that could cause actual results to differ include, without limitation, the uncertain and costly research and development process, including the risk that preclinical results may not be indicative of any future clinical trials, to the effects of macroeconomic factors or financial challenges, including as a result of ongoing overseas conflicts, tariffs, geopolitical instability, inflation and fluctuations in interest rates on the global business environment, healthcare systems and business and operations of us and our collaborators, including the initiation and operation of clinical trials; the research and development process; the uncertain timing and unpredictable results of clinical trials, including whether preliminary or initial clinical trial data will be representative of final clinical trial data and whether final clinical trial data will validate the safety, efficacy and durability of product candidates; the impacts of clinical trial delays, pauses and holds on clinical trial timelines and commercialization of product candidates; the unpredictable regulatory approval process for product candidates across multiple regulatory authorities; the potential for Sangamo to cease development of the Hemophilia A program, whether due to its inability to secure options to bring the program forward or otherwise; the manufacturing of products, product candidates and capsids; the commercialization of approved products; the potential for technological developments that obviate technologies used by us and our collaborators; the potential for us or our collaborators to breach or terminate collaboration agreements; the potential for us to fail to realize our expected benefits of our collaborations; the uncertainty of our future capital requirements, financial performance and results, our lack of capital resources to fully develop, obtain regulatory approval for and commercialize our product candidates, including our ability to secure collaboration for some of our programs, our ability to secure the funding required to advance our preclinical programs in a timely manner or at all; and our lack of capital resources and need for substantial additional funding to execute our operating plan and to operate as a going concern, including the risk we will be unable to obtain the funding or partnerships, in particular for our Fabry disease program, or additional collaboration partners necessary to advance our preclinical and clinical programs and to otherwise operate as a going concern in which case we may be required to cease operations entirely, liquidate all or portion of our assets and/or seek protection under applicable bankruptcy laws middle all or a portion of out. There can be no assurance that we and our collaborators will be able to develop commercially viable products. These risks and uncertainties are described more fully in our Annual Report on Form 10-K for the fiscal year ended December 31, 2024 and our Quarterly Report on Form 10-Q for the quarter ended March 31, 2025, as filed with the Securities and Exchange Commission ("SEC") and future reports filed with the SEC. Forward-looking statements contained in this presentation speak only as of the date hereof, and we undertake no duty to update such information except as required under applicable law. This presentation concerns investigational product candidates that are under preclinical and/or clinical investigation, and which have not yet been approved for marketing by any regulatory agency. They are currently limited to investigational use, and no representations are made as to their safety or efficacy for the purposes for which they are being investigated. Any discussions of safety or efficacy are only in reference to the specific results presented here and may not be indicative of an ultimate finding of safety or efficacy by regulatory agencies.

Sangamo is a differentiated genomic medicine company focused on treating debilitating neurological diseases



Potent zinc finger epigenetic regulation technology, with neurology programs advancing towards the clinic



Industry-leading AAV capsid discovery platform has demonstrated non-invasive intrathecal and intravenous delivery to the brain



Powerful research platform **continually innovates in new modes of genome modulation** to support value creation opportunities for both wholly owned programs and potential partners



Strong roster of current partners and a **clear regulatory pathway to Accelerated Approval** agreed with **U.S. FDA in Fabry disease**, with partner negotiations ongoing

SHARP STRATEGIC FOCUS IN NEUROLOGY

OPTIMIZING ASSET VALUE

Why neurology genomic medicines?

- Widespread, debilitating diseases, largely unserved by current approaches
- Many neurology indications are single-gene or gene-associated
- Genomic medicines are well suited to neurology:
 - Targeting diseases at the DNA level reduces therapeutic complexity
 - Gene expression can be fine-tuned to the level needed for proper brain function
 - Potential for durable effect as most brain cells do not divide
- Addressing the issues of widespread brain delivery is critical to creating an effective neurology medicine



Sangamo pairs the epigenetic regulation *and* capsid delivery capabilities needed to create neurology genomic medicines

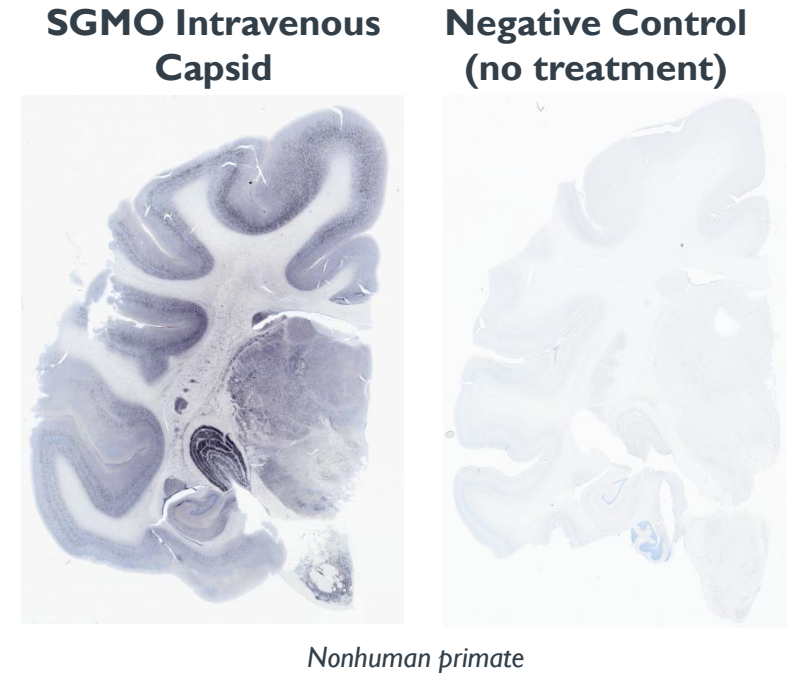
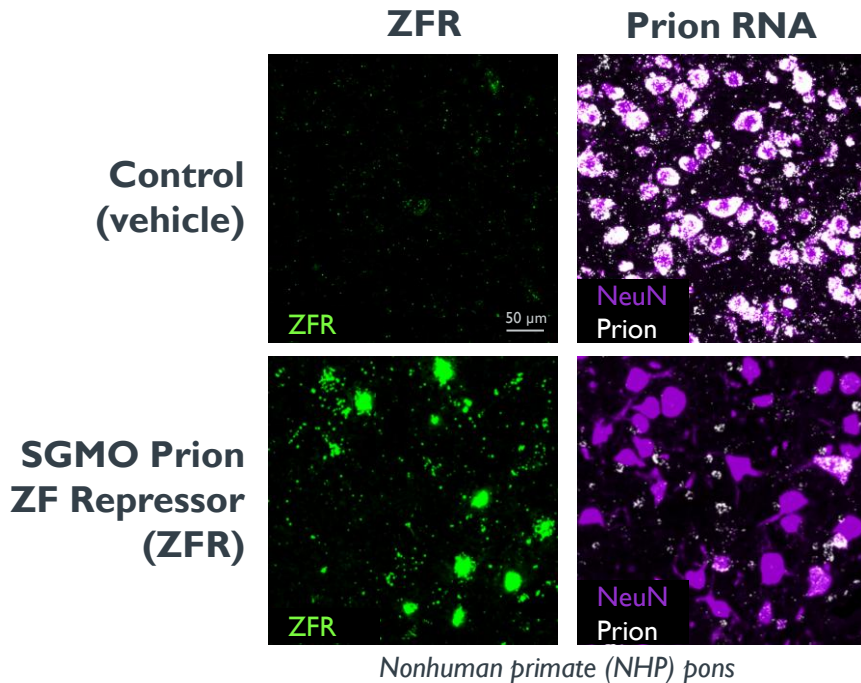
Genome-Targeting Cargo

Epigenetic regulation platform



Capsid Delivery Engine

AAV capsid delivery platform via intravenous delivery



Future of Neurology Genomic Medicines

Company pipeline and business development opportunities

NEUROLOGY PIPELINE – WHOLLY OWNED

| Indication | Preclinical | Phase I/2 | Pivotal | Partner | Commentary |
|--|-------------|-----------|---------|---------|--|
| Idiopathic Small Fiber Neuropathy (ST-503) | <div></div> | | | - | IND cleared, patient enrollment and dosing planned mid-2025. |
| Prion Disease | <div></div> | | | - | CTA submission anticipated in Q1 2026 |
| Undisclosed neurology target(s) | <div></div> | | | - | |

NEUROLOGY PIPELINE – PARTNERED

| Partnered Indication | Preclinical | Phase I/2 | Pivotal | Partner | Commentary |
|---|-------------|-----------|---------|---|---|
| Tauopathies   | <div></div> | | |  <small>A Member of the Roche Group</small> | August 2024: Announced epigenetic regulation and capsid delivery license agreement |
| Undisclosed neurology target   | <div></div> | | |  <small>A Member of the Roche Group</small> | |
| Undisclosed neurology target  | <div></div> | | |  | December 2024: Announced capsid license agreement for up to five neurological diseases |
| Undisclosed CNS target  | <div></div> | | |  | April 2025: Announced capsid license agreement for up to five diseases of the CNS |
| ALS/FTD  | <div></div> | | |  <small>AstraZeneca Rare Disease</small> | |
| Huntington's Disease  | <div></div> | | |  | |

OTHER PROGRAMS

| Indication | Preclinical | Phase I/2 | Pivotal | Partner | Commentary |
|--|-------------|-----------|---------|---------|---|
| Hemophilia A (Giroctogene fitelparvovec) | <div></div> | | | * | July 2024: Positive readout in Phase 3 AFFINE trial. |
| Fabry Disease (Isaralgagene civaparvovec) | <div></div> | | | - | BLA submission expected as early as 1Q 2026. |

Gateway neurology indication: ST-503 for chronic neuropathic pain



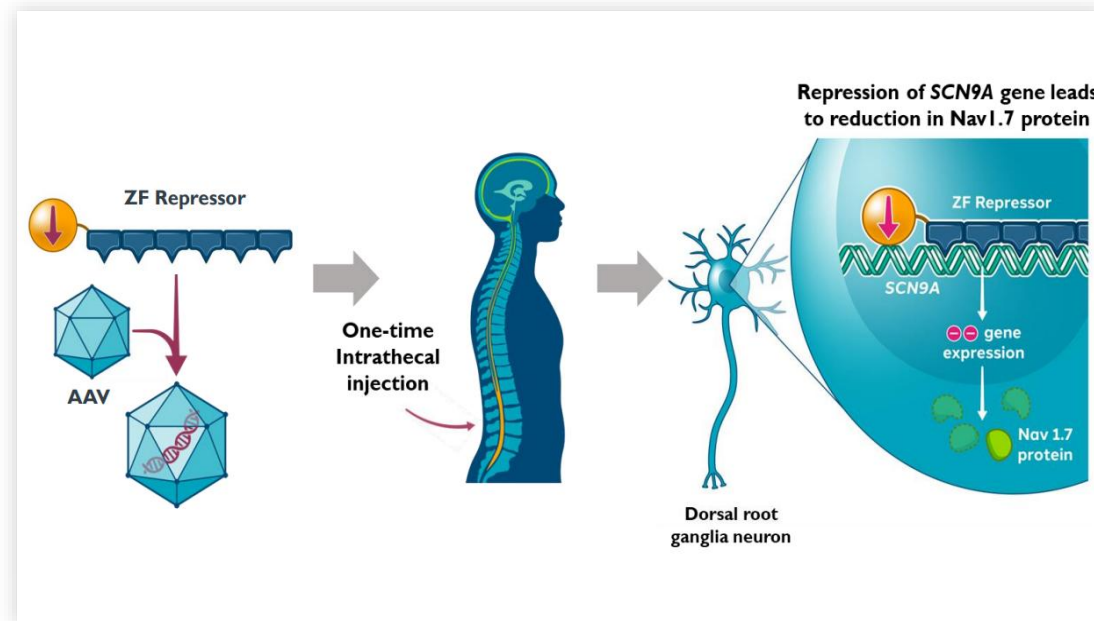
Epigenetic regulation

has the potential to fundamentally reshape the treatment of chronic intractable pain, which impacts millions globally, with few adequate treatment options

KEY ANTICIPATED MILESTONES

Mid-2025: Initiate patient enrollment and dosing

Q4 2026: Preliminary proof of efficacy data



- Starting in **idiopathic small fiber neuropathy (iSFN)**, a debilitating chronic neuropathic pain impacting **43,000 in the U.S.**
- **Nav1.7 sodium channel**, encoded by the **SCN9A gene**, is involved in a spectrum of inherited neuropathies
- Engineered **ZFR** resulted in **~70% repression of SCN9A gene** and **reduced pain hypersensitivity in mice**, with **high level of Nav1.7 specificity**
- Intrathecal delivery of **ZFR in NHPs** by AAV9 demonstrated up to **60% repression of SCN9A** in dorsal root ganglia (DRG) tissue
- **Short timescale** to expected preliminary clinical efficacy readout
- **Gateway pain indication:** if successful, ST-503 could be broadened to other types of chronic neuropathic pain e.g. trigeminal neuralgia

Gateway neurology indication: Prion disease



Clear path

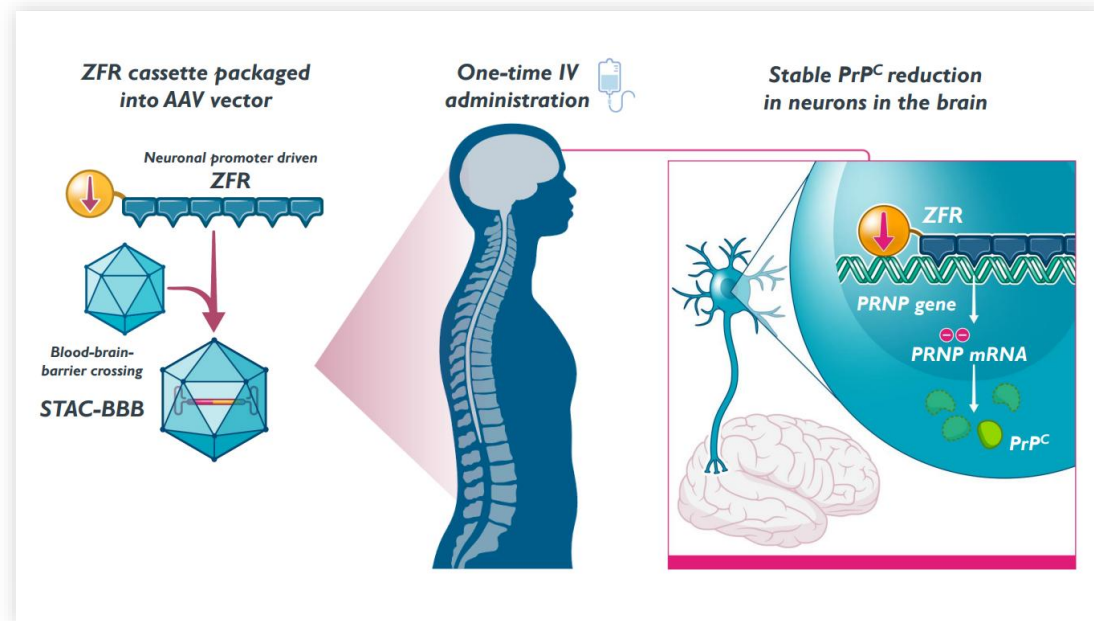
to potential clinical validation in a devastating disease with no current approved treatment options

