Delivering the Future of Genomic Medicines

August 6, 2024

Forward-Looking Statements

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 of our product candidates and engineered capsids, including the ability of STAC™-BBB to unlock significant potential for the treatment of various neurological diseases, our plans to focus on epigenetic regulation and capsid engineering, 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, the MINT platform, SIFTER and other technologies to develop durable, safe and effective therapies and capsids, the potential for us to benefit and earn upfront fees, development and commercial milestone and royalty payments from our collaborations and the timing of any such benefits and payments, the potential for Genentech to complete clinical development, regulatory interactions, manufacturing and global commercialization of any resulting products, Pfizer's continued advancements of the giroctocogene fitelparvovec program, including the potential for Pfizer to complete clinical development, regulatory interactions, manufacturing and global commercialization of any resulting products, anticipated revenues from existing and new collaborations and the timing thereof, plans and expectations to seek partners or collaborators for certain of our programs, plans regarding our financial resources, including the sufficiency thereof and 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, risks and uncertainties related to macroeconomic factors, including as a result of ongoing overseas conflicts, disruptions in access to bank deposits and lending commitments due to bank failure, 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 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 and/or initiate a potential registrational trial of isaralgagene civaparvovec in a timely manner or at all; and our 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 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, 2023, as supplemented by Sangamo's Quarterly Reports on Form 10-Q for the quarters ended March 31, 2024 and June 30, 2024, 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

Sangamo THERAPEUTICS

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

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

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

SHARP STRATEGIC FOCUS IN NEUROLOGY

Successful partnership track record with $50 million in expected near-term payments from Genentech and $220 million in potential milestone payments* from Pfizer. **Fabry partner discussions ongoing, with clear pathway to potential registration.**

OPTIMIZING ASSET VALUE

Sangamo THERAPEUTICS

**beginning in 2025, upon the achievement of certain regulatory and commercial milestones. Subject to customary reductions.*

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

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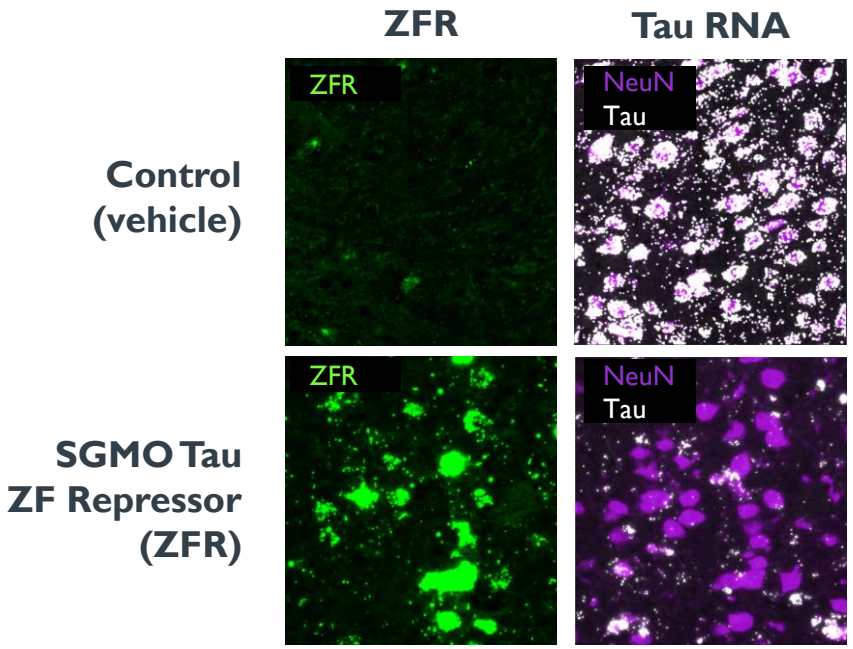
Sangamo pairs the epigenetic regulation *and* capsid delivery capabilities needed to create neurology genomic medicines

Genome-Targeting Cargo

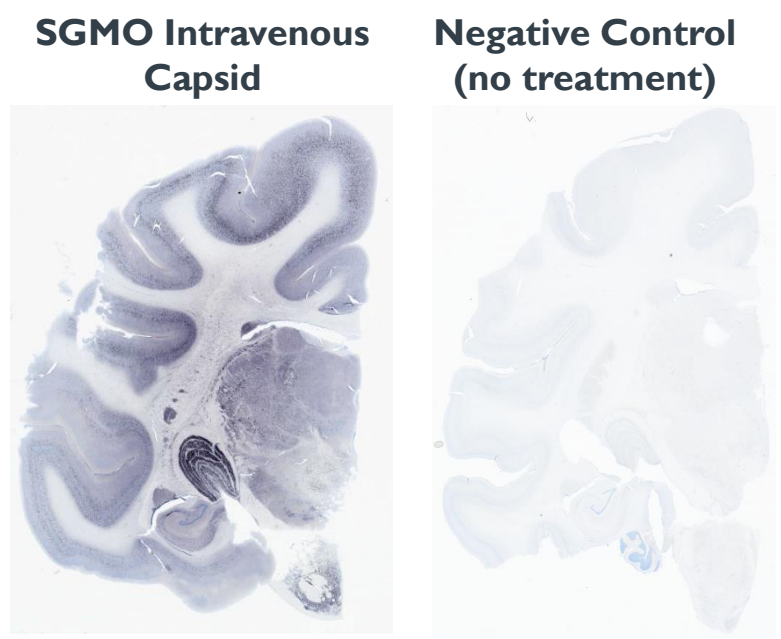
Epigenetic regulation platform

Capsid Delivery Engine

AAV capsid delivery platform via intravenous delivery



Non-human primate brainstem



Non-human primate

Future of Neurology Genomic Medicines

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						
AVAILABLE CARGO TARGETS ENABLED BY STAC-BBB	**Phelan-McDermid Syndrome** SHANK3	**Dravet Syndrome** SCN1A	**Angelman Syndrome** UBA3A	**Myotonic Dystrophy Type I** DMPK	**ALS** SOD1	**Charcot Marie Tooth 2A** MFN2	**Charcot Marie Tooth 1A** PMP22	**Haploin-sufficiency Syndrome** SCN2A
PARTNERED PROGRAMS	**ALS** C9orf72 ALEXION AstraZeneca Rare Disease	**Huntington's Disease** HTT Takeda	**Tauopathies** MAPT Genentech A Member of the Roche Group	**Undisclosed** Genentech A Member of the Roche Group				

Cerebrospinal fluid (CSF) capsid

Intravenous (IV) capsid

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

Gateway indications unlock broader neurology pipeline

- ✓ Targets validated by human genetics
- ✓ Well-defined patient populations
- ✓ Delivery achievable with AAV
- ✓ Quantifiable patient outcomes on a rapid timeline

Chronic Neuropathic Pain (Nav1.7)

Est. 43,000+ Patients in US**

- Significant unmet medical need
- Highly specific repression, with no impact to other Nav channels
- Starting with small fiber neuralgia. Potential to broaden to other indications.
- Potentially rapid development pathway given short timescale to clinical efficacy readout

Prion Disease

Est. 1,500+ Patients Per Year***

- Devastating condition. Rapidly progressive and always fatal.
- Highly potent repression of prion in mice brains, significantly extending survival in a disease mouse model
- Potential for accelerated regulatory and commercialization pathway

** Subject to our ability to secure adequate funding*
***With Small Fiber Neuralgia*
****US (per CDC) and Europe (https://www.eurocjd.ed.ac.uk/)*

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Company pipeline and business development opportunities

CORE NEUROLOGY PIPELINE

Indication	Preclinical	Phase 1/2	Pivotal	Partner	Commentary
Chronic Neuropathic Pain *(Nav1.7)*	*Data presented at ASGCT 23*			-	Nav1.7 IND-enabling activities continue to advance
Prion Disease	*Data presented at ASGCT 24*			-	Prion CTA-enabling activities continue to advance
Tauopathies	*Data presented at ASGCT 24*			Genentech A Member of the Roche Group	**August 2024:** Announced epigenetic regulation and capsid delivery license agreement with Genentech
Undisclosed				Genentech A Member of the Roche Group	
ALS/FTD	*Data presented at ASGCT 24*			Alexion AstraZeneca Rare Disease	
Huntington's Disease				Takeda	

OTHER PROGRAMS

Indication	Preclinical	Phase 1/2	Pivotal	Partner	Commentary
Hemophilia A (Giroctogene fitelparvovec)	*Data presented at ASH 2023*			Pfizer	**July 2024:** Positive topline readout in Phase 3 AFFINE trial. Pfizer plans to discuss data with regulatory authorities in coming months.
Fabry Disease (Isaralgagene civaparvovec)	*Data presented at WORLDSymposium 2024*			-	Continue to amass encouraging clinical data. Potential partnership discussions ongoing.

Multiple biopharma collaborations demonstrate our platform's potential and have provided significant economics for Sangamo

Gene Therapy	Pfizer
Genome Engineering	ALEXION AstraZeneca Rare Disease; Takeda; Genentech A Member of the Roche Group; Prevail Therapeutics A Wholly Owned Subsidiary of Eli Lilly and Company; CHROMA MEDICINE

$817m
cash received from partners to date

Up to $3.8b
in potential future milestones and exercise fees assuming exercise of all options and targets

Additional potential product royalties

Numerous Benefits of Partnerships:

Large pharma 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 cargo and novel AAV capsids for high-value gateway neurology diseases like chronic neuropathic pain and prion disease

Proprietary AAV blood-brain barrier penetrant capsid (STAC™-BBB) with industry leading CNS tropism in non-human primates

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

Pfizer collaboration in Hem A brings revenue-bearing opportunity – $220m potential milestones and 14-20% potential sales royalties, if approved and commercialized

Fabry program generating compelling Phase 1/2 clinical data. Ready for potential registrational study, with abbreviated clinical pathway aligned with U.S. FDA. Advancing potential collaboration partner discussions.

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2Q24 Business Updates

2Q24 Key Takeaways

Announced global license agreement with Genentech to develop novel genomic medicines for neurodegenerative diseases

Entered into a global epigenetic regulation and capsid delivery license agreement with Genentech to develop novel genomic medicines for neurodegenerative diseases, focused on the tau gene, which is critically involved in Alzheimer's disease and other tauopathies, as well as a second undisclosed neurology target.