KEY ANTICIPATED MILESTONES

Q1 2026: Prion CTA submission

Mid-2026: Clinical trial enrollment and dosing

Q4 2026: Preliminary clinical data



- Progressive condition leading to **rapid neurodegeneration and death**, with **no disease modifying therapy**
- At least **1,300 new cases each year in U.S. and Europe***
- Caused by the **misfolding of the prion protein (PrP)** into toxic species
- **ZFR-driven reduction of neuronal PrP expression** in prion-inoculated mice **profoundly extended survival**, reduced PrP in the brain and **improved biomarker and behavioral readouts**
- Widespread ZFR expression and **prion gene repression seen in NHP** brains following intravenous (IV) **STAC-BBB** administration
- **First-in-human** trial of novel **STAC-BBB** capsid, which if successful, could validate broader neurology pipeline

* US (per CDC) and Europe (<https://www.eurocjed.ac.uk/>)

Widespread CNS delivery is challenging with conventional AAVs

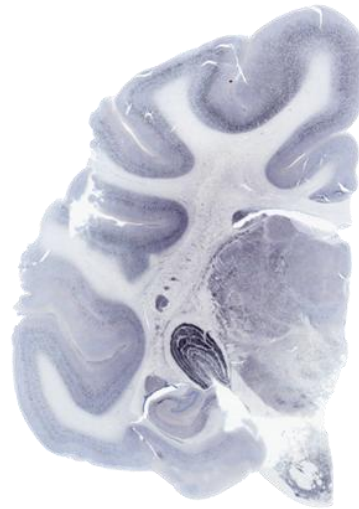
Our capsid engineering platform has demonstrated the ability to expand delivery, with industry-leading results



STAC-BBB

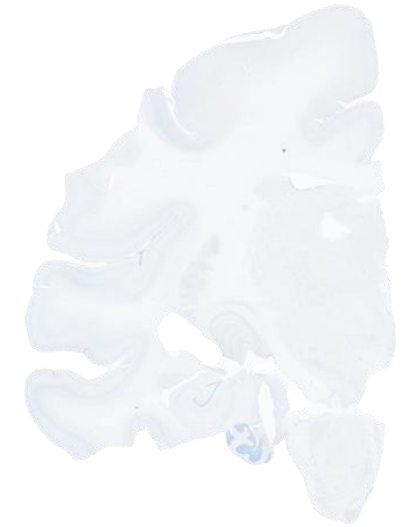
Showed robust penetration of the BBB and widespread transgene expression throughout the brain in NHPs following intravenous administration

STAC-BBB (Nuclear-localized GFP)



2e13 vg/kg STAC-BBB, 19 days post administration

Negative control (no AAV treatment)



- Enabled **strong expression** of zinc-finger cargo throughout the brain, including **all key brain regions**
- **Industry-leading** performance: **700-fold higher** transgene expression than benchmark capsid AAV9
- **Capsid-enabled delivery of zinc finger payloads** targeting prion disease and tauopathies resulted in **widespread repression** of target genes
- Vector genomes were **enriched in the CNS** and appear **de-targeted from the DRG and the liver**
- STAC-BBB is already the subject of **three blue-chip pharma agreements** (Genentech, Astellas and Lilly) with the potential for additional partnerships

Biopharma agreements have demonstrated industry interest in STAC-BBB and could provide significant economics for Sangamo

STAC-BBB partnerships

Genentech
A Member of the Roche Group

 **astellas**

Lilly

Potential for additional STAC-BBB license agreements

\$88m

cash received from
partners to date

Up to \$4.6b

in potential future milestones and
exercise fees assuming exercise of
all options and targets

**Additional
potential product
royalties**

Numerous Benefits of Partnerships:

Partner buy-in validates the
science

Provides potential non-dilutive
capital to advance pipeline

Leverages partner domain
expertise

Promotes optimal resource
allocation to advance late-stage
clinical development

Company Highlights



Advancing epigenetic regulation for important gateway neurology diseases like chronic neuropathic pain and prion disease, with preliminary clinical data anticipated in Q4 2026 for both



Proprietary AAV blood-brain barrier penetrant capsid (STAC-BBB) with industry leading CNS tropism in NHPs. Already the subject of license agreements with Genentech, Astellas and Lilly, with potential for additional partnerships.



STAC-BBB potentially unlocks multiple neurology epigenetic programs that could be advanced ourselves or with partners



Novel next-generation modular integrase (MINT) platform allows targeting of a serine recombinase engineered to enable large-scale genome editing



Fabry program generating compelling Phase I/2 clinical data. Clear pathway to Accelerated Approval with FDA, with potential BLA submission as early as 1Q 2026 (3-year acceleration). Engaged in potential commercialization partner negotiations.

1Q25 Business Updates



1Q25 Key Takeaways

Announced capsid license agreement with Lilly to deliver genomic medicines for up to five diseases of the CNS plus pricing of a \$23 million underwritten registered direct equity offering.



Received \$18 million upfront license fee from Lilly for first target and eligible to earn up to \$1.4 billion in additional licensed target fees and milestone payments, plus tiered royalties on potential net sales.

Neurology Pipeline

- Advanced preparations for Phase I/2 study of ST-503 for treatment of intractable pain due to idiopathic small fiber neuropathy (iSFN), a type of chronic neuropathic pain.
- Expect to commence patient enrollment and dosing for ST-503 in mid-2025, with preliminary proof of efficacy data anticipated in Q4 2026.
- CTA enabling activities continue to advance for ST-506 in prion disease, with a submission expected in 1Q26.
- Continue to engage in potential business development discussions related to STAC-BBB.
- Nine abstracts accepted for presentation at ASGCT (May 13-17), showcasing advances in neurology pipeline.

Fabry Disease

- All dosed patients in Phase I/2 STAAR study data have now completed at least 52-weeks of follow-up – preliminary analysis across all 32 dosed patients indicates mean eGFR slope remains positive.
- A pivotal data readout is expected by end of the second quarter of 2025.
- Held productive Type B CMC meeting with U.S. FDA, providing Sangamo with a clear CMC pathway to a planned BLA submission as early as the first quarter of 2026.
- Discussions with the European Medicines Agency (EMA) are ongoing.



Financial Highlights

- Received from Lilly an **\$18 million upfront license fee**. Eligible to earn up to **\$1.4 billion in additional licensed target fees and milestone payments, plus tiered royalties on net sales**.
- Approximately **\$25.2 million in cash and cash equivalents** as of March 31, 2025, which, together with the \$18.0 million upfront license fee received from Lilly, the anticipated net proceeds from the underwritten offering announced today, and our at-the-market offering program since March 31, 2025, will be sufficient to fund our planned operations into **late in the third quarter of 2025**.



Q1 Pipeline Progress & Anticipated Milestones

CORPORATE UPDATES

- ✓ Announced capsid license agreement with Lilly to deliver genomic medicines for up to five diseases of the CNS. Received an \$18 million upfront license fee.
- Continue to engage in potential business development discussions related to STAC-BBB.
- Announced pricing of \$23 million underwritten registered direct equity offering.
- Continue to seek a potential collaboration partner for Hemophilia A, following a decision by Pfizer to terminate the global collaboration and license agreement.

NEUROLOGY

- ✓ Advanced preparations for Phase 1/2 study of ST-503 for treatment of intractable pain due to idiopathic small fiber neuropathy (iSFN), a type of chronic neuropathic pain.
- Expect to commence patient enrollment and dosing for ST-503 in mid-2025.
- Preliminary ST-503 proof of efficacy data anticipated in Q4 2026.
- ✓ Continued to advance CTA-enabling activities for prion disease, leveraging STAC-BBB.
- A CTA submission for prion is expected in Q1 2026.
- Preliminary prion clinical data anticipated in Q4 2026.
- ✓ Nine Sangamo abstracts accepted for presentation at ASGCT (May 13-17), showcasing advances in neurology pipeline.
- ✓ One abstract accepted as platform presentation in prestigious Presidential Symposium showcasing the potent combination of epigenetic regulation and capsid delivery technology for the treatment of prion disease in animal models.

FABRY DISEASE

- ✓ All dosed patients in Phase 1/2 STAAR study data have now completed at least 52-weeks of follow-up - preliminary analysis across all 32 dosed patients indicates mean eGFR slope remains positive.
- ✓ Clear regulatory pathway to Accelerated Approval from FDA using data from ongoing Phase 1/2 STAAR study.
- A pivotal data readout is expected by the end of the second quarter of 2025.
- ✓ Held productive Type B CMC meeting with U.S. FDA, providing Sangamo with a clear CMC pathway to BLA submission.
- A potential BLA submission is anticipated as early as the first quarter of 2026.
- Discussions with the EMA are ongoing.

Financial metrics

Historical

\$910m

Cash received from
partners to date

\$32.5m*

Non-GAAP OpEx – Q1 2025

~\$25.2m

Cash and cash equivalents balance
as of 3/31/25

Forward Looking

Up to \$6.1b

In potential future milestones and exercise fees, assuming exercise of all
options and targets

\$125m – \$145m (2025)**

Non-GAAP OpEx guidance excludes certain non-cash charges as noted
below***



Engineering Versatile Zinc Finger Payloads for Neurology

Sangamo has the tools needed to advance a next-generation neurology genomic medicine company



Potent Zinc Finger Cargo

Level of potency is precisely customizable to the indication being targeted



Versatility and Exquisite Specificity

We believe any gene in the genome is targetable for up- or down-regulation



All Human Derived

Potentially avoids issues with immunogenicity



Small Size. Easily Packaged.

Zinc fingers can be easily packaged into viral vectors



Powerful AAV Delivery Platform

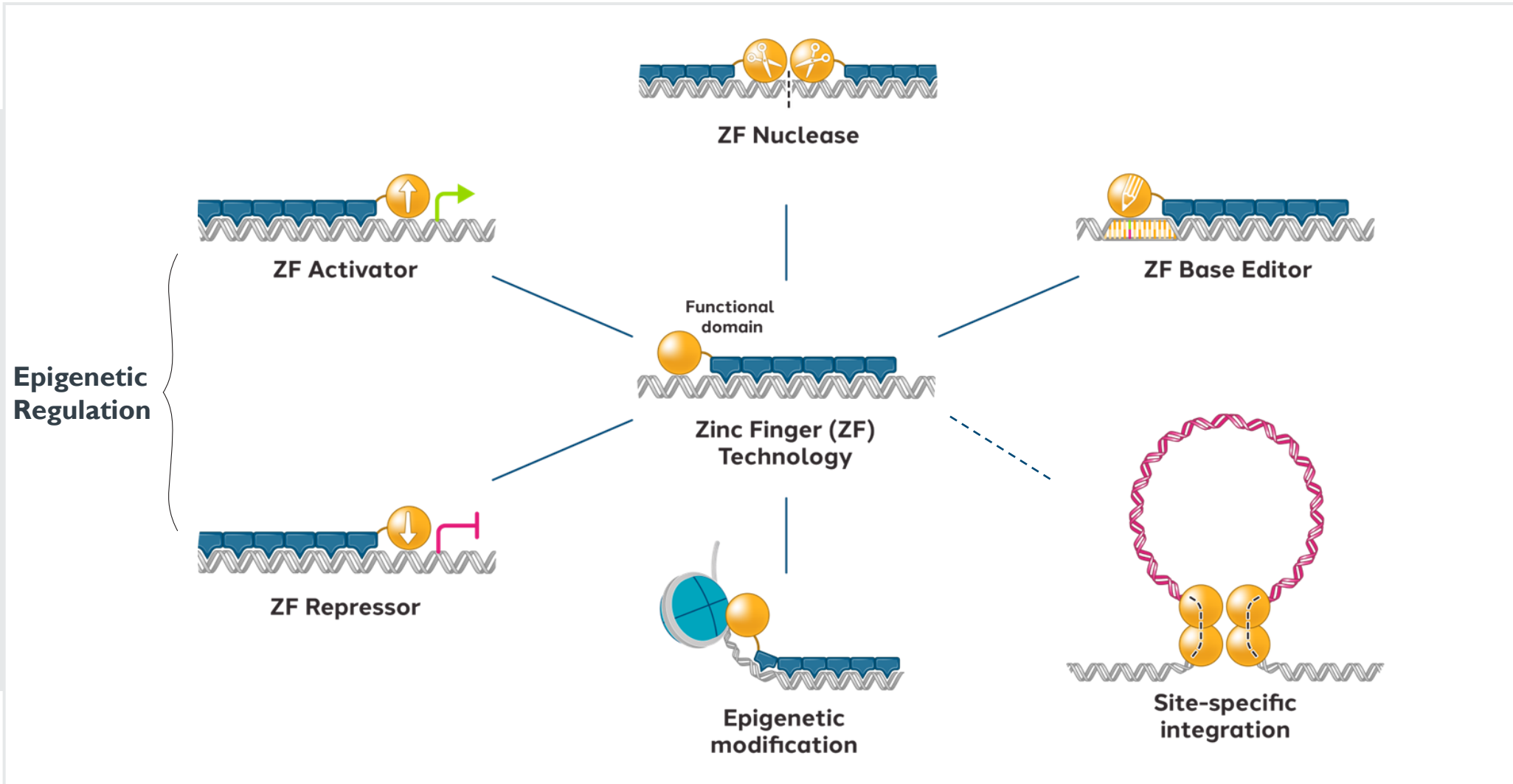
Widespread zinc-finger 'cargo' delivery – via both intravenous AND intrathecal delivery



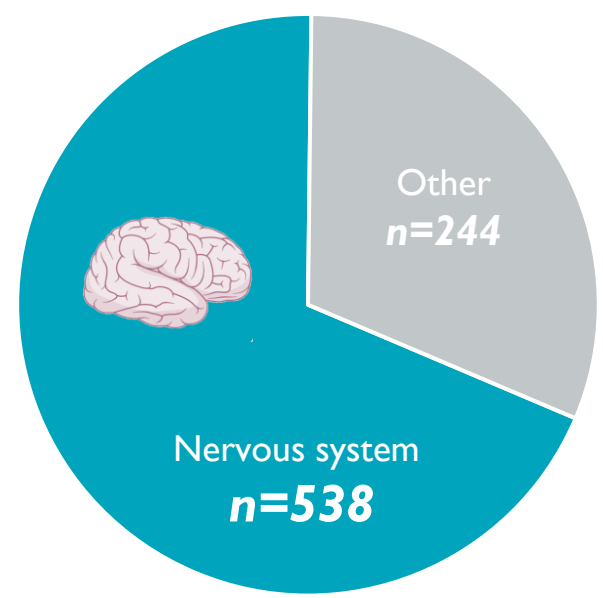
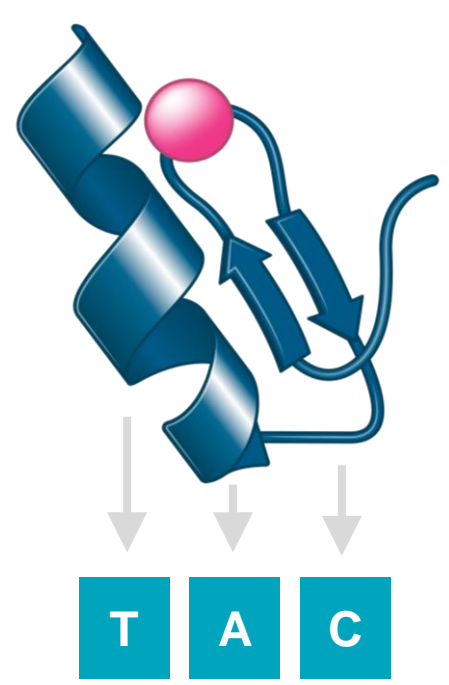
Industry Leading CNS Tropism



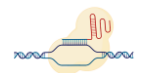
Robust penetration of the blood-brain barrier and widespread brain distribution in NHPs

Sangamo's differentiated genomic engineering platform is flexible, creating specific tools for the needs of each target



Zinc finger epigenetic regulators are the ideal cargo for neurology-focused genomic medicines



| |  ZFR/ZFA |  ASO |  CRISPR |
|-------------------------|---|---|--|
| Single administration | ✓ | ✗ | ✓ |
| Human derived | ✓ | ✗ | ✗ |
| Target any sequence | ✓ | ✗ | ✗ |
| Cell-type specificity | ✓ | ✗ | ~ |
| Compact / multiplexing | ✓ | ~ | ✗ |
| Supplement with cDNA | ✓ | ✗ | ✗ |
| All RNA / protein forms | ✓ | ~ | ✓ |
| Allele specific | ✓ | ✗ | ~ |

Zinc Fingers are natural proteins that bind DNA with high specificity
















At least 782 human genes encode Zinc Finger Proteins

Most regulate the epigenetic state of other genes


Zinc fingers are differentiated in key therapeutic features for potentially treating neurologic diseases

n=782 C2H2 ZF-containing genes
Sources: Ensembl human genes; GTEx: CNS (>5 TPM)
ASO: antisense oligonucleotide

Sangamo's neurology portfolio provides opportunities for wholly owned program advancement and potential partnering opportunities

| | | | | | | | |
|--|---|--|--|---|---|--|---|
| WHOLLY OWNED PRIORITY PROGRAMS | Chronic Neuropathic Pain Nav1.7  | Prion Disease PRNP  | | | | | |
| CURRENTLY PAUSED CARGO PROGRAMS ENABLED BY STAC-BBB | Phelan-McDermid Syndrome SHANK3  | Dravet Syndrome SCN1A  | Myotonic Dystrophy Type I DMPK  | ALS SOD1  | Charcot Marie Tooth 2A MFN2  | Charcot Marie Tooth 1A PMP22  | Haploinsufficiency Syndrome SCN2A  |
| PARTNERED PROGRAMS | ALS C9orf72  | Huntington's Disease HTT  | Tauopathies MAPT  | Undisclosed neurology  | Undisclosed neurology  | Undisclosed CNS  | |

ALS: Amyotrophic Lateral Sclerosis; CMT: Charcot-Marie Tooth

 Cerebrospinal fluid (CSF) capsid

 Intravenous (IV) capsid



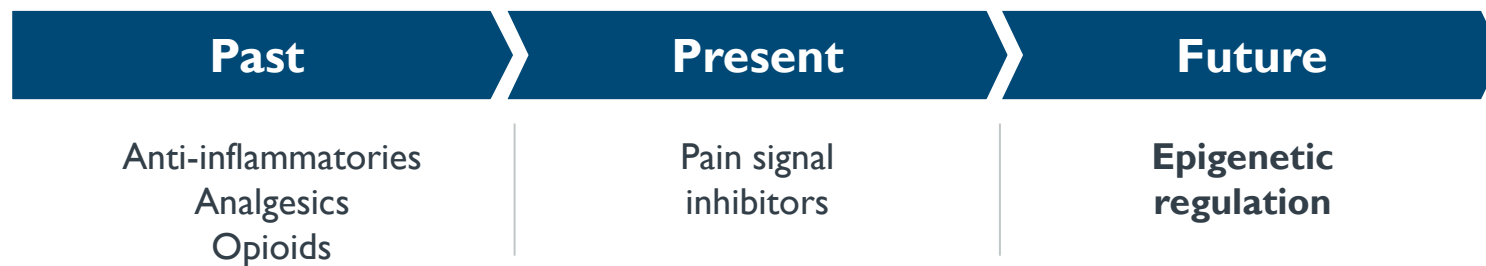
Epigenetic regulation to address chronic neuropathic pain

The urgent need for novel chronic neuropathic pain therapeutics



Epigenetic regulation

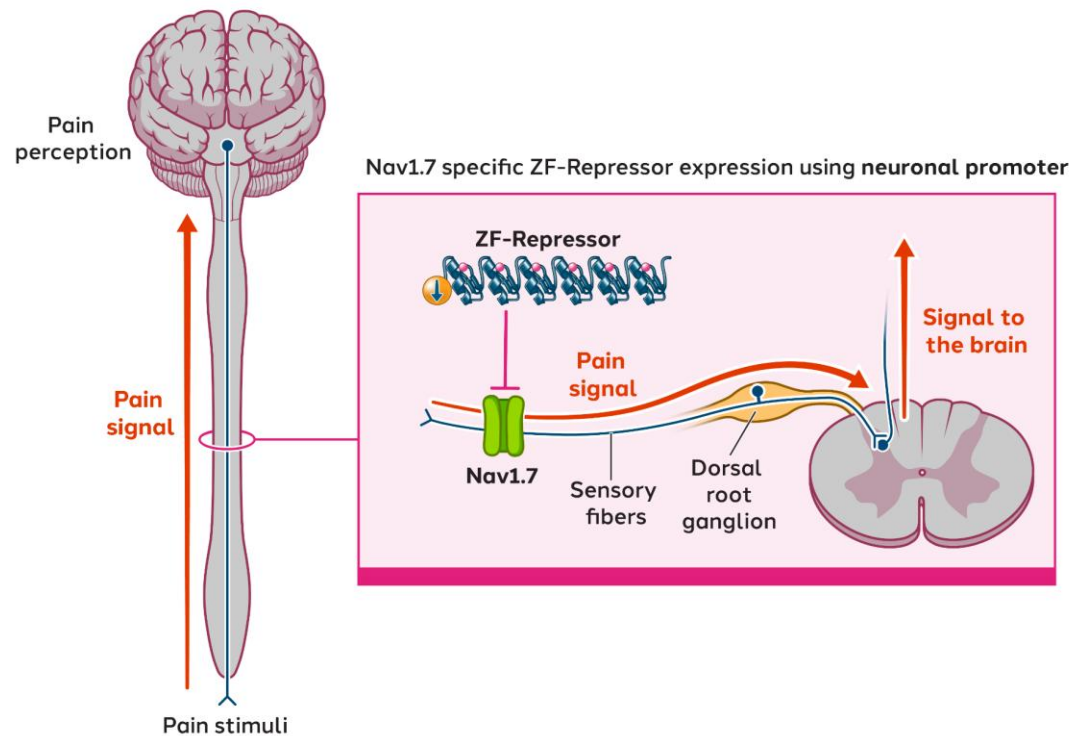
has the potential to fundamentally reshape the treatment of intractable pain



- > ST-503 is an **investigational epigenetic regulator** for the treatment of **intractable, chronic neuropathic pain**
- > **Peripheral neuropathies** are estimated to affect **~40 million Americans**
- > Our **first study** assesses ST-503 in **idiopathic small fiber neuropathy (iSFN)**, a type of chronic neuropathic pain
- > iSFN is a **chronic, highly debilitating** pain syndrome, with an estimated prevalence of at least **43,000 patients in the U.S**
- > **High unmet medical need**, with insufficient current treatment options (anticonvulsants, opioids and topical therapies)
- > **Short timescale** to expected clinical efficacy readout
- > **Gateway indication:** if successful, ST-503 could be **broadened** to other types of **chronic neuropathic pain**

Targeting the Nav1.7 pathway at the DNA level, we seek to succeed where others have failed

ST-503 targets a gene validated by human genetics and leverages an AAV delivery capsid already in the clinic



- A significant body of evidence implicates **sodium channels** in mediating the **pathophysiology of neuropathic pain**
- **Nav1.7** is a voltage gated sodium channel expressed in the Dorsal Root Ganglion (DRG)
- Blocking Nav1.7 in the DRG is expected to prevent the **transmission of nociceptive pain signals** to the brain
- This allows us to target multiple **neuropathic pain indications**, regardless of the cause of the pain
- Reducing pain by inhibiting Nav1.7 is not predicted to be associated with **any neurological side effects**
- Administered **intrathecally via AAV9**, a well-established, well-tolerated capsid

Zinc finger repressors potently reduced Nav1.7 in human neurons with high level of specificity



iPSC-derived
neurons

+

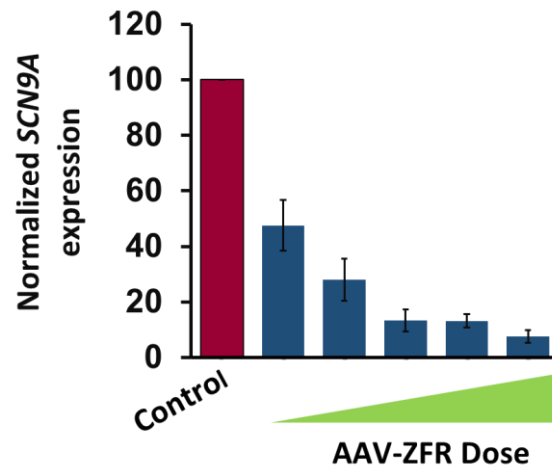


AAV + ZFR

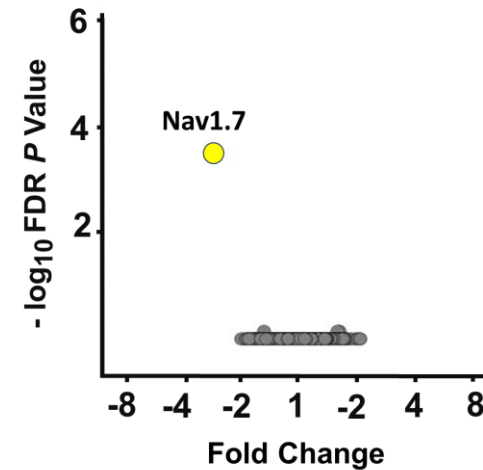
↓ 30d

Nav1.7 expression,
Off-target
assessment

Potent and dose-dependent
repression of *SCN9A* gene,
which encodes Nav1.7

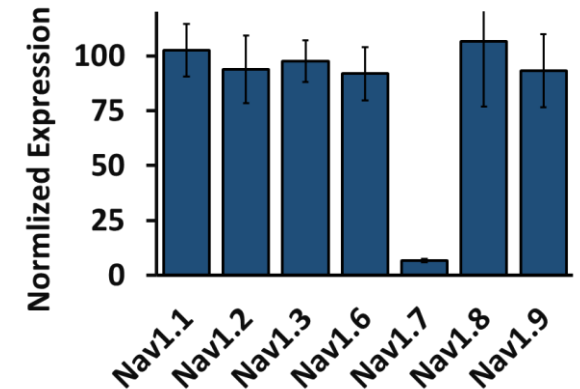


Selective repression
of *SCN9A* as shown
by global transcriptome analysis



Differential expression of
20,000 genes was evaluated

Specific repression of Nav1.7
without impacting other sodium
channels



Data presented at ASGCT 2023

Nav1.7 repressor reversed neuropathic pain in preclinical mouse models



Intrathecal
lumbar injection



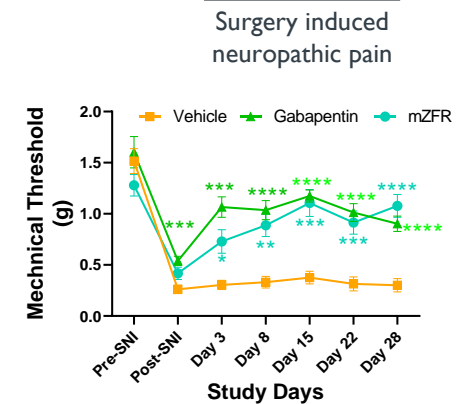
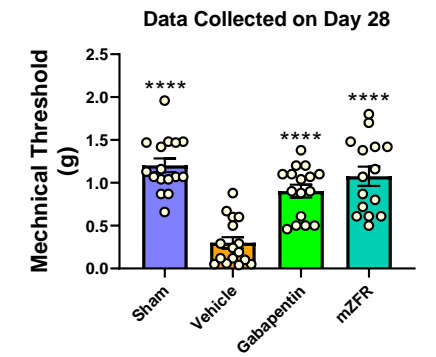
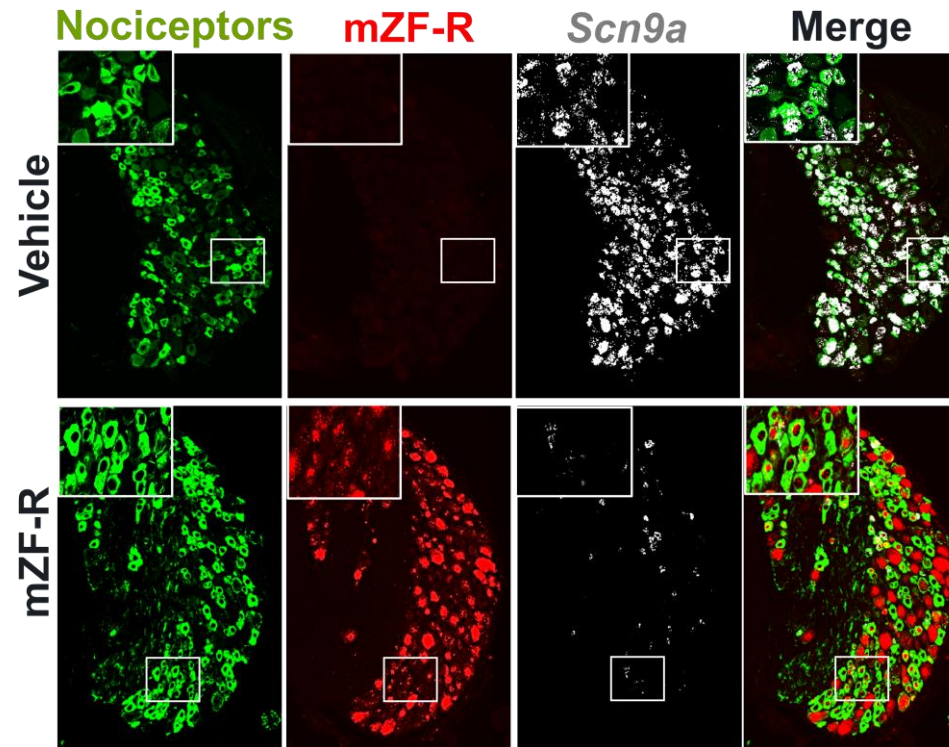
AAV-mZFR