Hem A (Pfizer)

- Positive topline results reported from the Phase 3 AFFINE trial evaluating giroctocogene fitelparvovec, an investigational gene therapy that Sangamo is co-developing with and licensing to Pfizer.
- Sangamo is eligible to earn from Pfizer up to $220 million in milestone payments* upon the achievement of certain regulatory and commercial milestones and product sales royalties of 14% - 20% if giroctocogene fitelparvovec is approved and commercialized**.

Fabry Disease

- Dosing complete for the Phase 1/2 STAAR study, with seventeen out of eighteen patients withdrawn from Enzyme Replacement Therapy (ERT) to date.
- Continue to amass encouraging clinical data, including evidence of improvements in kidney function.
- Met with European Medicines Agency (EMA) on proposed pathway to potential approval.
- Engaged in ongoing discussions with potential Fabry collaboration partners.

Financial Highlights

- Expect to receive from Genentech **$50 million in near-term upfront license fees and milestone payments**. Eligible to earn up to **$1.9 billion in development and commercial milestones, plus tiered royalties on net sales**.
- Approximately **$28 million in cash and cash equivalents** as of June 30, 2024.
- We believe that our available cash and cash equivalents, in combination with the expected near-term Genentech payments, will be sufficient to fund our planned operations **into the first quarter of 2025.**

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**beginning in 2025. **subject to customary reductions*

Q2 Pipeline Progress & Anticipated Milestones

CORPORATE UPDATES

- ✓ Announced global epigenetic regulation and capsid delivery license agreement with Genentech, a member of the Roche Group, to develop novel genomic medicines for neurodegenerative diseases.
- ✓ Granted an exclusive license to Genentech for Sangamo's proprietary zinc finger repressors that are directed to the genes associated with tau and a second undisclosed neurology target. Agreed to also exclusively license, for the same targets, Sangamo's proprietary, neurotropic AAV capsid, STAC-BBB.
- ✓ Expect to receive from Genentech $50 million in near-term upfront license fees and milestone payments.
- • Eligible to earn up to $1.9 bn in development and commercial milestones, spread across multiple potential products.

NEUROLOGY

- ✓ Continued to advance IND-enabling activities for Nav1.7 for chronic neuropathic pain
- ✓ Continued to advance CTA-enabling activities for prion disease.
- • Engaged in ongoing business development discussions with new potential collaborators for STAC-BBB, epigenetic regulation and modular integrases capabilities.

HEMOPHILIA A (PFIZER)

- ✓ Pfizer announced positive topline results from the Phase 3 AFFINE trial, meeting primary and key secondary endpoints.
- • Eligible to earn from Pfizer up to $220.0 million in milestone payments* upon the achievement of certain regulatory and commercial milestones for giroctocogene fitelparvovec and product sales royalties of 14% - 20% if giroctocogene fitelparvovec is approved and commercialized**.
- • Pfizer plans to discuss these data with regulatory authorities in the coming months.

FABRY DISEASE

- ✓ Enrollment, screening and dosing complete – 33 patients total.
- ✓ Seventeen out of eighteen patients now successfully withdrawn from ERT.
- ✓ Continue to amass encouraging clinical data, including evidence of improvements in kidney function with a statistically significant rise in both mean and median eGFR levels observed in 18 male and female patients treated >1year.
- ✓ Held a productive meeting in June 2024 with the EMA on proposed pathway to potential approval in Europe.
- • Engaged in ongoing discussions with potential Fabry collaboration partners.

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*beginning in 2025. **subject to customary reductions

We have focused resources and reduced Non-GAAP OpEx by ~45% year-on-year. We expect further reductions in 2025 as we transition our legacy programs.

Historical

$817m
Cash Received from Partners to date

$31.9m*
Non-GAAP OpEx – Q2 2024

~$27.8m
Cash and Cash Equivalents Balance as of 6/30/24

Forward Looking

Up to $3.8b
In potential future milestones and exercise fees, assuming exercise of all options and targets

Up to $220m
in potential milestone payments from Hemophilia A†, plus 14-20% in potential sales royalties

$125 – $145m** *(2024)*
Reiterated Non-GAAP OpEx Guidance excludes certain non-cash charges as noted below***

** On a GAAP basis, the Q2 2024 operating expenses were $37.4 million which included impairment of long-lived assets of $1.2 million, depreciation and amortization of $1.2 million and stock-based compensation expense of $3.1 million.*
*** Assuming additional funding.*
**** On a GAAP basis we expect our 2024 operating expenses to be in the range of $150 - $170 million, including impairment of long-lived assets of $6 million, depreciation and amortization of $5 million and stock-based compensation expense of $13 million.*
† Currently being co-developed with Pfizer

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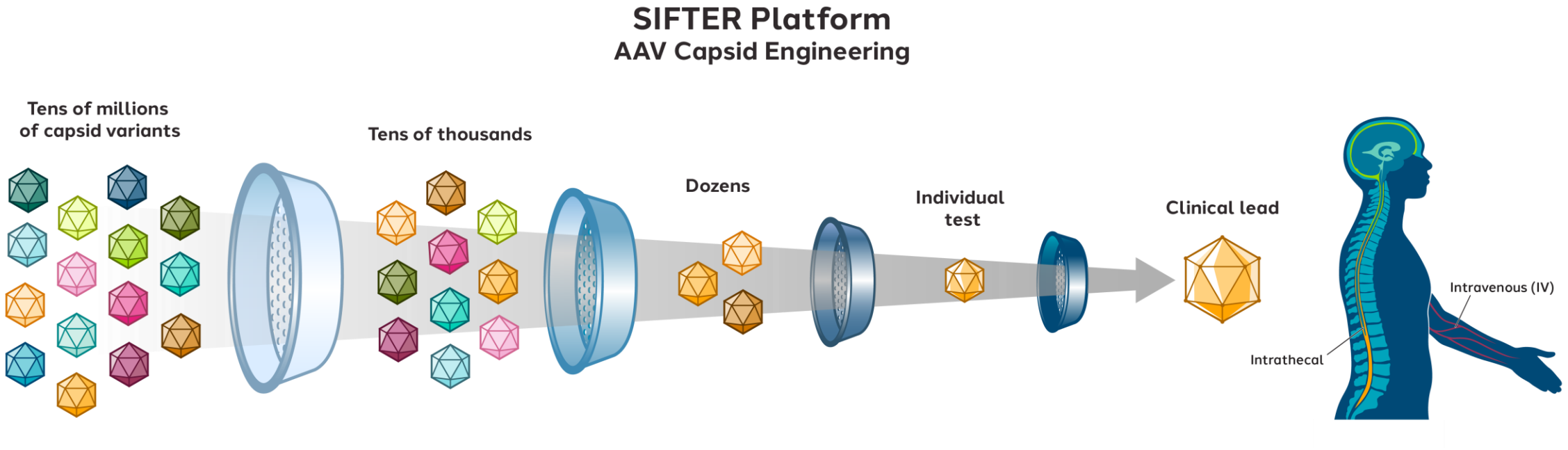
Achieving Widespread Central Nervous System Delivery for Optimal Therapeutic Benefit

Widespread central nervous (CNS) delivery is challenging with conventional AAVs. Our SIFTER platform enables selection of neurotropic AAV capsids to potentially advance our innovative preclinical programs to the clinic.



SIFTER: *Selecting In vivo For Transduction and Expression of RNA*

Key characteristics of a blood-brain barrier (BBB) penetrant capsid

- Broad brain coverage
- Enhanced enrichment in the brain compared to other published capsids
- Widespread neuronal transduction
- Neuronal transduction in key brain regions integral to disease pathology
- Consistency in results across animal subjects
- Clear dose response curve for ZF expression
- Clear dose response curve of target reduction
- De-targeting of the liver, dorsal root ganglia and other organs
- Easily manufacturable at scale

Brain regions *and associated disease*

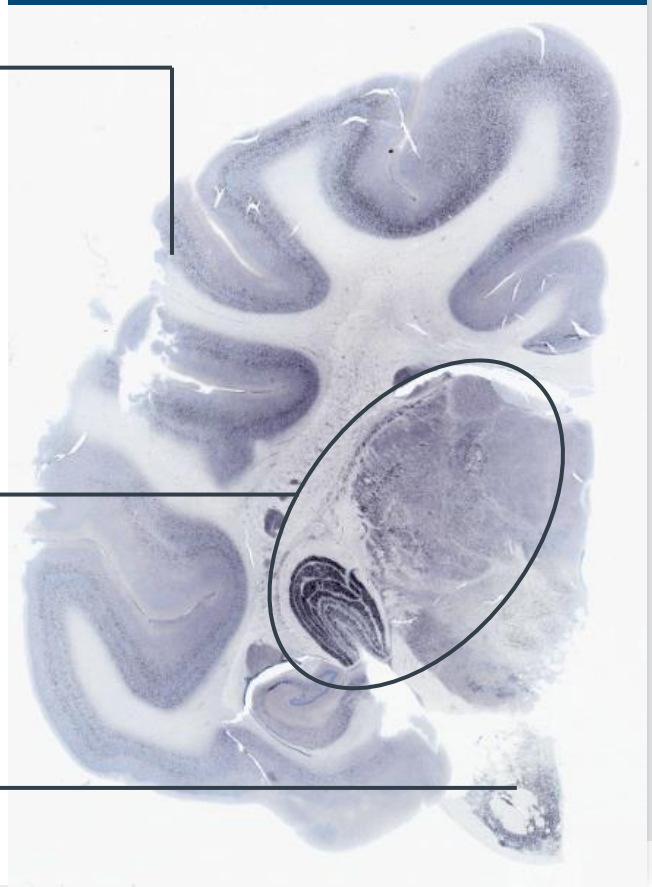
Cortical regions (e.g. postcentral gyrus)
Alzheimer's disease
Parkinson's disease
ALS, Dravet syndrome

Thalamic regions (e.g. LGN, thalamus)
Prion disease
Alzheimer's disease

Globus pallidus
Parkinson's disease
Progressive supranuclear palsy (tau)

Cerebellar nuclei (e.g. dentate nucleus)
Friedreich's ataxia
Spinocerebellar ataxia