Nav1.7 expression,
Pain assessment

Potent *Scn9a* mRNA repression in mouse
Lumbar DRG nociceptors

Full restoration of normal
sensitivity to mechanical pain

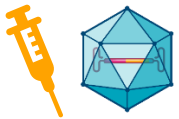


mZFR: mouse ZFR

Potent and selective repression of *SCN9A* observed in NHPs, with no clinical signs of toxicity or adverse clinical pathology



Intrathecal lumbar injection

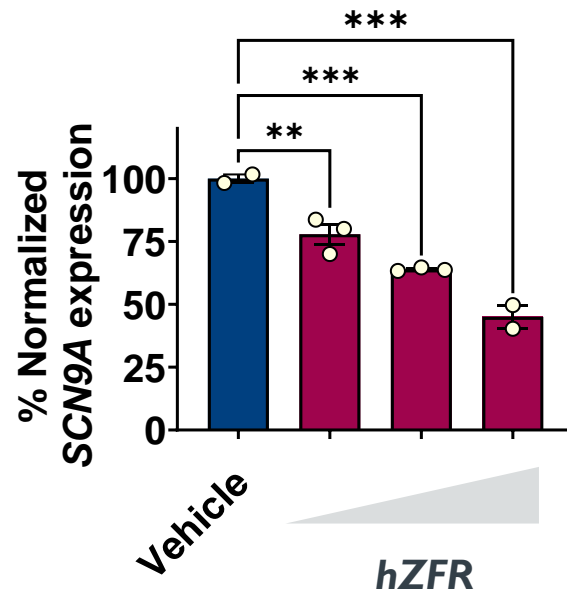


AAV-hZFR

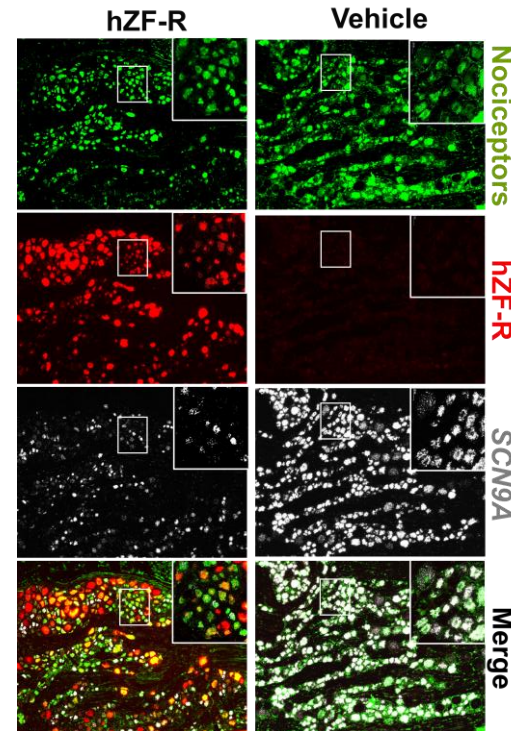
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Nav1.7 expression

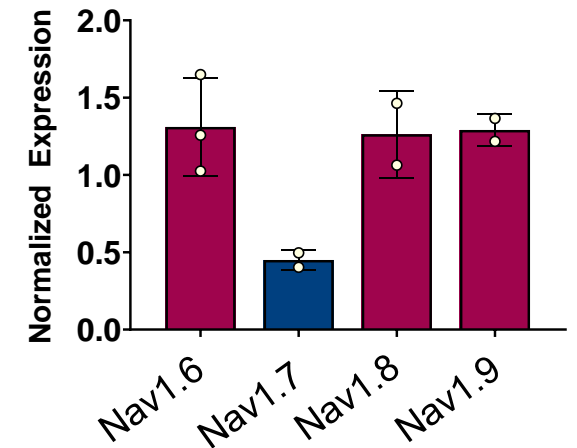
Potent and dose-dependent repression of *SCN9A* gene, which encodes Nav1.7



Selective repression of *SCN9A* as shown by single cell analysis

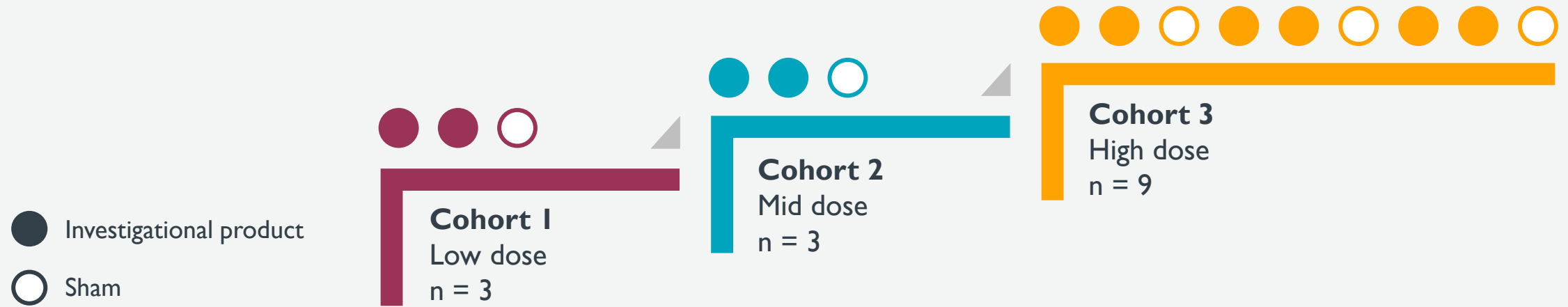


Specific repression of Nav1.7 without impacting other sodium channels



hZFR: human ZFR

Clinical study preparations are advancing, with preliminary proof of efficacy data anticipated in Q4 2026



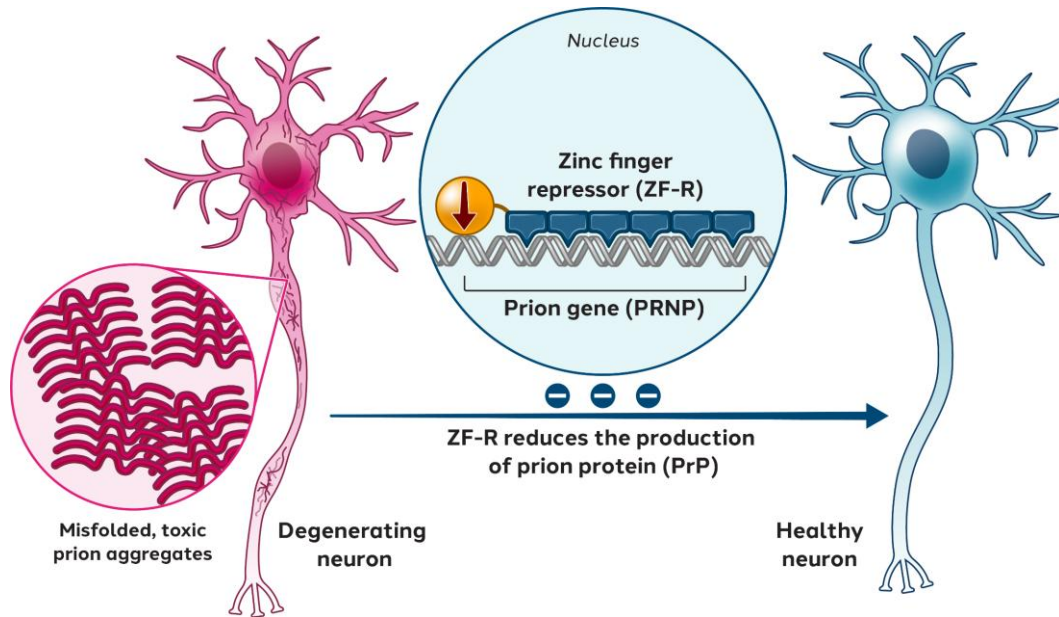
- > FDA **clearance of IND** received November 2024 to assess **ST-503** in **iSFN** patients
- > Preparing for **double-blind, randomized, sham-controlled dose escalation** study to determine safety and tolerability of single dose **intrathecal ST-503** gene therapy
- > Dose escalation protocol with a **2:1 randomization** of investigational product to sham
- > Plan to initiate patient enrollment and **dosing by mid-2025**
- > Anticipate preliminary **proof of efficacy data in Q4 2026**



Epigenetic regulation to address prion disease, leveraging STAC-BBB

Prion disease is rapidly progressive and always fatal

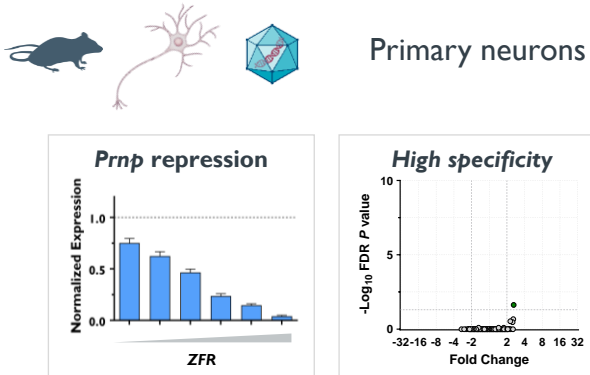
Path to potential clinical validation in a devastating disease with no current approved treatment options



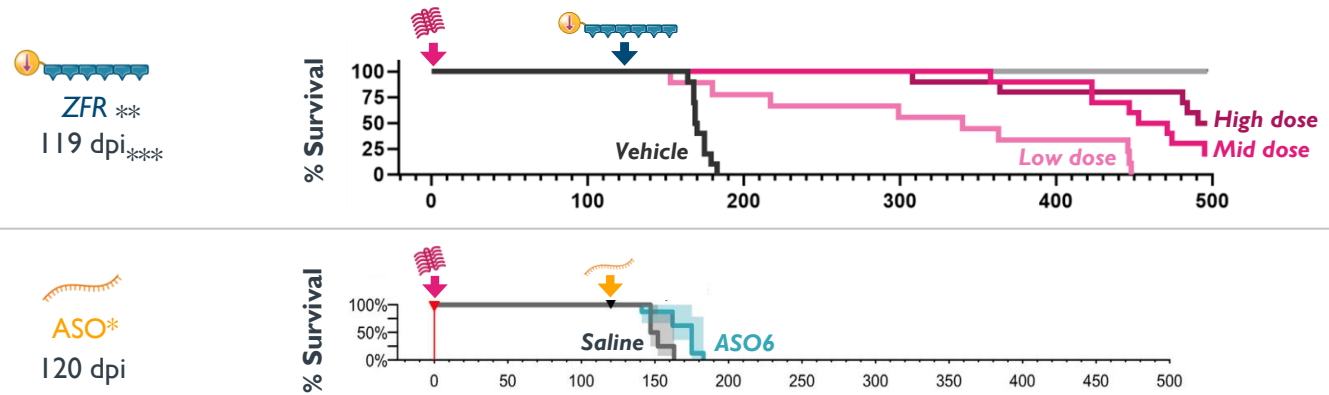
- Progressive condition, with **no disease modifying therapy**
- Caused by the misfolding of the prion protein (PrP) into toxic species, **leading to neurodegeneration and death**
- At least **1,300 new cases** each year in **U.S. and Europe***
- **Sporadic, inherited and acquired** forms
- **Well-defined** patient population
- **Excellent fit** for a zinc finger repression approach
 - Prion knockout animals do not get disease
 - Prion reduction can delay disease
- Repression of prion expression in the brain **should slow or halt disease progression and neurodegeneration**
- **First-in-human** trial of **STAC-BBB** capsid, which if successful, could validate broader wholly owned and partnered programs

Zinc finger repressors extended survival in a mouse model of aggressive prion disease, even when administered post-symptomatically

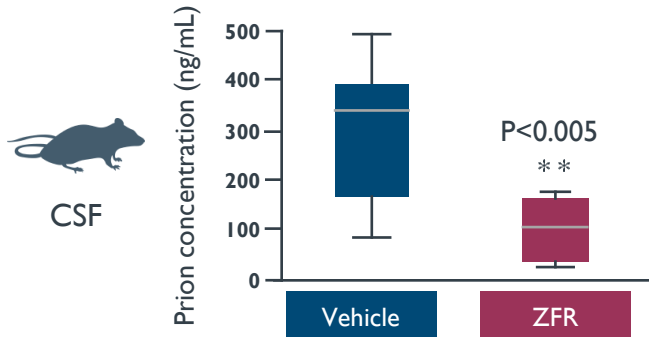
Potent and specific repression



Mouse survival extended, even when administered post-symptomatically



Reduction of CSF biomarker



Sustained brain-wide PrP knockdown in prion disease mice

Black: PrP
protein
antibody
labeling

(scale bar = 1 mm)

No treatment control
Assessment at 164 dpi

ZFR at 60dpi (pre-symptomatic)
Assessment at 500 dpi

ZFR at 122dpi (symptomatic)
Assessment at 500 dpi

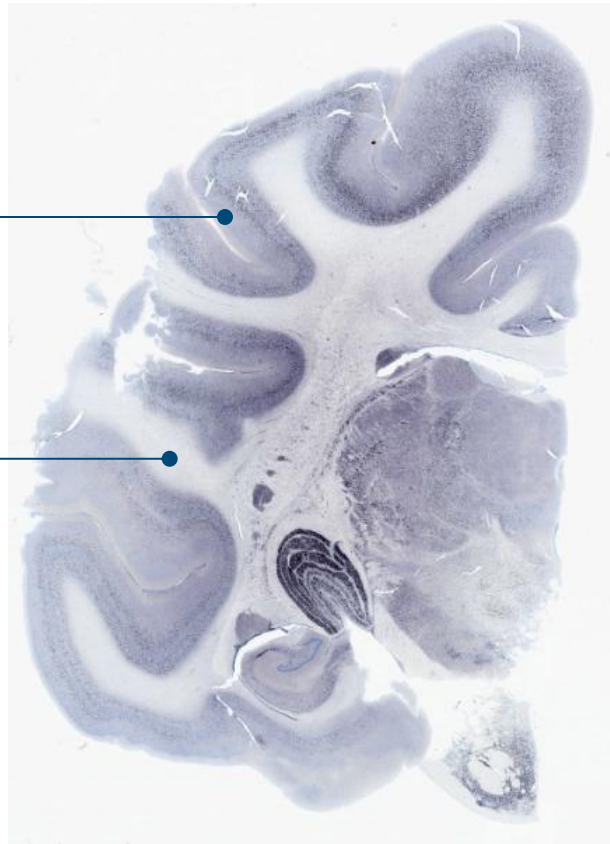
Data presented at ASGCT 2023, Prion 2024

* Antisense oligonucleotide (ASO) data from Minikel et al 2020
** ZFR administered intravenously using PHPB capsid *** dpi: days post inoculation

STAC-BBB demonstrated widespread and robust expression throughout the nonhuman primate brain

STAC-BBB

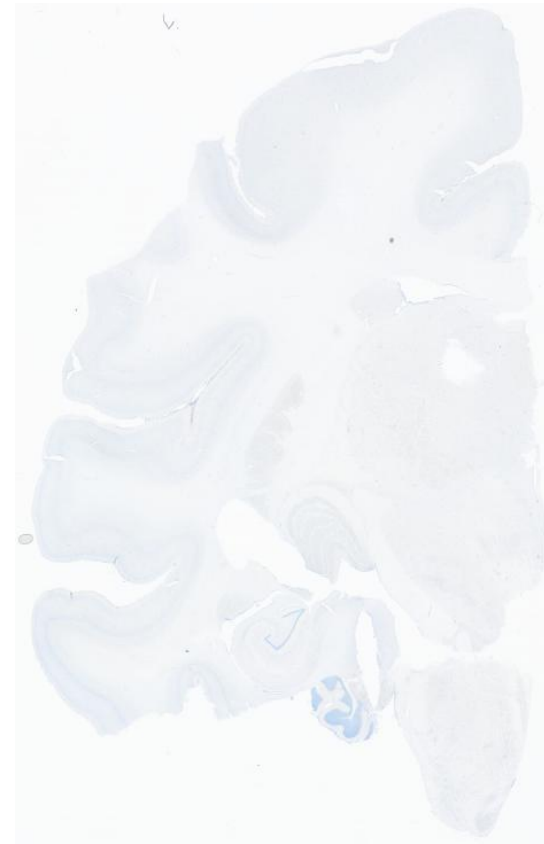
(Nuclear-localized GFP)



2e13 vg/kg STAC-BBB, 19 days post administration

Negative control

(no AAV treatment) – No signal



Grey matter
(cell bodies)

White matter
(nerve fibers)

Nissl staining (light blue):

All cell nuclei

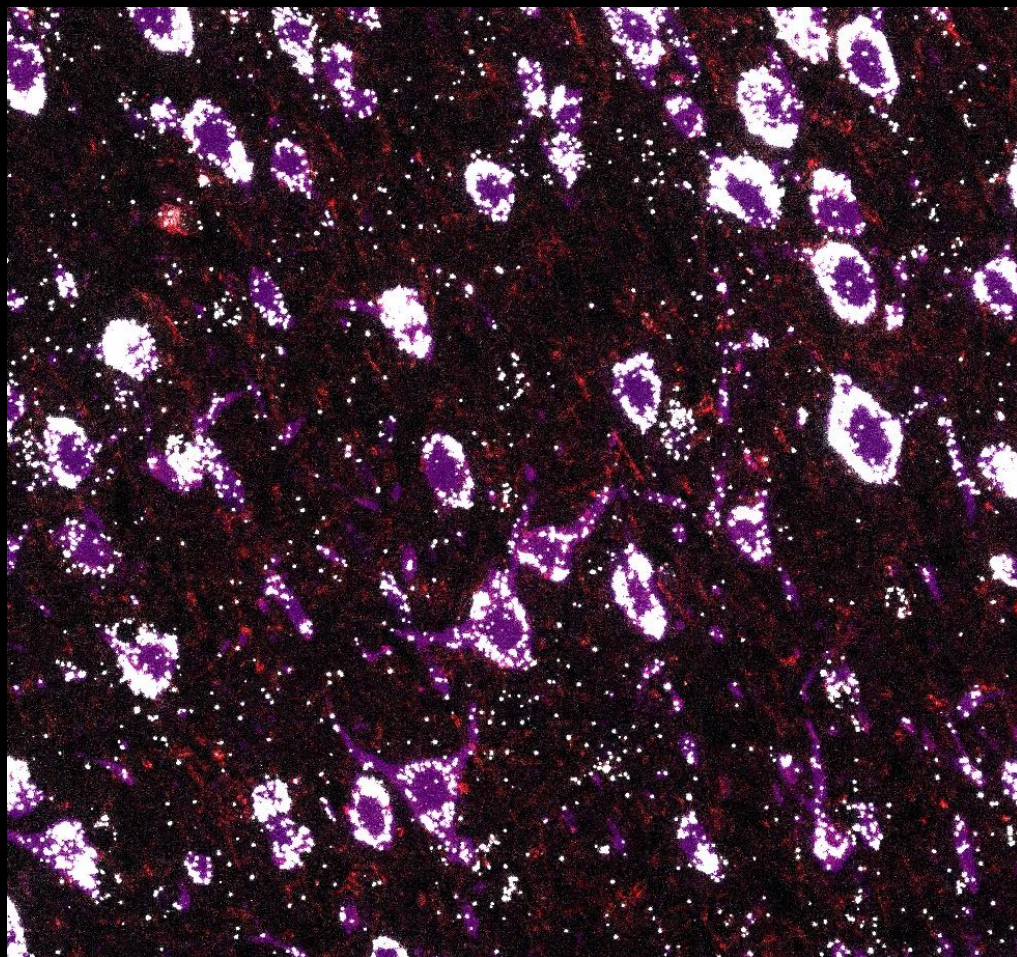
*Antibody labeling
for green fluorescent protein
(GFP) expression (black):*

**Cells transduced
with STAC-BBB**

STAC-BBB mediated ZFR expression and Prion repression in the NHP brain

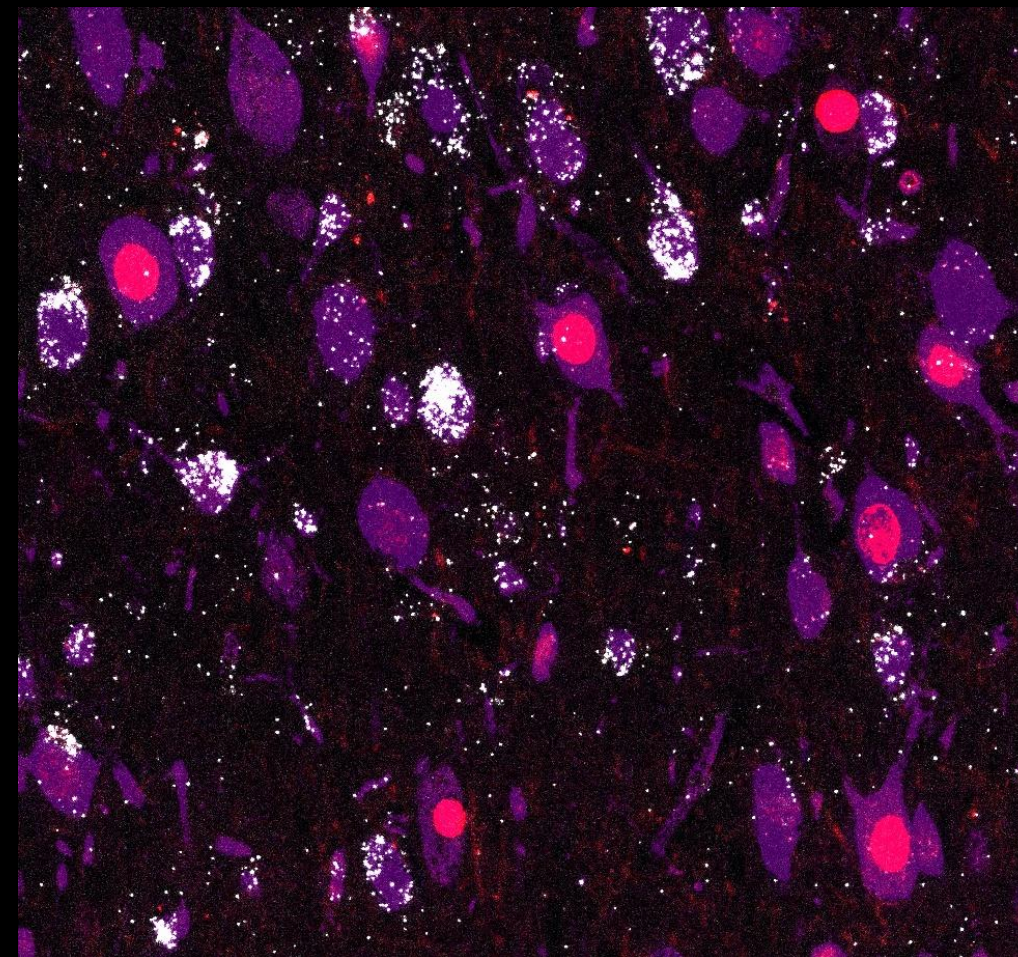
ZFR+ cells (GFP)
Neurons (NeuN)
Prion mRNA

Vehicle Control



Motor cortex

STAC-BBB



Brain-wide PRNP repression seen in NHPs in the range of that associated with marked survival in mouse



STAC-BBB

**STAC-BBB capsid
with human-specific
ZFR 2e13 vg/kg**



PHP.B

**PHP.B capsid with
mouse-specific ZFR**

1e13 vg/kg

3e13 vg/kg

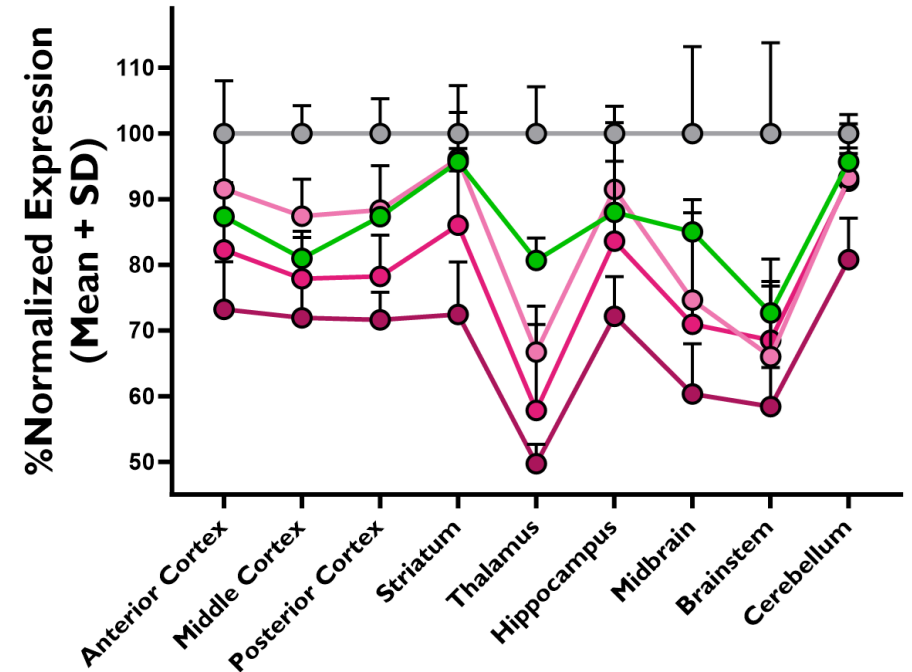
1e14 vg/kg

Vehicle

Higher doses in NHP are feasible and should provide higher repression of PRNP

Prnp mRNA repression seen across key brain regions:

- **Pink:** repression in mouse survival study at three doses
- **Green:** repression in NHP study at 2e13 vg/kg dose
- Prion repression in NHP similar to mouse at comparable doses
- Anticipate greater repression with clinical manufacturing process and higher doses in NHP



Data presented at ASGCT 2023, Prion 2024

Phase 1/2 CTA-enabling activities and clinical study preparations are ongoing

| Item | Category criteria | Score |
|--|--|-------|
| Bowel function | At least one episode of incontinence in last 7 days | 0 |
| | Continent for last 7 days | 1 |
| Bladder function | Always incontinent or catheterized | 0 |
| | Continent or occasional accidents | 1 |
| Toilet use | Fully dependent | 0 |
| | Needs some help | 1 |
| | Independent | 2 |
| Bathing | Fully dependent or needs some help | 0 |
| | Independent | 1 |
| Feeding | Unable or NG/PEG/RIG fed (takes nothing by mouth) | 0 |
| | Needs help but can swallow (even if unsafe) | 1 |
| | Independent | 2 |
| Transfers and mobility | Bedbound, unable to sit | 0 |
| | Can sit, but cannot mobilize or transfer without help (from person or walking aid) | 1 |
| | Can transfer or mobilize independently or both | 2 |
| Stairs | Unable | 0 |
| | Needs help | 1 |
| | Independent | 2 |
| Best verbal response | Mute | 0 |
| | Incomprehensible sounds | 1 |
| | Single words | 2 |
| | Sentences, but difficulty in finding words, uses incorrect words or is often disoriented/confused | 3 |
| | Normal conversation | 4 |
| Memory and orientation to surroundings | Shows no awareness of surroundings or any evidence of memory | 0 |
| | Evidence of retaining some highly learned material (e.g. recognizing familiar people) or awareness of surroundings but no evidence of acquiring new material | 1 |
| | Able to retain some new information but memory consistently impaired | 2 |
| | Memory normal or some impairment off and on | 3 |
| Judgement and problem solving | Unable to show any judgement or problem-solving | 0 |
| | Able to show some judgement or problem-solving, even if this is severely impaired | 1 |
| Use of tools | Unable to use any tools or objects | 0 |
| | Able to use some tools or objects, with help if necessary | 1 |

NG = nasogastric; PEG = percutaneous endoscopic gastrostomy; RIG = radiologically inserted gastrostomy.

MRC Prion Disease Rating Scale

➤ **CTA submission** anticipated in **Q1 2026**

➤ Clinical study expected to be a **Bayesian Optimal Interval (BOIN) design** to assess safety and efficacy, while potentially enabling rapid escalation to maximum tolerated dose

➤ Study will use the **MRC prion disease rating scale** to assess efficacy of the ZFR and **compare to matched historic controls**

➤ **Aim is to delay progression of disease**, offering potential for meaningful extension of survival

➤ Plan to initiate clinical study in **mid-2026**

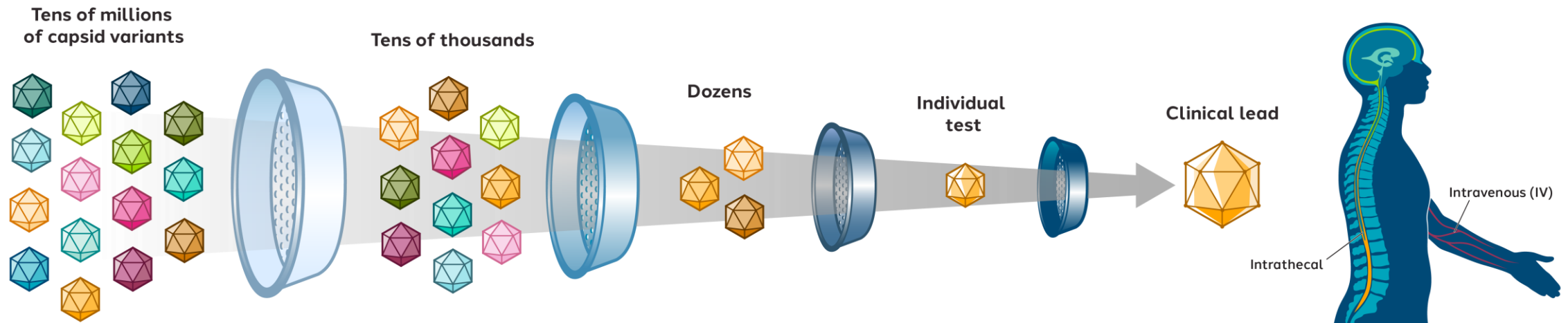
➤ Anticipate **preliminary clinical data** in **Q4 2026**



Achieving Widespread Central Nervous System Delivery for Optimal Therapeutic Benefit

Widespread CNS delivery is challenging with conventional AAVs. Our SIFTER platform is designed to enable the selection of neurotropic AAV capsids to potentially advance our innovative preclinical programs to the clinic.