Brainstem (e.g. pons, substantia nigra)
Progressive supranuclear palsy (tau)
Rett syndrome
Parkinson's disease



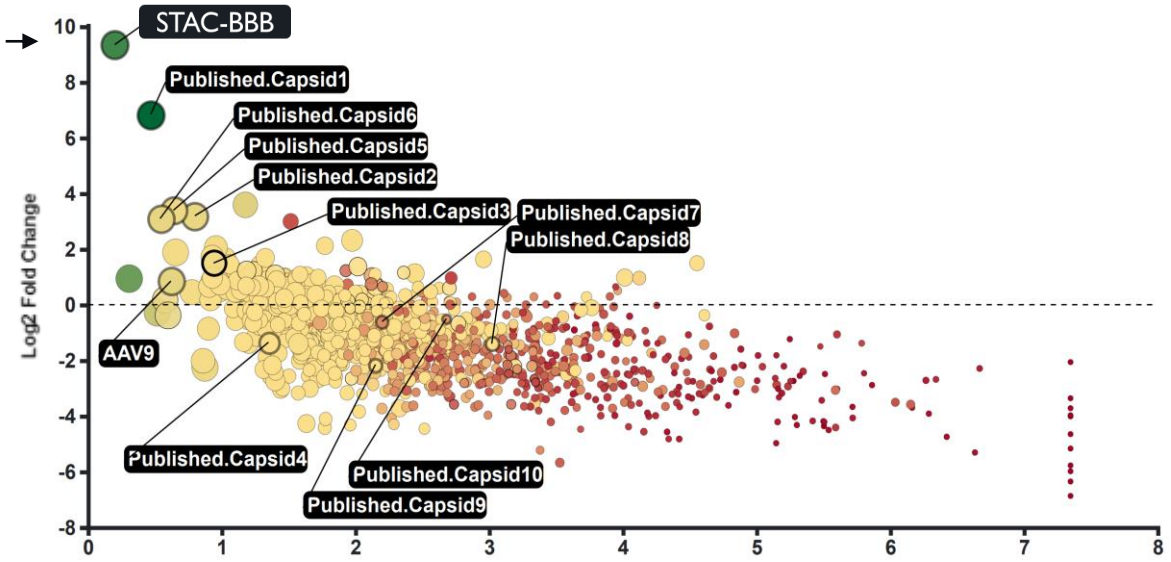
Sangamo STAC-BBB findings exceeded expectations for a successful blood-brain barrier penetrant capsid

- STAC-BBB achieves robust penetration of the blood-brain barrier and **widespread distribution** throughout the brain
- 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**
- Enables **robust expression** of zinc-finger cargo throughout the brain, including **all key brain regions**
- **Clear dose response curve** for both ZF expression and repression of the disease target
- 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 identifies STAC-BBB as the top performing BBB-penetrant capsid for delivery to the brain

Capsid-mediated expression of cargo in neurons

644-fold enrichment in brain →



Log_2 Fold Change (Y-axis): Enrichment score relative to the administered library
Larger value is better

Coefficient of Variation (X-axis): Variation in performance across tissue samples that were evaluated
Smaller value is better

WHOLE BRAIN ASSESSMENT

5112
4544
3976
3408
2840
2272
1704
1136
568
1

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, hSyn1)

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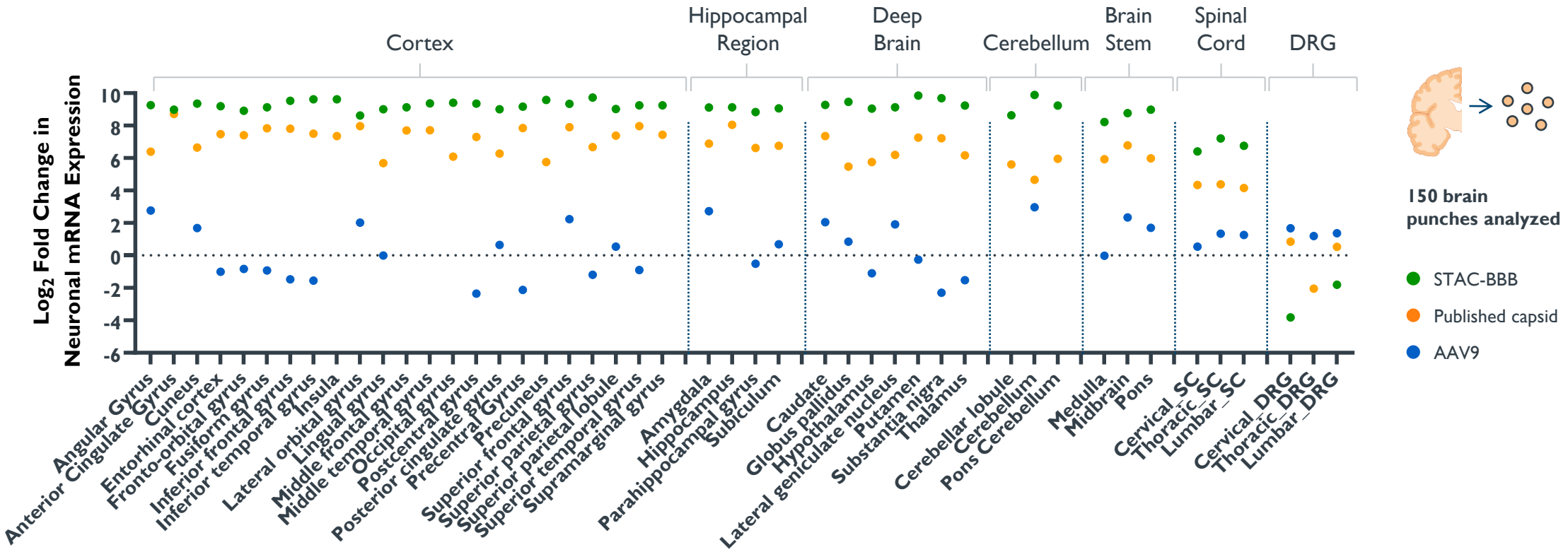
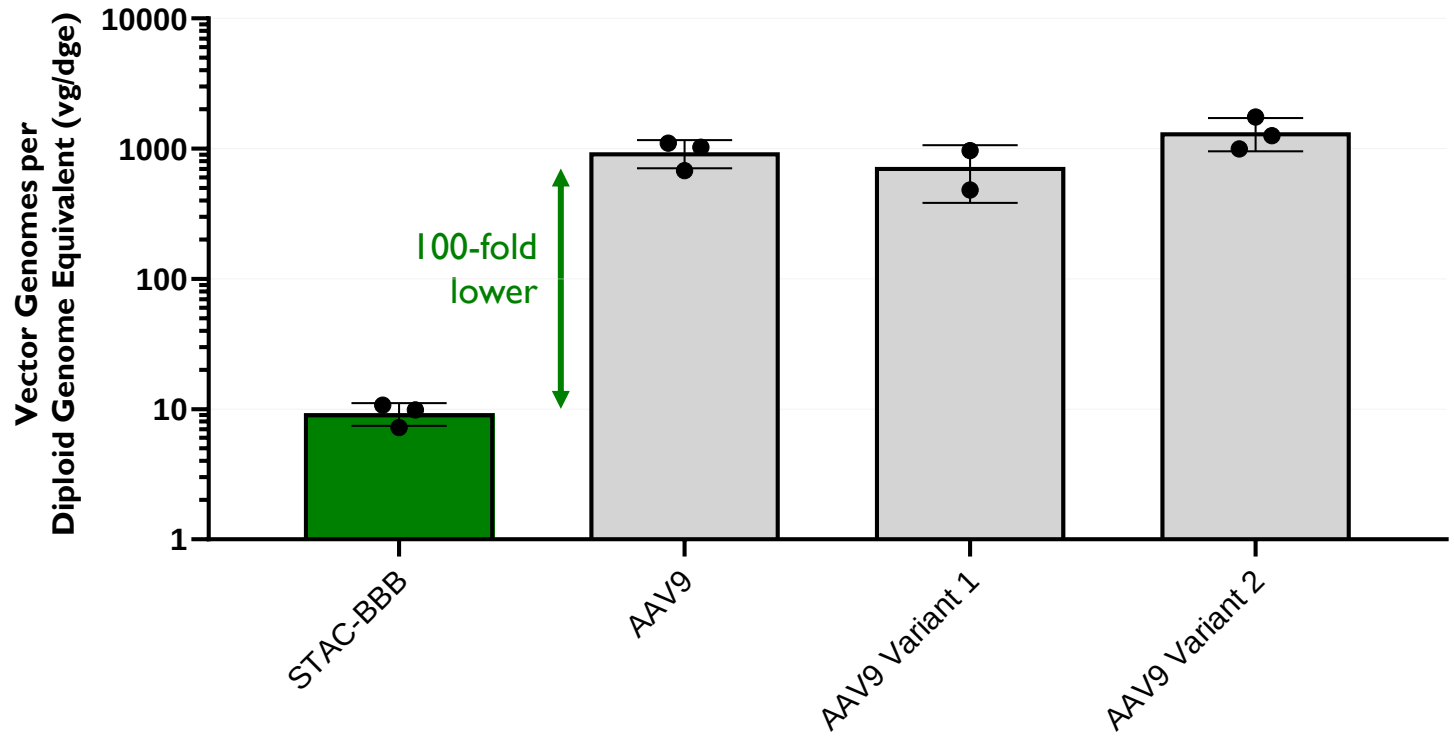
STAC-BBB is enriched in neuronal RNA expression in all CNS regions

Capsid-mediated expression of cargo in neurons



Neuronal RNA expression (3-week study, hSyn1)

STAC-BBB exhibits profound liver de-targeting relative to AAV9



Comparison is relative to historical Sangamo studies, all data shown is for a 1e14 vg/kg dose

High liver exposure after intravenous administration is a limitation of conventional AAV serotypes including AAV9

STAC-BBB achieves efficient CNS delivery while maintaining low peripheral exposure in liver and dorsal root ganglia (DRG)