SIFTER Platform AAV Capsid Engineering



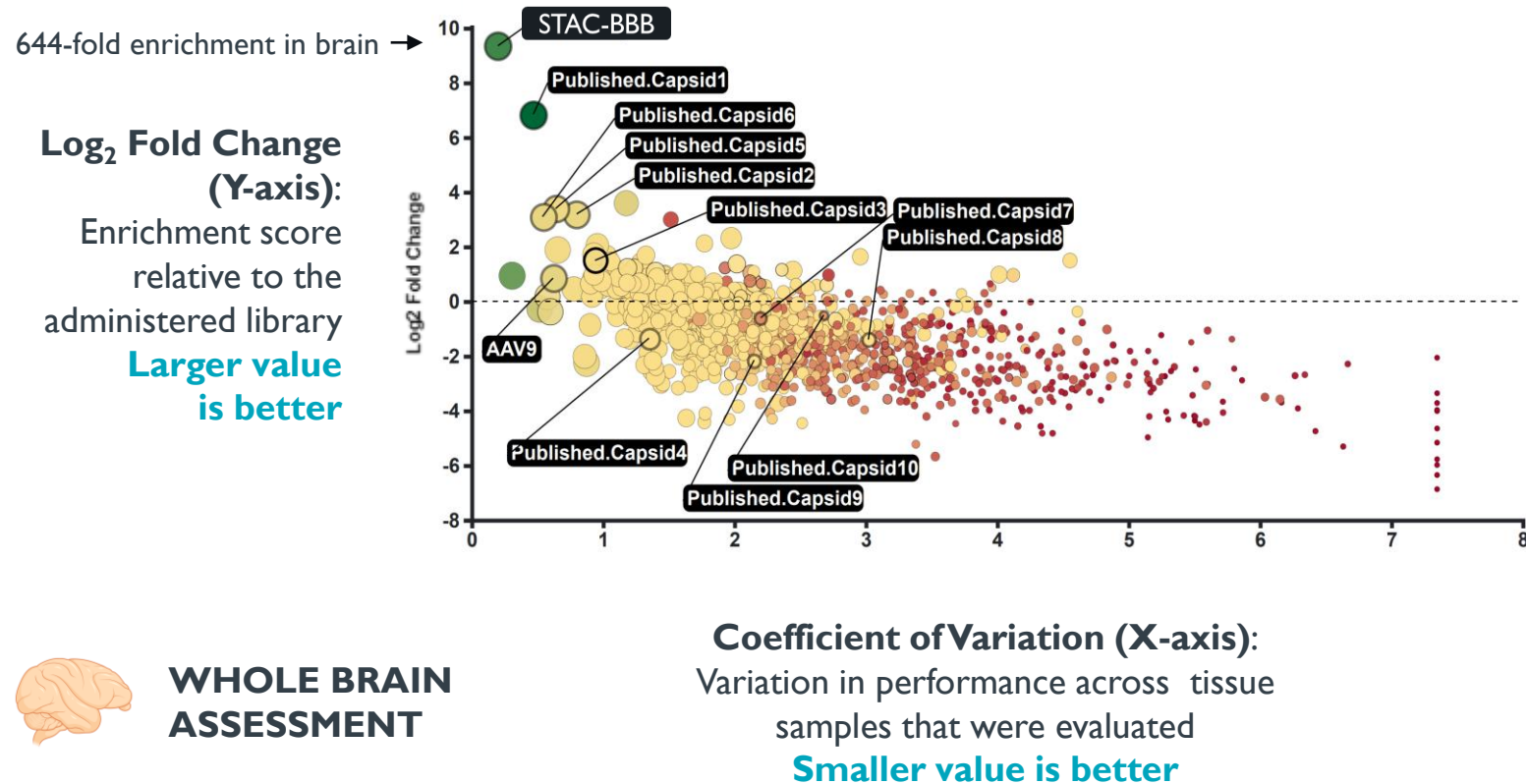
SIFTER: Selecting In vivo For Transduction and Expression of RNA

Sangamo STAC-BBB findings exceeded expectations for a successful blood-brain barrier penetrant capsid

- ✓ STAC-BBB achieved robust penetration of the blood-brain barrier and widespread distribution throughout the brain in NHPs
- ✓ Industry-leading performance: 700-fold better enrichment than the benchmark AAV9
- ✓ Appears to primarily target neurons regardless of promoter
- ✓ Results are consistent across individual animals and groups
- ✓ Enabled robust expression of zinc-finger cargo throughout the brain, including all key brain regions
- ✓ Vector genomes are enriched in the CNS and appear de-targeted from the DRG and the liver
- ✓ We believe STAC-BBB is manufacturable at scale

In vivo library evaluation in cynomolgus macaques identified STAC-BBB as the top performing BBB-penetrant capsid, with additional enhancements in progress

Capsid-mediated expression of cargo in neurons



Unique Molecular Identifier count (Color):
Informs number of unique AAV transduction events
Darker green is better

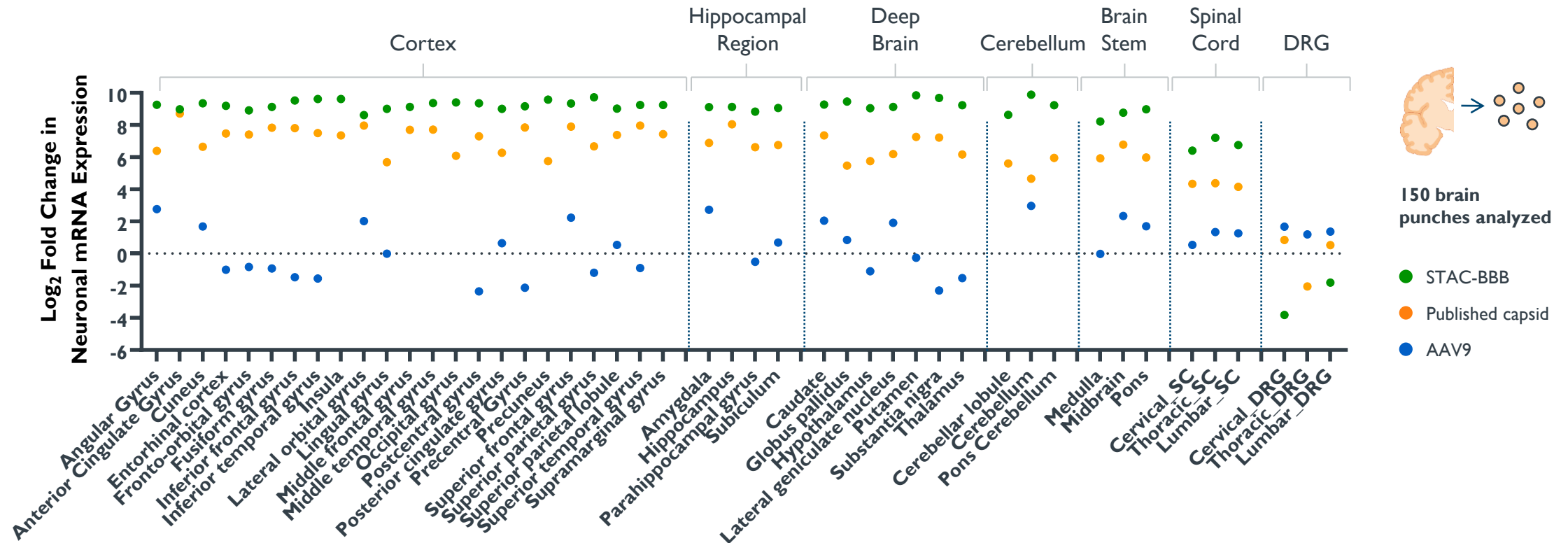


Fraction of replicates found (Bubble size):
Informs consistency of replicate recovery
Larger circle is better

Neuronal RNA expression (3-week study, hSyn I)

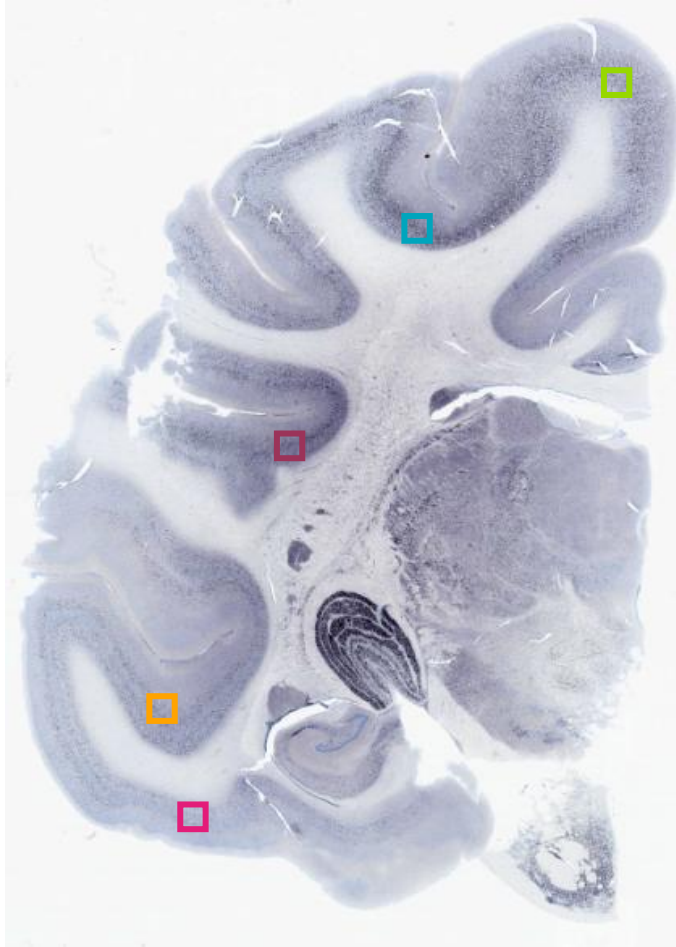
STAC-BBB was enriched in neuronal RNA expression in all CNS regions

Capsid-mediated expression of cargo in neurons

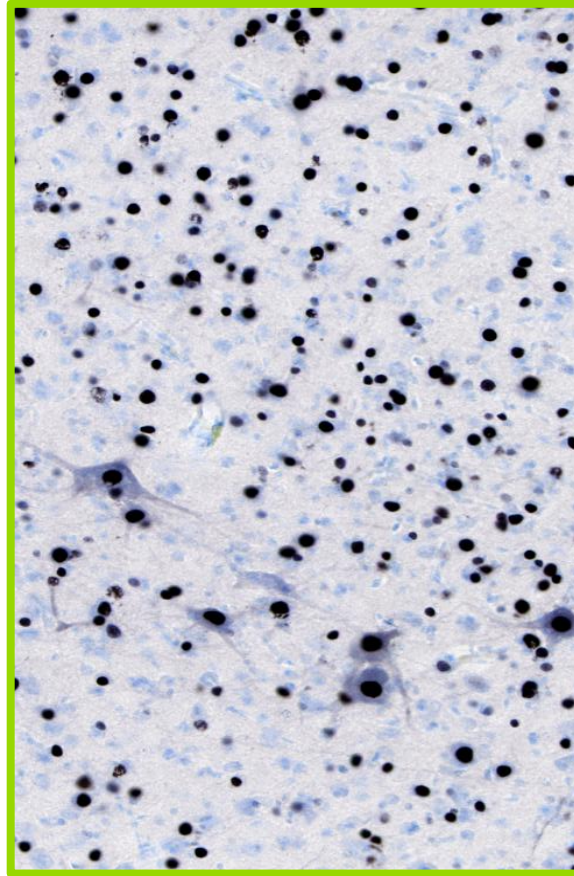


Neuronal RNA expression (3-week study, hSyn I)

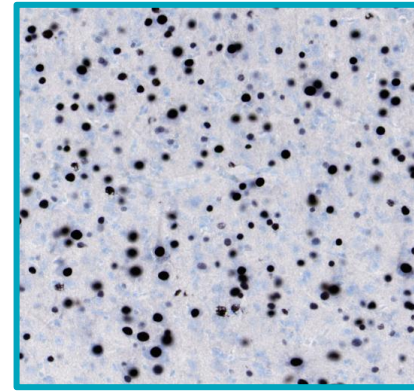
STAC-BBB showed widespread neuronal transduction across all cortical regions



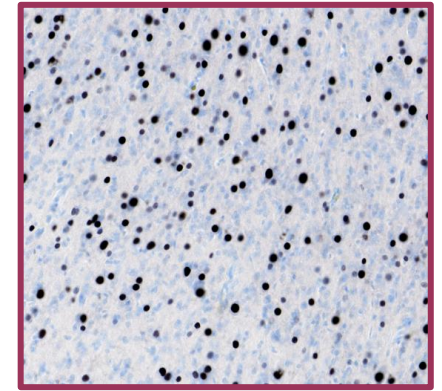
Precentral Gyrus (Motor Cortex)



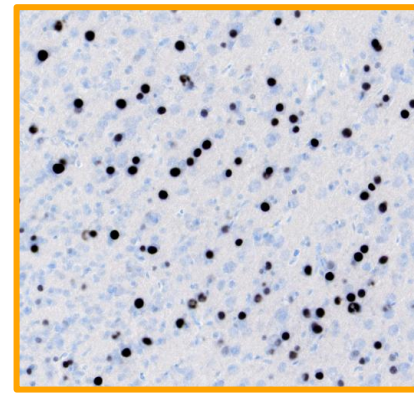
Postcentral Gyrus



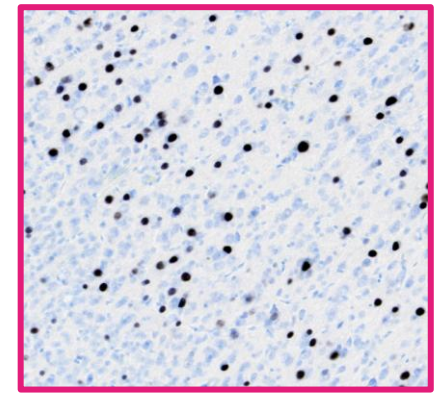
Superior Temporal Gyrus



Middle Temporal Gyrus

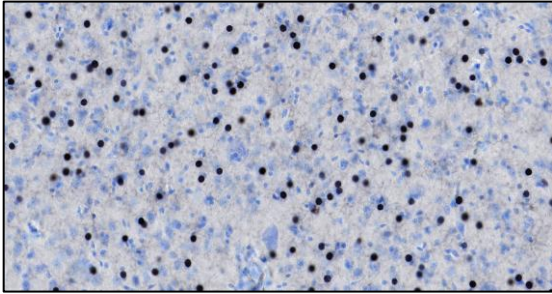


Inferior Temporal Gyrus

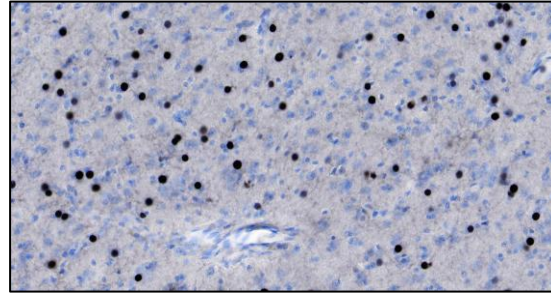


STAC-BBB mediated widespread brain transduction

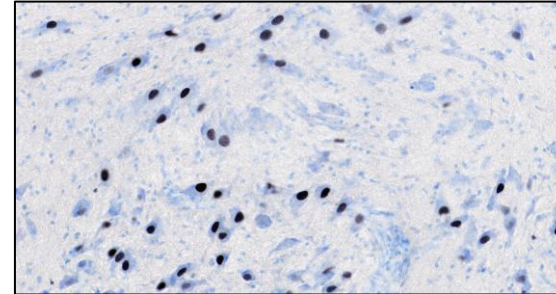
Putamen



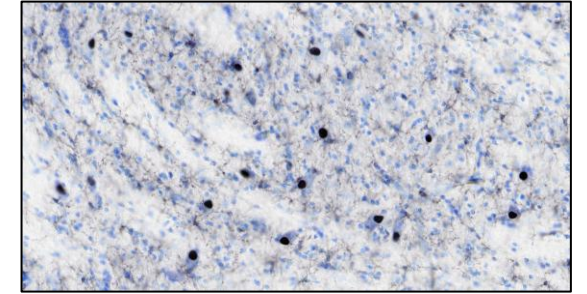
Caudate



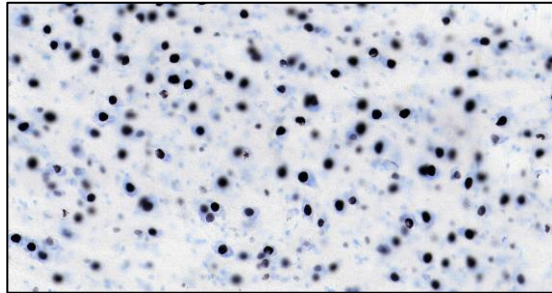
Substantia nigra



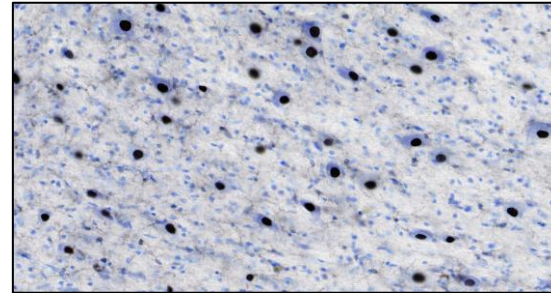
Globus pallidus



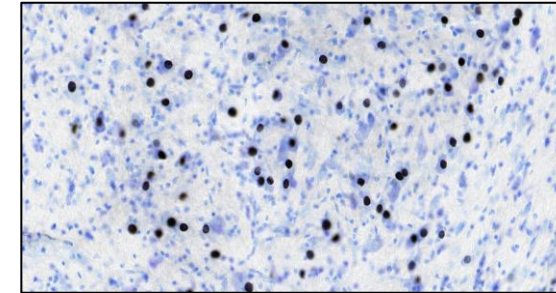
Pons



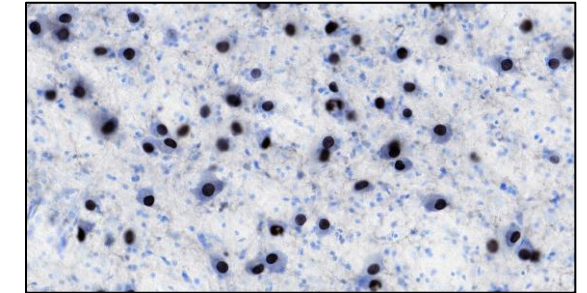
Dentate nucleus



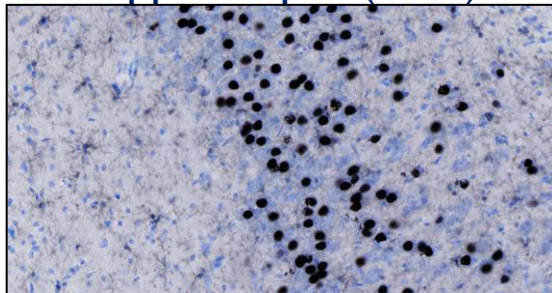
Cuneate nucleus



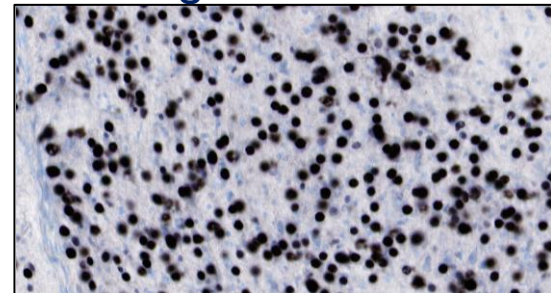
Thalamus



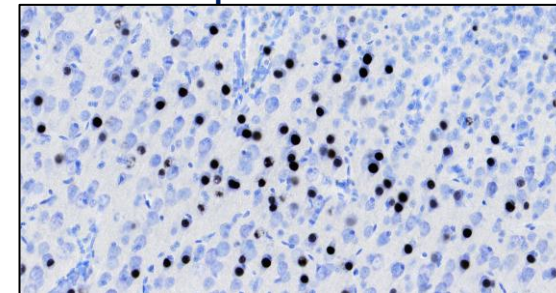
Hippocampus (CA2)



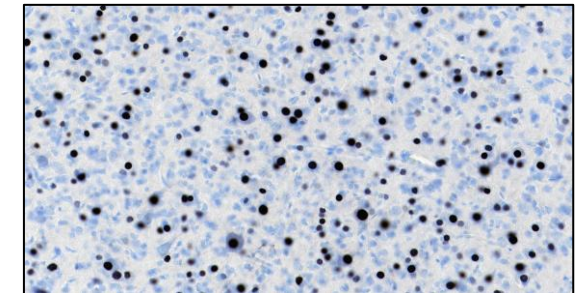
Lateral geniculate nucleus



Temporal cortex



Motor cortex



Neurons were widely transduced in regions integral to disease pathology

Putamen



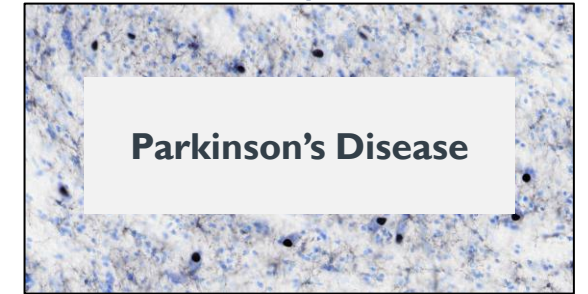
Caudate



Substantia nigra



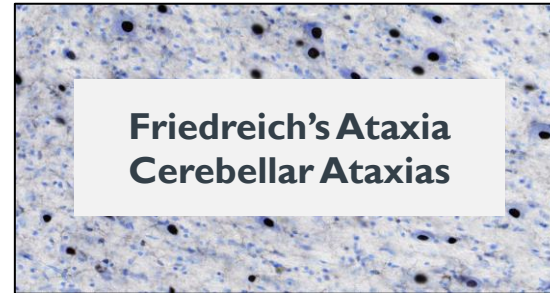
Globus pallidus



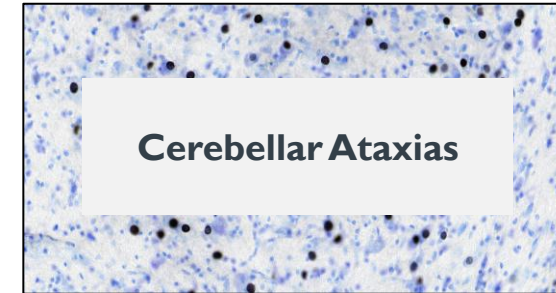
Pons



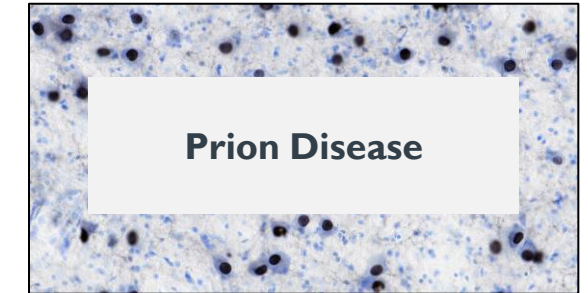
Dentate nucleus



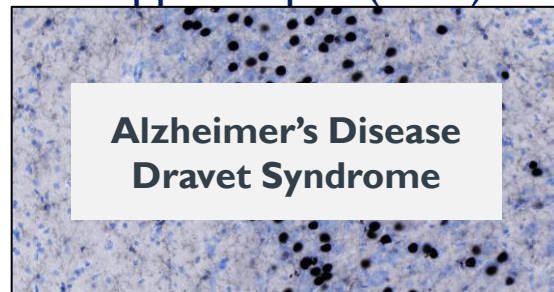
Cuneate nucleus



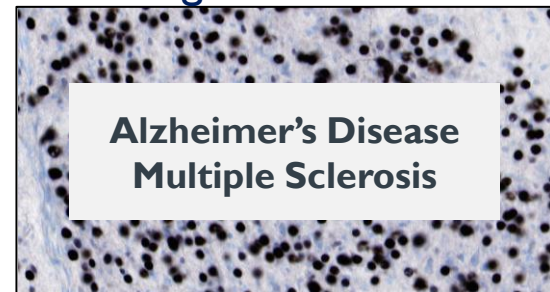
Thalamus



Hippocampus (CA2)



Lateral geniculate nucleus



Temporal cortex




Motor cortex



— We believe STAC-BBB is manufacturable at scale

- Capsid manufacturability is critical to create a successful potential commercial drug product for patients
- We believe STAC-BBB is:
 - Manufacturable at commercial scale using standard cell culture and purification processes
 - Soluble using known excipients
 - Can be characterized using available analytics
- We have successfully manufactured up to 50-liter scale, and further scale up to 500-liter is in progress



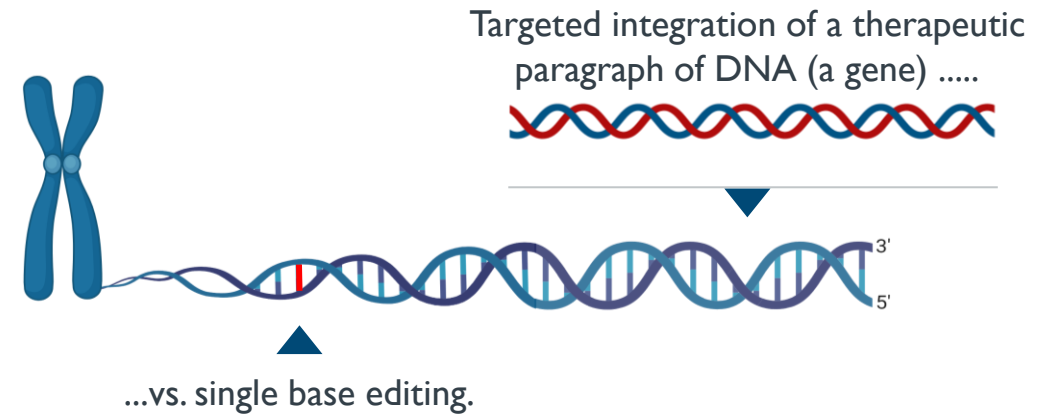


Advancing Next-Generation Genome Engineering

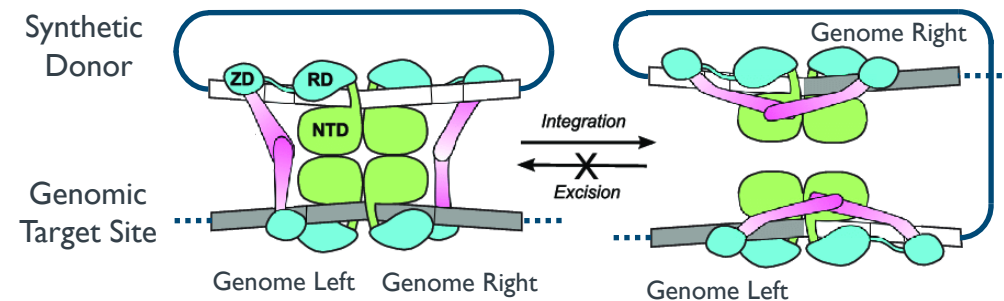
What is an integrase and why is it important?