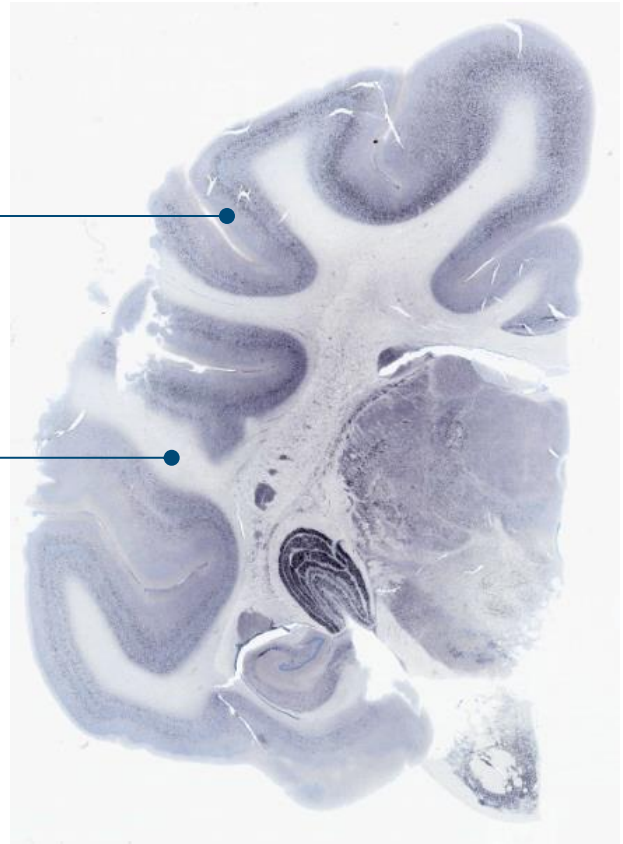
This is the ideal profile for a CNS-targeted capsid

STAC-BBB drives widespread and robust expression throughout the brain

Grey matter (cell bodies)

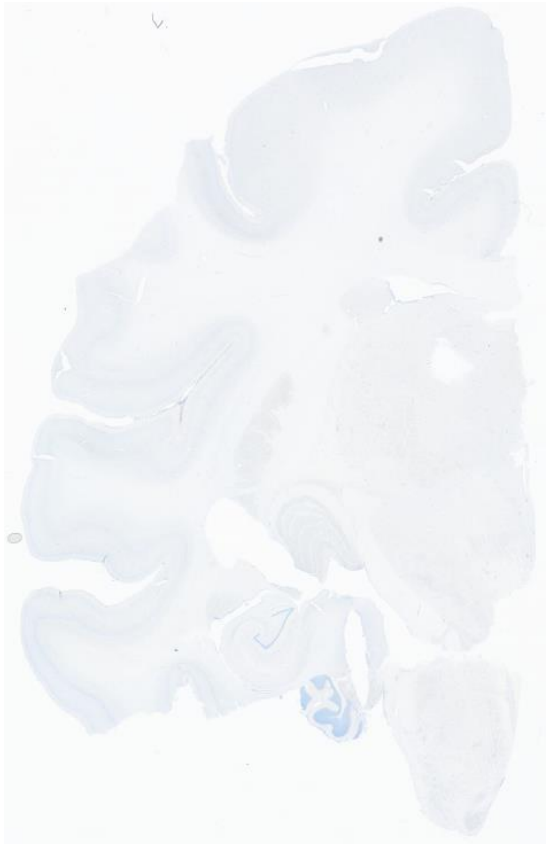
White matter (nerve fibers)

STAC-BBB
(Nuclear-localized GFP)



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

Negative control
(no AAV treatment) – No signal



Nissl staining (light blue):

All cell nuclei

Antibody labeling for green florescent protein (GFP) expression (black):

Cells transduced with STAC-BBB

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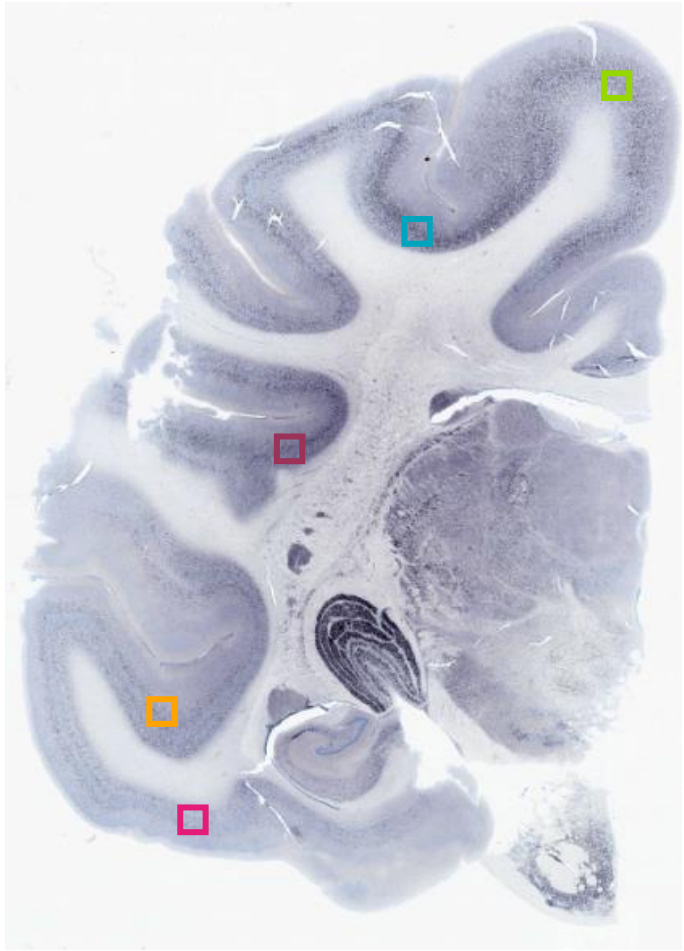
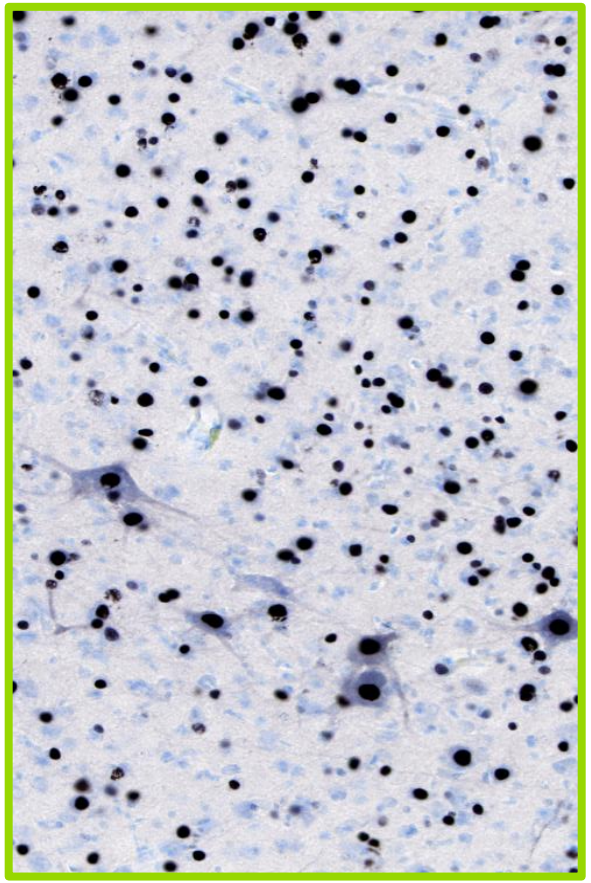
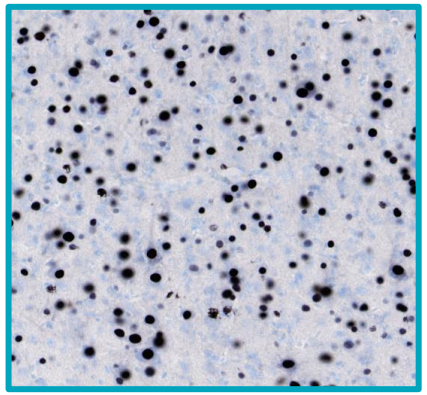
STAC-BBB shows widespread neuronal transduction across all cortical regions



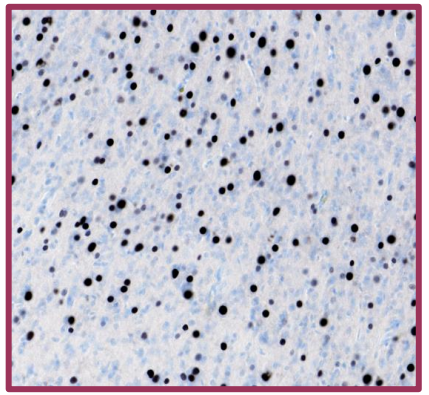
Precentral Gyrus (Motor Cortex)



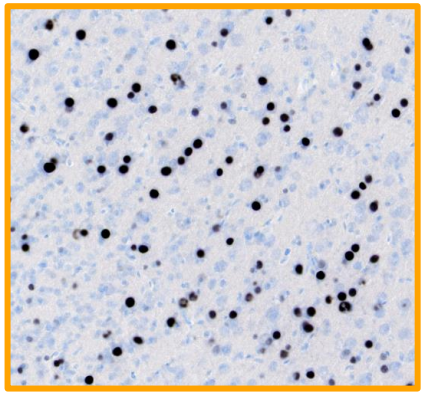
Postcentral Gyrus



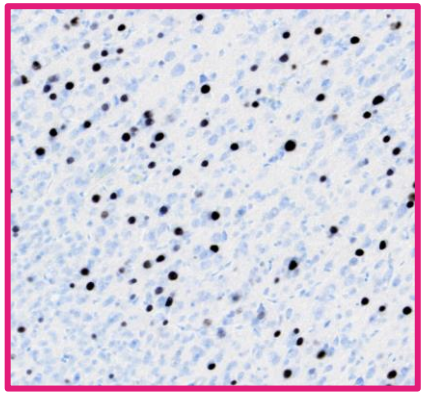
Superior Temporal Gyrus



Middle Temporal Gyrus

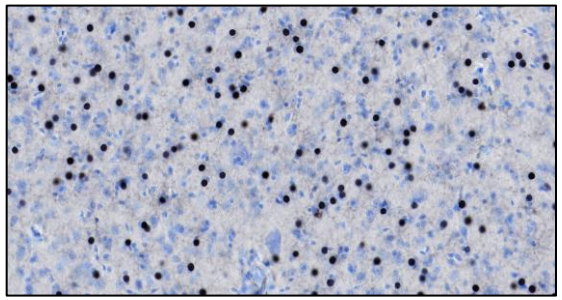


Inferior Temporal Gyrus

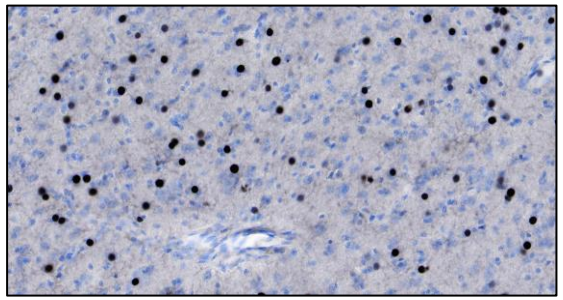


STAC-BBB mediates widespread brain transduction at the 2e13 vg/kg dose

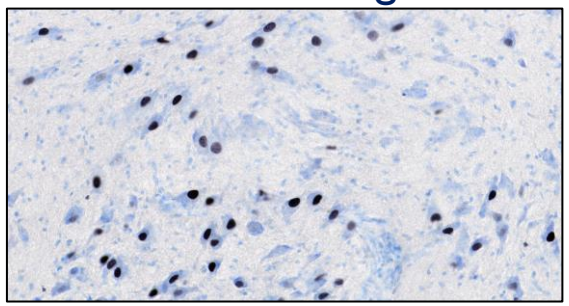
Putamen



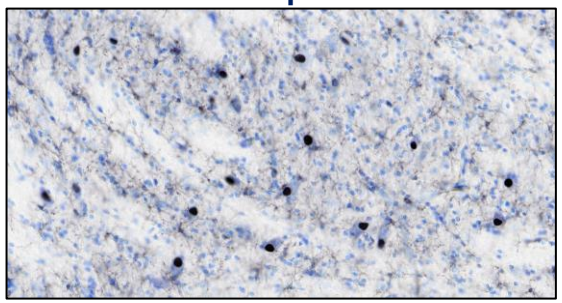
Caudate



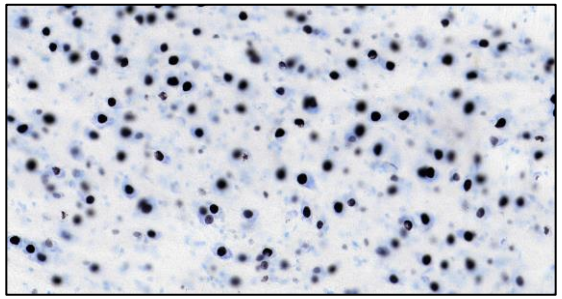
Substantia nigra



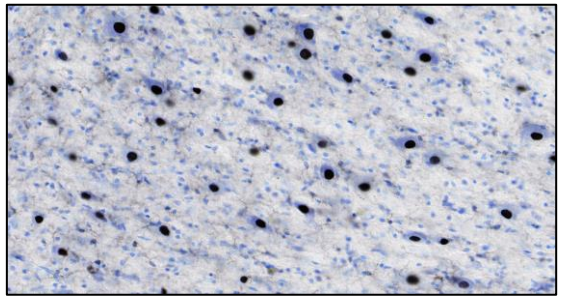
Globus pallidus



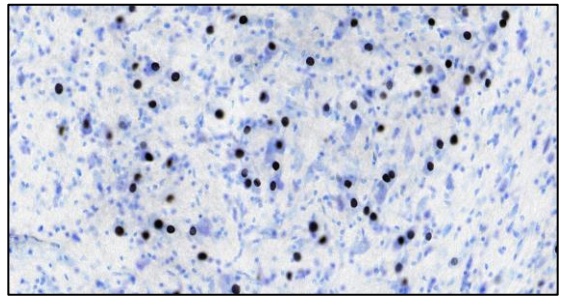
Pons



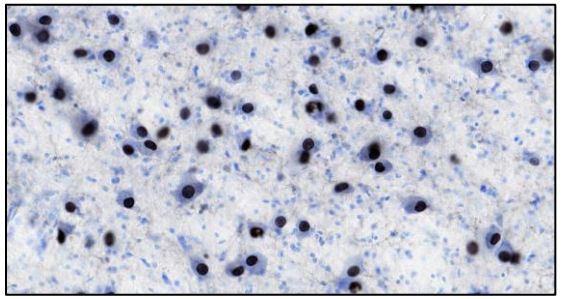
Dentate nucleus



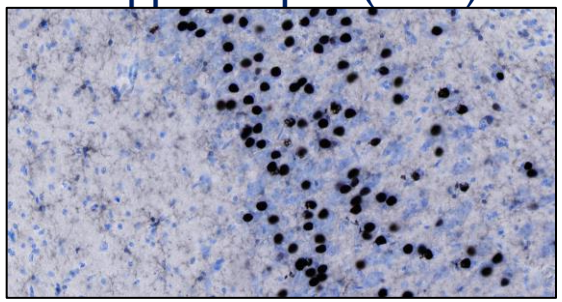
Cuneate nucleus



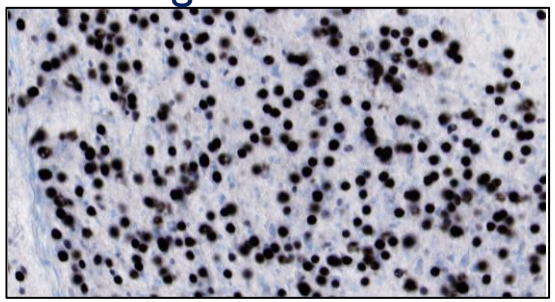
Thalamus



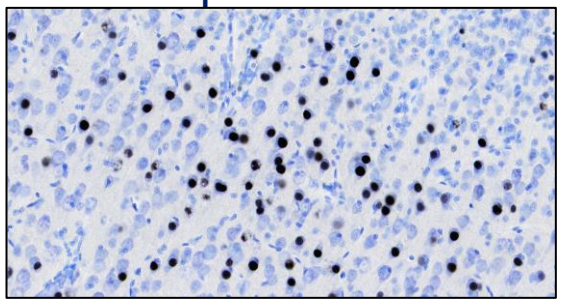
Hippocampus (CA2)



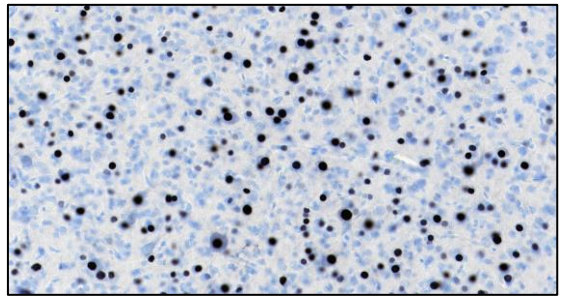
Lateral geniculate nucleus



Temporal cortex



Motor cortex



Sangamo THERAPEUTICS

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

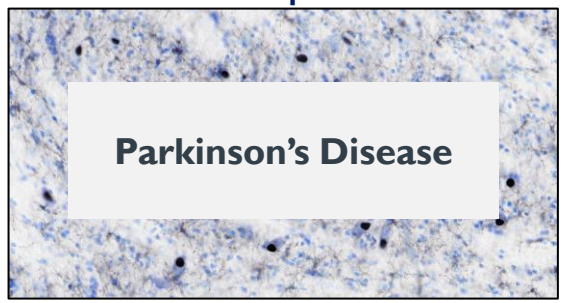
Neurons are widely transduced in regions integral to disease pathology