Targeted integration enables large-scale genome editing

- ✓ Capable of delivering large payloads - 10 kb+
- ✓ No copying required - low error rate
- ✓ Self sufficient - no dependence on cell DNA repair machinery
- ✓ No DNA breaks - reduced translocation risk



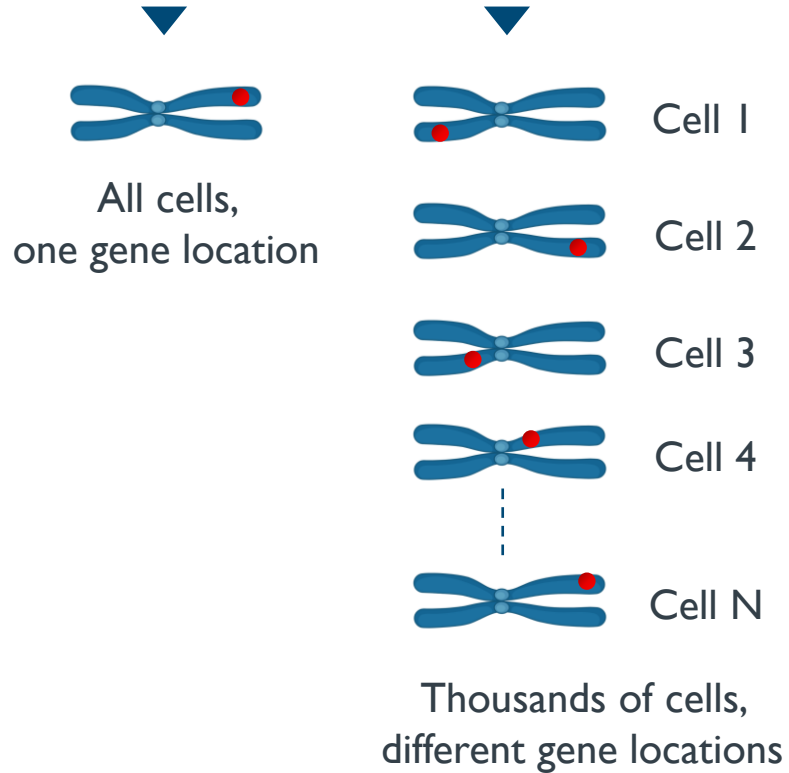
BxbI Integration Mechanism



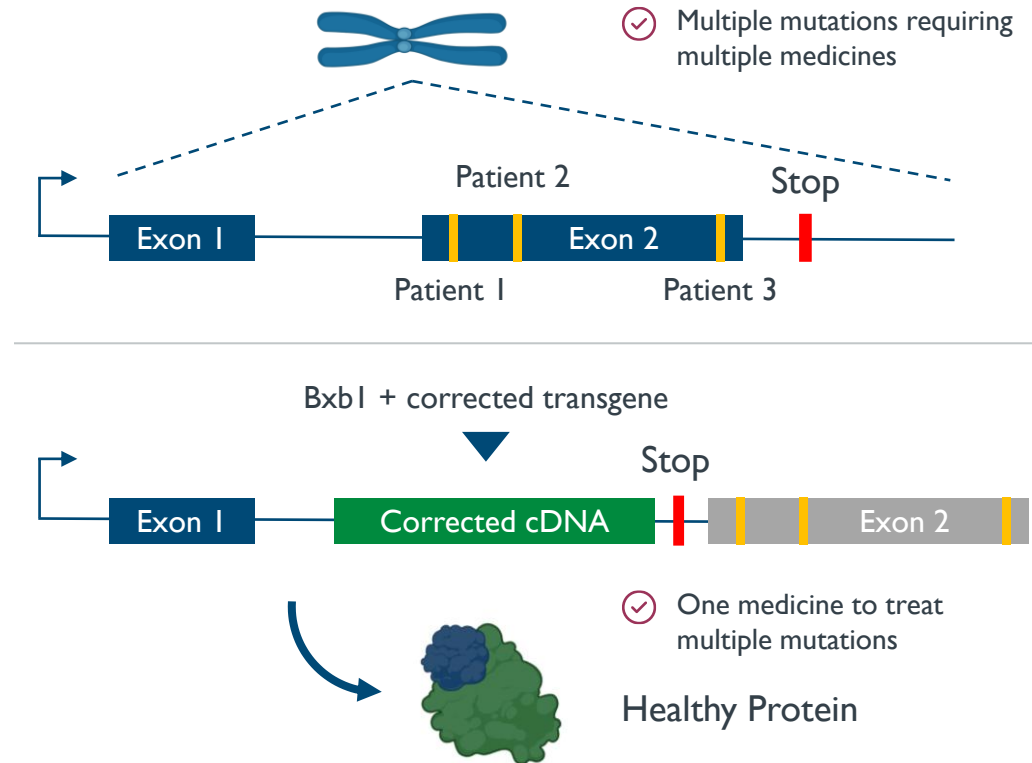
Adapted from Gupta et al., NAR (2017)
doi: 10.1093/nar/gkx474

Targeted integration improves existing therapies, and enables new therapies

Targeted vs. Random Integration



One medicine vs. multiple variants for each mutation



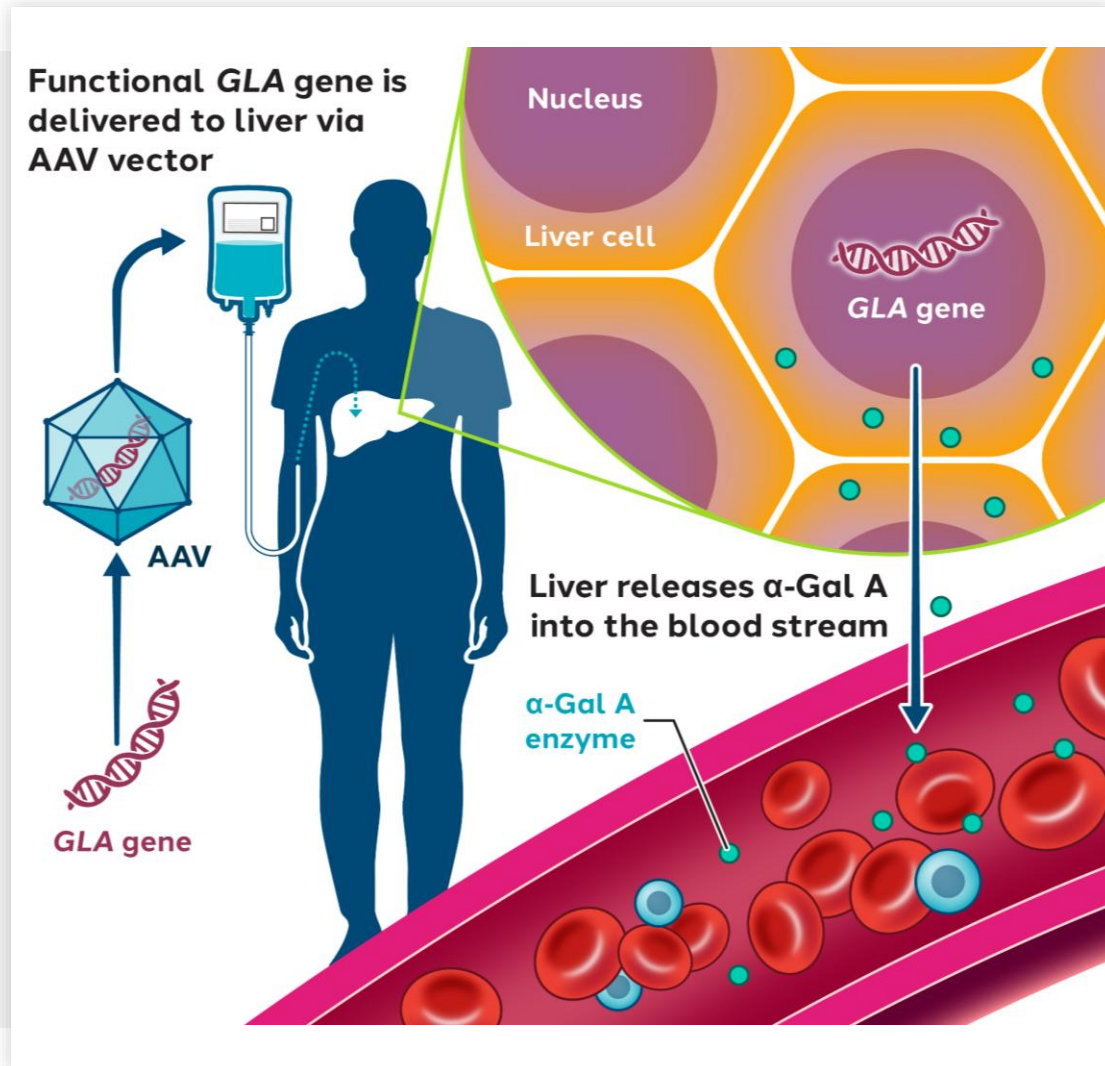
Images by Biorender

Optimizing Value of Clinical Programs



Fabry Disease: Isargagene civaparvovec (ST-920)

Abbreviated clinical pathway supports efforts to secure a commercialization partner



- **Largest known gene therapy program in Fabry disease**
 - Dosing complete in Phase I/2 STAAR study – all 32 patients have achieved at least 52-weeks follow-up
- **Compelling clinical data**
 - Continue to amass encouraging clinical data, including preliminary analysis of a positive mean eGFR slope in all 32 patients treated > 1yr
 - Pivotal readout expected later in Q2 2025
- **FDA alignment on Accelerated Approval pathway**
 - FDA confirmed that eGFR slope data at one year across all Phase I/2 patients can serve as primary basis for accelerated approval
 - Potential BLA submission expected as early as 1Q 2026
- **Discussions with EMA** on regulatory pathway ongoing
- Has **EMA PRIME** eligibility and **UK MHRA ILAP** status

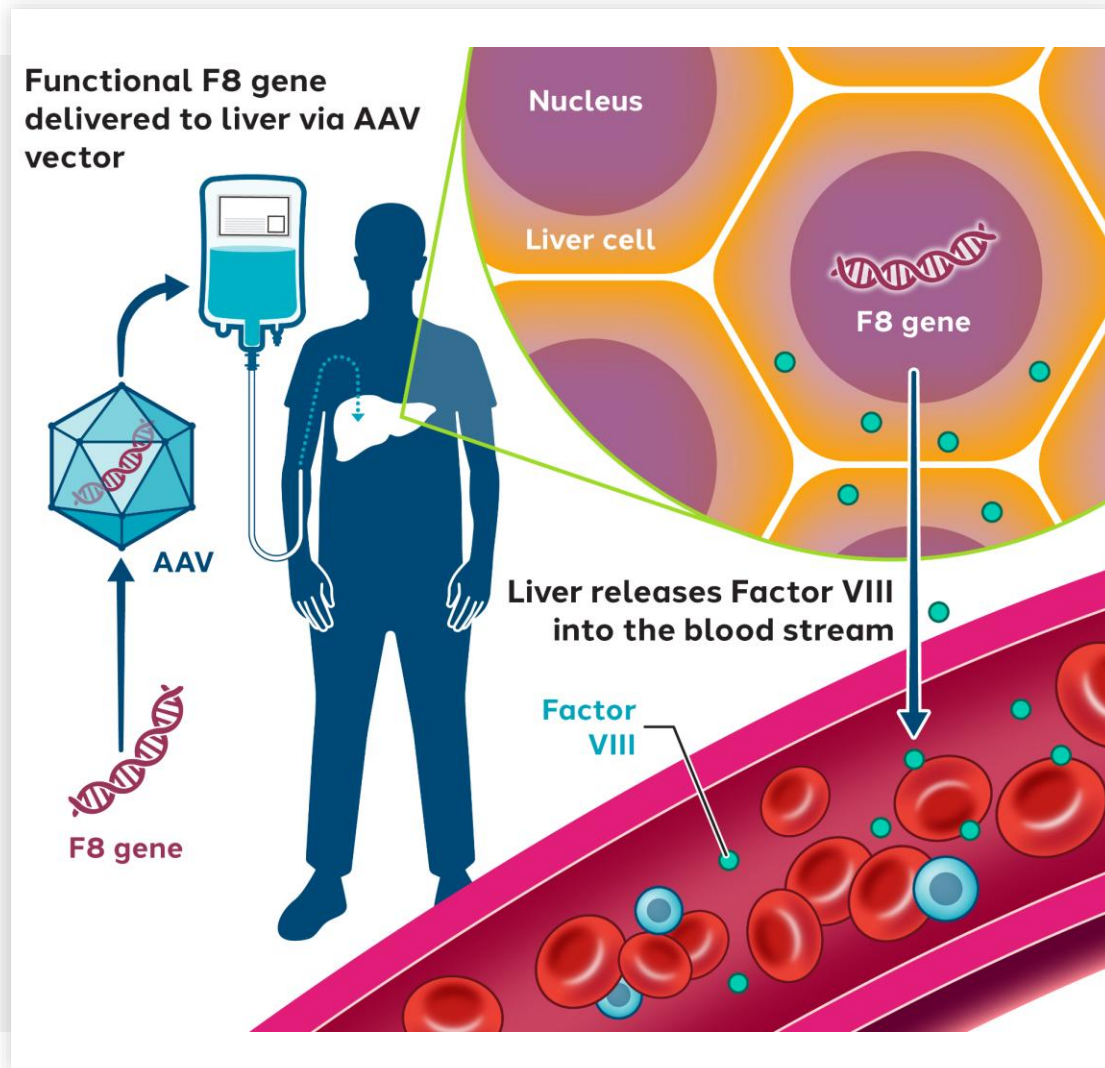
Fabry Disease: isargagene civaparvovec (ST-920)

Summary of updated Phase 1/2 STAAR study data, as presented at WORLDSymposium 2025

- ✓ ST-920 gene therapy was well-tolerated with a **favorable safety profile** in this population of adults with Fabry disease:
 - Mainly Grade 1 and 2 Adverse Events and no discontinuation based on ST-920
 - No prophylactic steroids or other immunomodulatory agents administered. No LFT elevations requiring steroids.
- ✓ **Durable benefit** was demonstrated with supraphysiological α -Gal A activity up to **27 months** for those receiving the top dose (2.63×10^{13} vg/kg) and **47 months** for all subjects independent of dose
- ✓ **Positive mean eGFR slope of 3.06 mL/min/1.73m²/year (95% confidence interval: 0.863, 5.258)** observed in the 23 patients that have reached 1-year follow-up, indicating improvements in renal function
- ✓ **Clinically and statistically significant QOL improvements**
 - 68 % improvement in FOS-MSSI
 - Improvement in SF-36 scores
 - Improvements in gastrointestinal symptoms
- ✓ All 18 subjects who discontinued ERT remain off ERT, for up to 33 months
- ✓ Total or neutralizing α -Gal A antibodies decreased markedly in 9 subjects and became undetectable in 7 (70%)
- ✓ ***ST-920 has potential as a one-time, durable treatment option for Fabry disease that can improve patient outcomes***

Hemophilia A: Giroctocogene fitelparvovec

Compelling readout for Phase 3 AFFINE trial



- > Pfizer reported positive topline results from the Phase 3 AFFINE trial in July 2024, which met primary and key secondary endpoints
- > Phase 3 data presented at ASH Annual Meeting and Exposition in December 2024 via platform and poster presentations
- > Sangamo announced in December 2024 that it is scheduled to regain development and commercialization rights to giroctocogene fitelparvovec following a decision by Pfizer to terminate the global collaboration and license agreement between the parties
- > Pfizer and Sangamo continue to work together to manage the transition of the collaboration which terminated on April 21, 2025

Sangamo is a differentiated genomic medicine company focused on treating debilitating neurological diseases



Potent zinc finger epigenetic regulation technology, with neurology programs advancing towards the clinic



Industry-leading AAV capsid discovery platform has demonstrated non-invasive intrathecal and intravenous delivery to the brain



Powerful research platform **continually innovates in new modes of genome modulation** to support value creation opportunities for both wholly owned programs and potential partners



Strong roster of current partners and a **clear regulatory pathway to Accelerated Approval** agreed with **U.S. FDA in Fabry disease**, with partner negotiations ongoing

SHARP STRATEGIC FOCUS IN NEUROLOGY

OPTIMIZING ASSET VALUE