Putamen

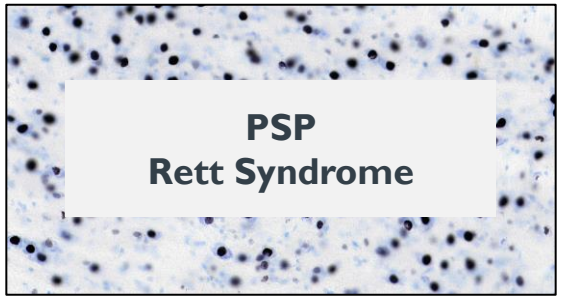
Caudate

Substantia nigra

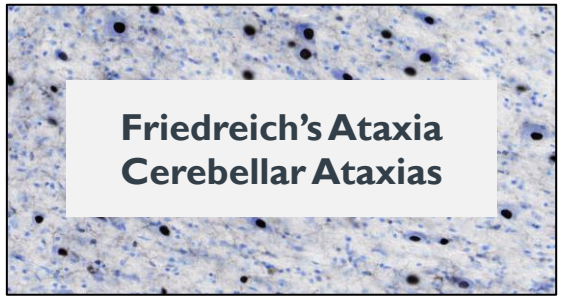
Globus pallidus



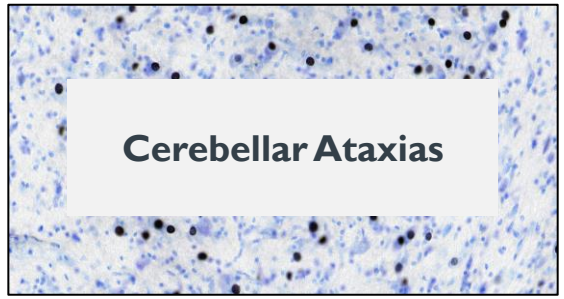
Pons



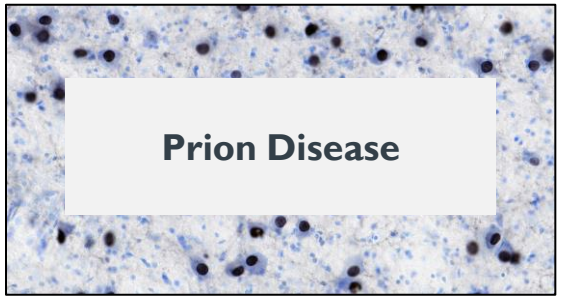
Dentate nucleus



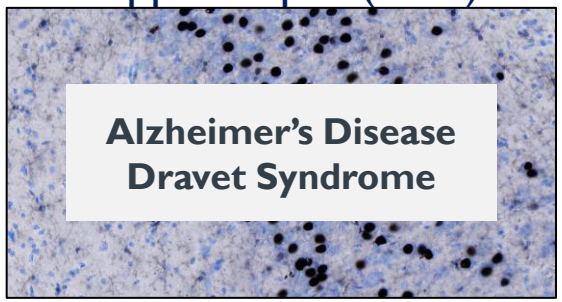
Cuneate nucleus



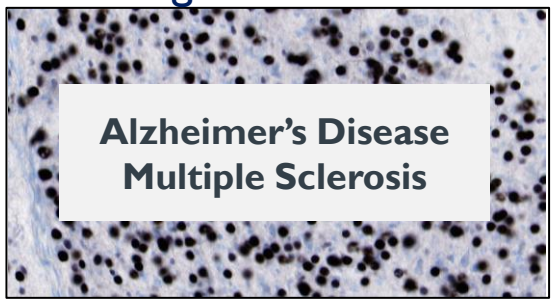
Thalamus



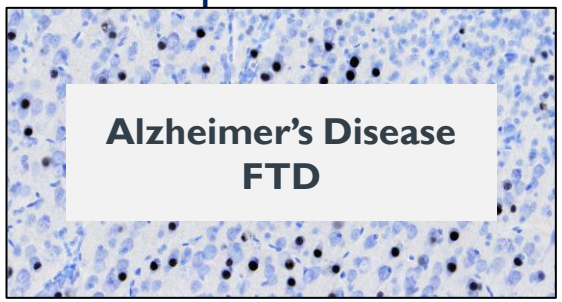
Hippocampus (CA2)



Lateral geniculate nucleus



Temporal cortex



Motor cortex

ALS: Amyotrophic lateral sclerosis; FTD: Frontotemporal dementia; PSP: Progressive supranuclear palsy
2e13 vg/kg STAC-BBB, 19 days post administration

Sangamo THERAPEUTICS

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

Sangamo THERAPEUTICS

Delivering Versatile Zinc Finger Payloads Throughout the CNS

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

Highly 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

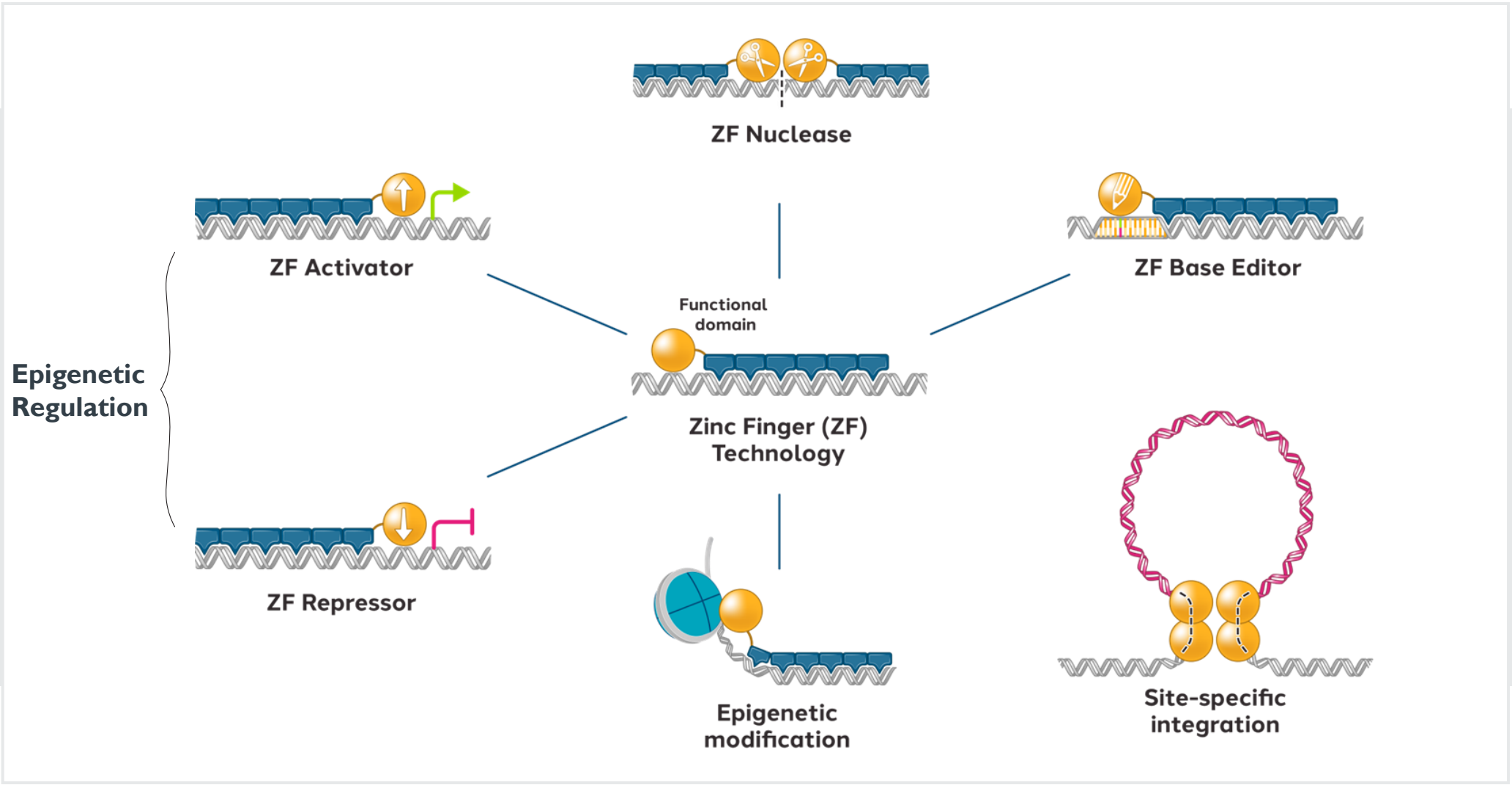
Powerful AAV Delivery Platform

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

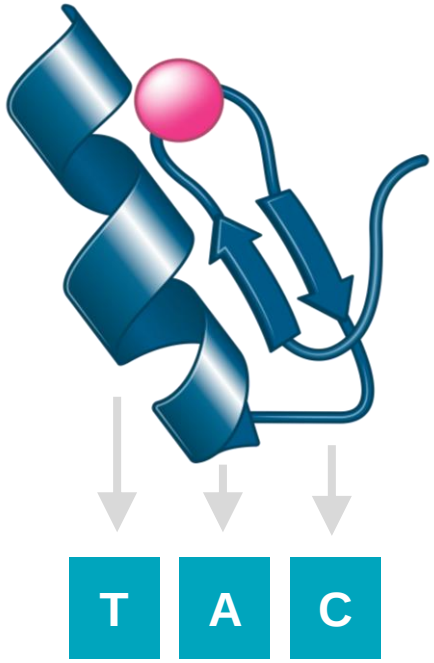
Potentially Industry Leading CNS Tropism

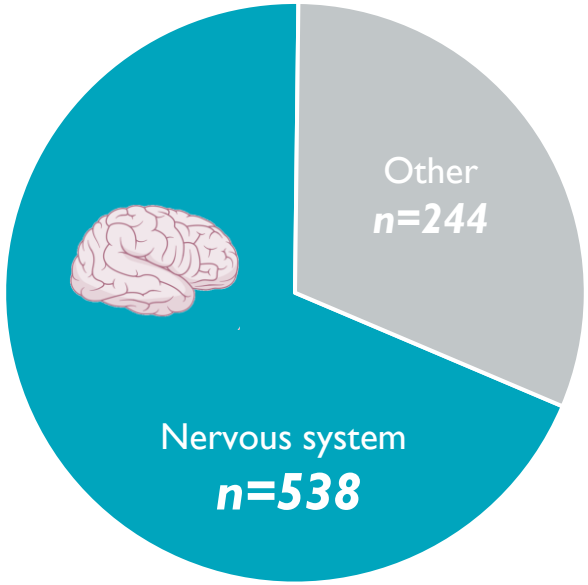
Robust penetration of the blood-brain barrier and widespread distribution throughout the brain

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

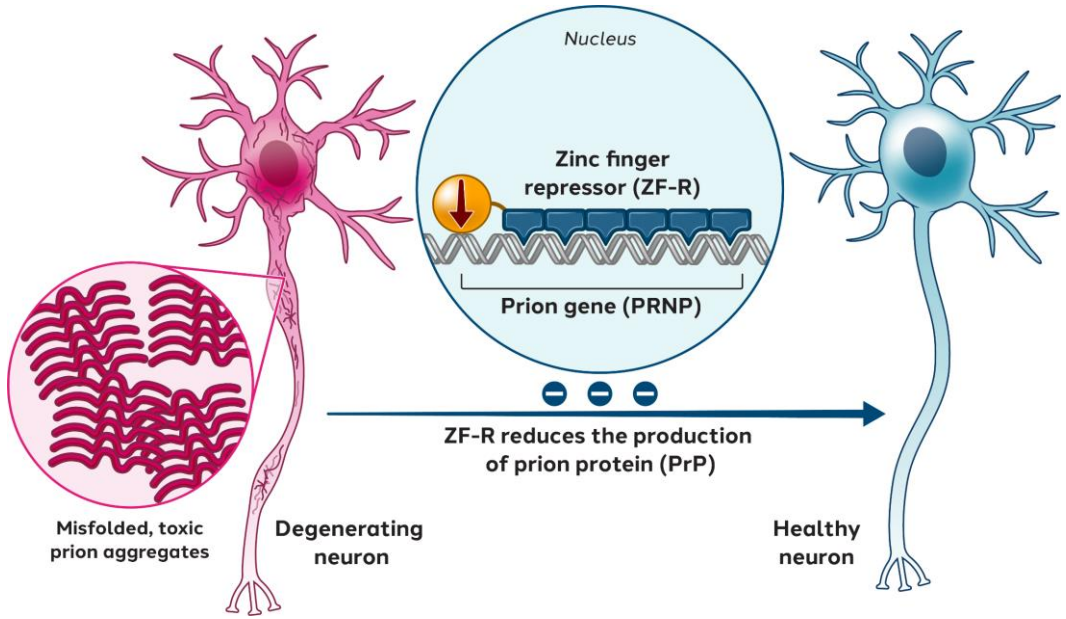
Zinc fingers are differentiated in key therapeutic features for potentially treating neurologic diseases

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

Sangamo THERAPEUTICS

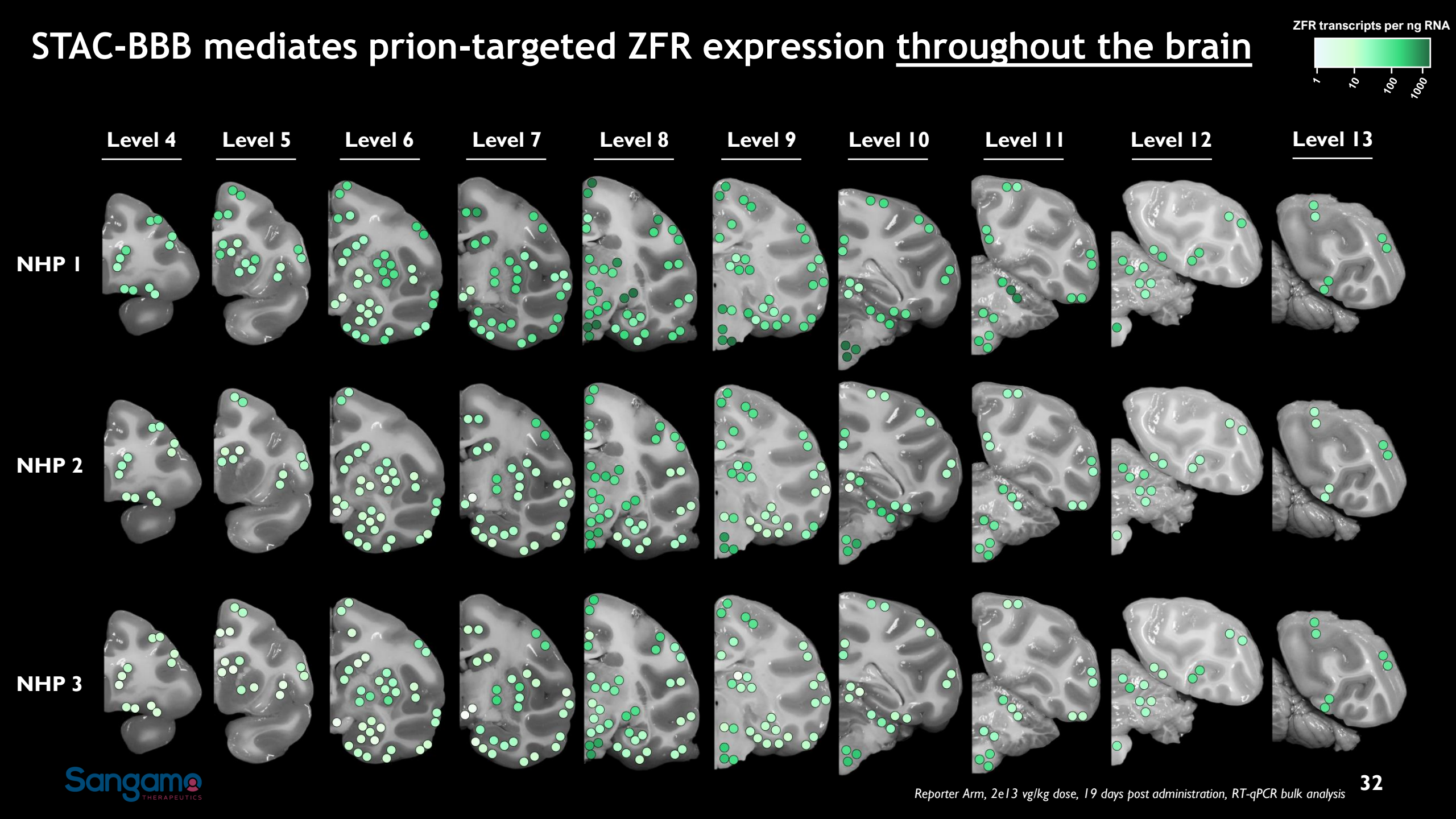
Prion disease is rapidly progressive and always fatal

Rapid path to clinical validation in a devastating disease with no current approved treatment options. Clear regulatory path and efficacy endpoints. Unlocks additional neurodegenerative indications.



- Progressive condition, with **no disease modifying therapy**
- Sporadic, inherited and acquired forms
- Very **well-defined** patient population
- Symptoms can include **cognitive, psychiatric and motor deficits**
- **Excellent fit** for a ZF repression approach
  - Prion knockout animals do not get disease
  - Prion reduction can delay or prevent disease
  - Neuronal PrP reduction prevents disease
- Repression of prion expression in the brain **may slow or halt disease progression and neurodegeneration**

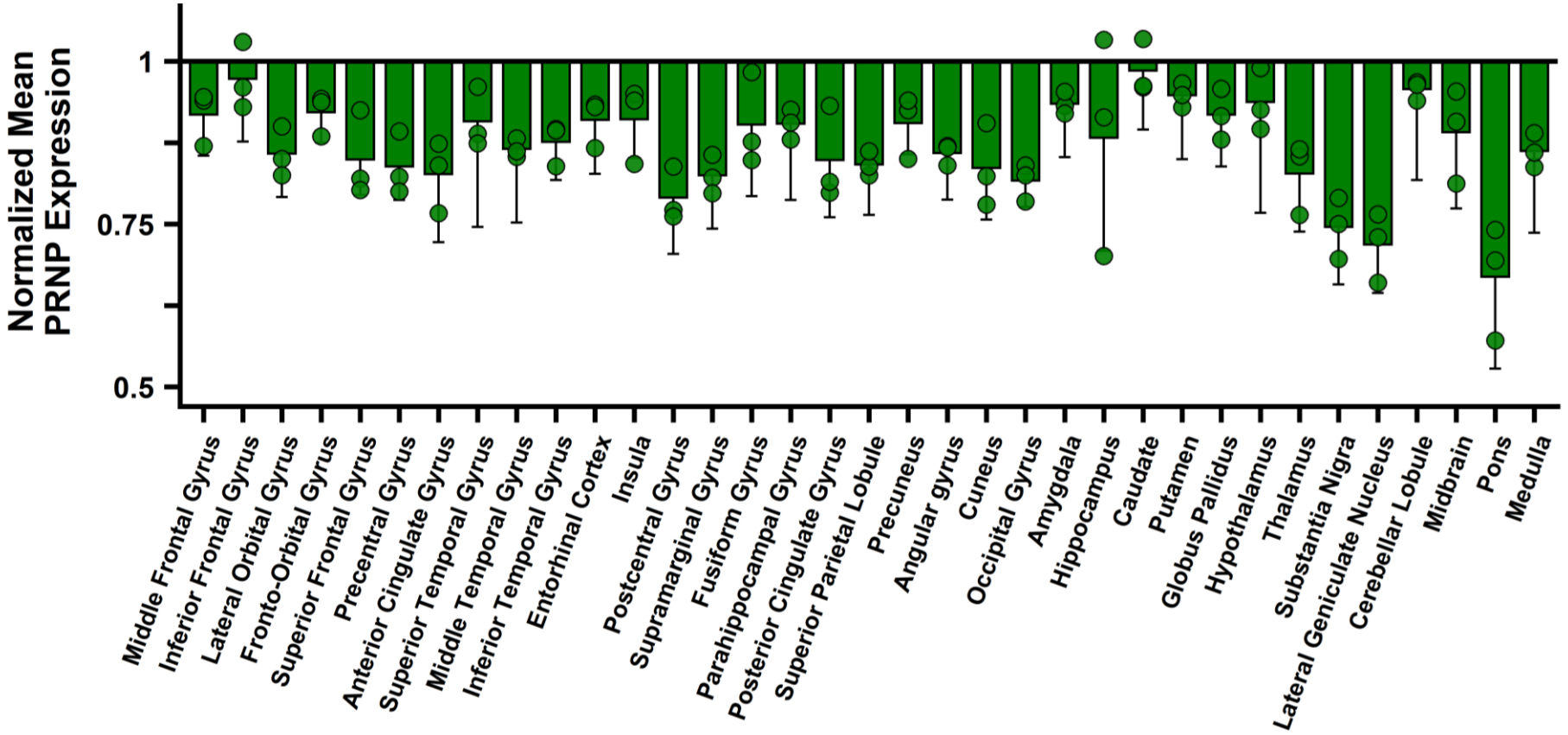
STAC-BBB mediates prion-targeted ZFR expression throughout the brain



Reporter Arm, 2e13 vg/kg dose, 19 days post administration, RT-qPCR bulk analysis

STAC-BBB mediated ZFR expression translates to brain-wide prion repression in all 35 brain regions analyzed

Prion gene expression, 19 days post administration, bulk analysis



← Prion expression in control animals is set to 1

STAC-BBB

2e13 vg/kg

Data analyses bulk brain punches.

Each bar is average of 3 animals.

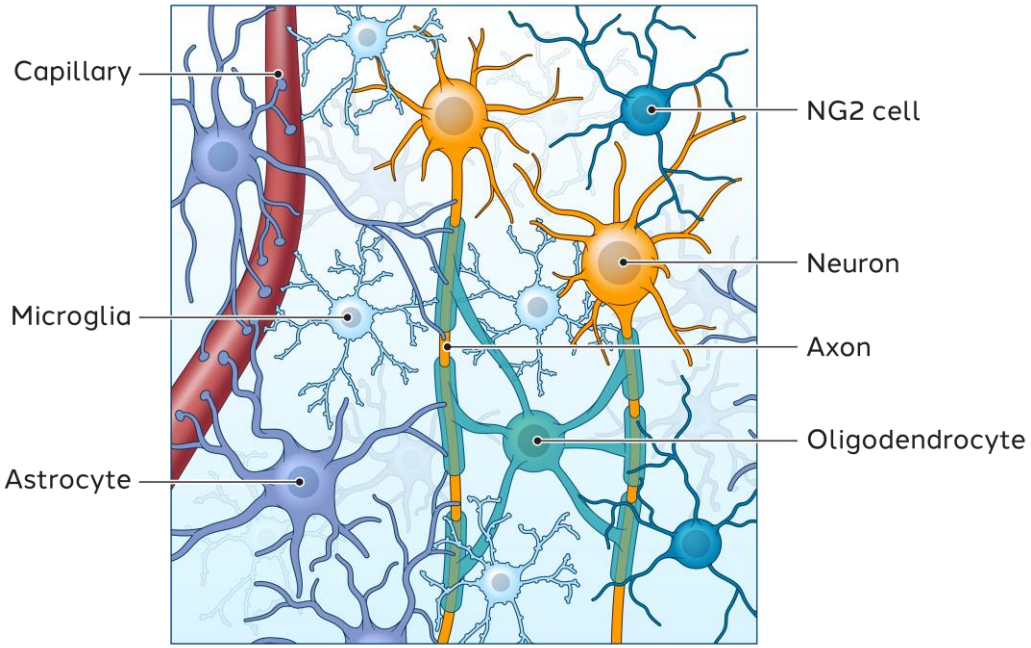
Each dot represents the average of multiple brain punches for one animal for the indicated region.

Genomic medicines enable cell-type specificity, critical for efficacy and safety when treating neurological diseases

Framework for understanding 'bulk analyses'

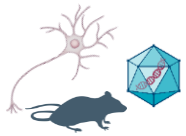
- Cell-type-specific promoters drive zinc finger expression **exclusively in neurons**
- Neurons are **critical drivers of disease pathology**, and key therapeutic targets
  - Non-neuronal cell types often express a gene involved in a disease, but either do not make the protein OR are not the disease drivers
- Neurons only make up **a percentage of overall** brain cell types (19-40%)
- This creates a **'floor effect'** for bulk analysis data due to the selectivity of our approach for gene repression in neurons

Prior experiments tell us even modest target repression in bulk brain tissue can lead to significant changes in disease progression

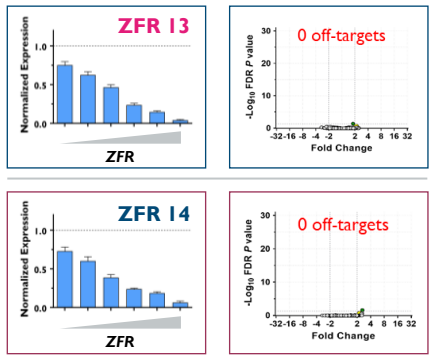


Zinc finger repressors extend survival in a mouse model of aggressive prion disease

Potent and specific ZFRs

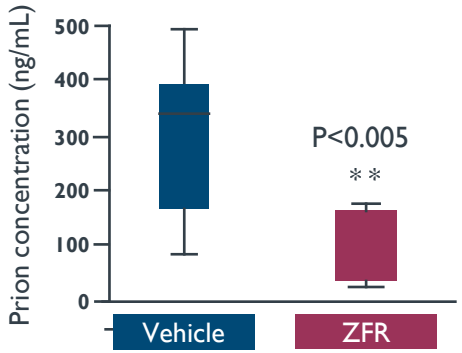


Primary neurons



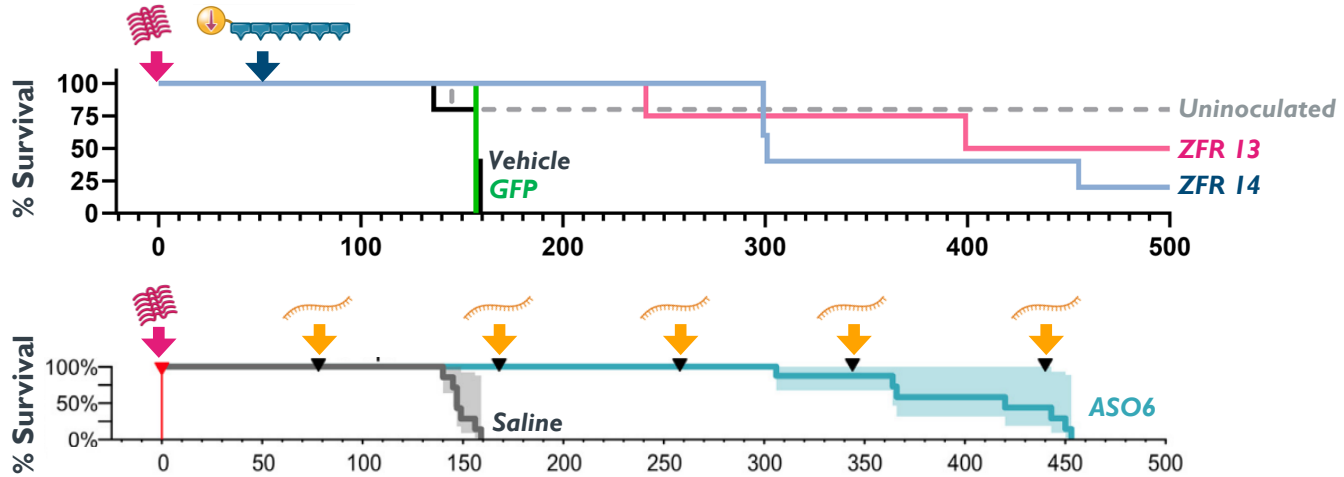
Reduction of CSF biomarker

CSF



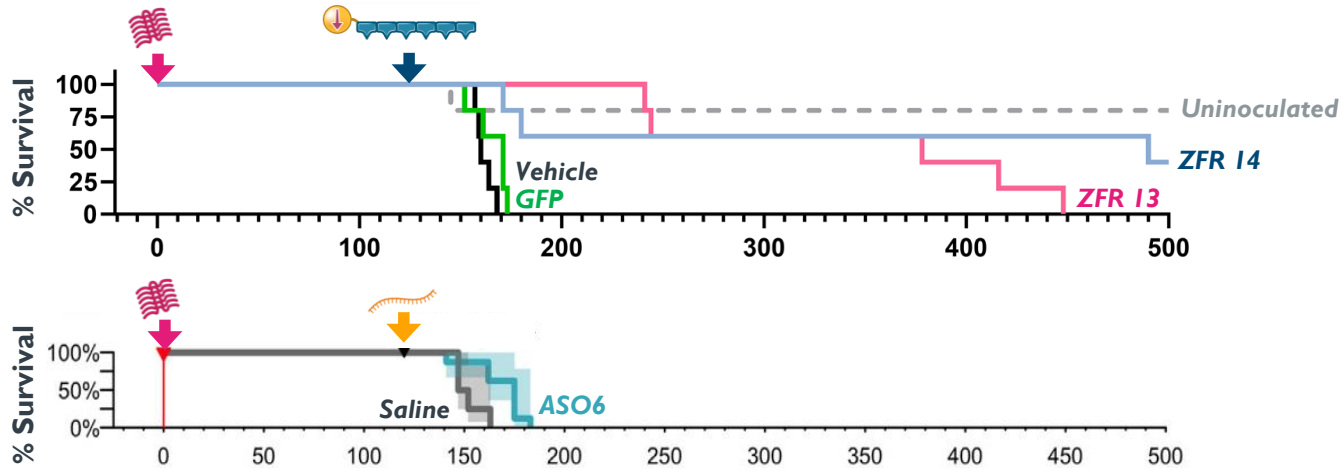
ZFR ** 60 dpi ***

ASO* 78, 168, 258, 348, 438 dpi



ZFR ** 122 dpi

ASO* 120 dpi



Data presented at ASGCT 2023

** ASO Data from Minikel et al 2020*
*** ZFR administered intravenously using PHPB capsid*
**** dpi: days post infection*

The prion program continues to advance towards CTA

Summary

- Clinical lead ZFR with >95% prion reduction per cell, no off-targets, and exceptional potency *in vitro* and *in vivo*
- Target engagement, durability and safety demonstrated in mouse and NHP studies
- Best-in-disease efficacy in gold standard survival model (Misfolded PrP^{Sc} infected mice)
- Clinical trial authorization (CTA) enabling activities continue to advance for Sangamo's program to treat prion disease, leveraging the novel STAC-BBB capsid.

Activity, Status	ZFR design, screening	In vitro validation	Rodent TE, safety	Rodent efficacy	NHP TE, safety	NHP GLP/TOX	CTA
Models	Human cell line Mouse cell line Human fibroblasts	Human iPSC neurons Mouse neurons	Wildtype mice *hPRNP* mice	PrP^{Sc} survival model @ -21, 60, or 120 days post infection	Cynomolgus NHP, IV administration		
Endpoints	*PRNP* mRNA Transcriptomics	*PRNP* mRNA Transcriptomics PrP protein	*PRNP* mRNA Transcriptomics PrP protein (tissue) PrP protein (CSF) Single-cell ISH/IHC Tolerability	Survival Plasma NfL PrP pathology *PrP* mRNA & protein Single-cell ISH/IHC Safety/pathology	*Prnp*, ZFR mRNA Single-cell ISH/IHC Biodistribution Safety/pathology		

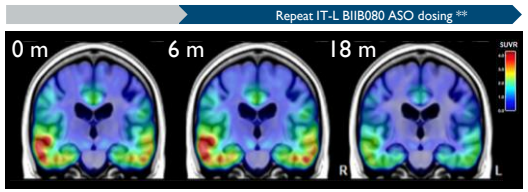
Neurodegenerative diseases, driven by tau pathology, impact millions of people globally

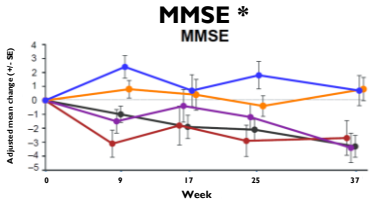
Leverages STAC-BBB delivery capsid. Targets a very large patient population with high unmet medical need. Unlocks multiple tauopathy indications, in addition to Alzheimer's disease.

Tauopathy disorders span indications including:

- AD – Alzheimer's disease
- PSP – Progressive supranuclear palsy
- FTD – Frontotemporal dementia
- CTE – Chronic traumatic encephalopathy
- CBS – Corticobasal syndrome
- LBD – Lewy body disease (+ alpha synuclein)

Lowering tau expression can reverse established tau pathology and potentially halt AD progression in humans



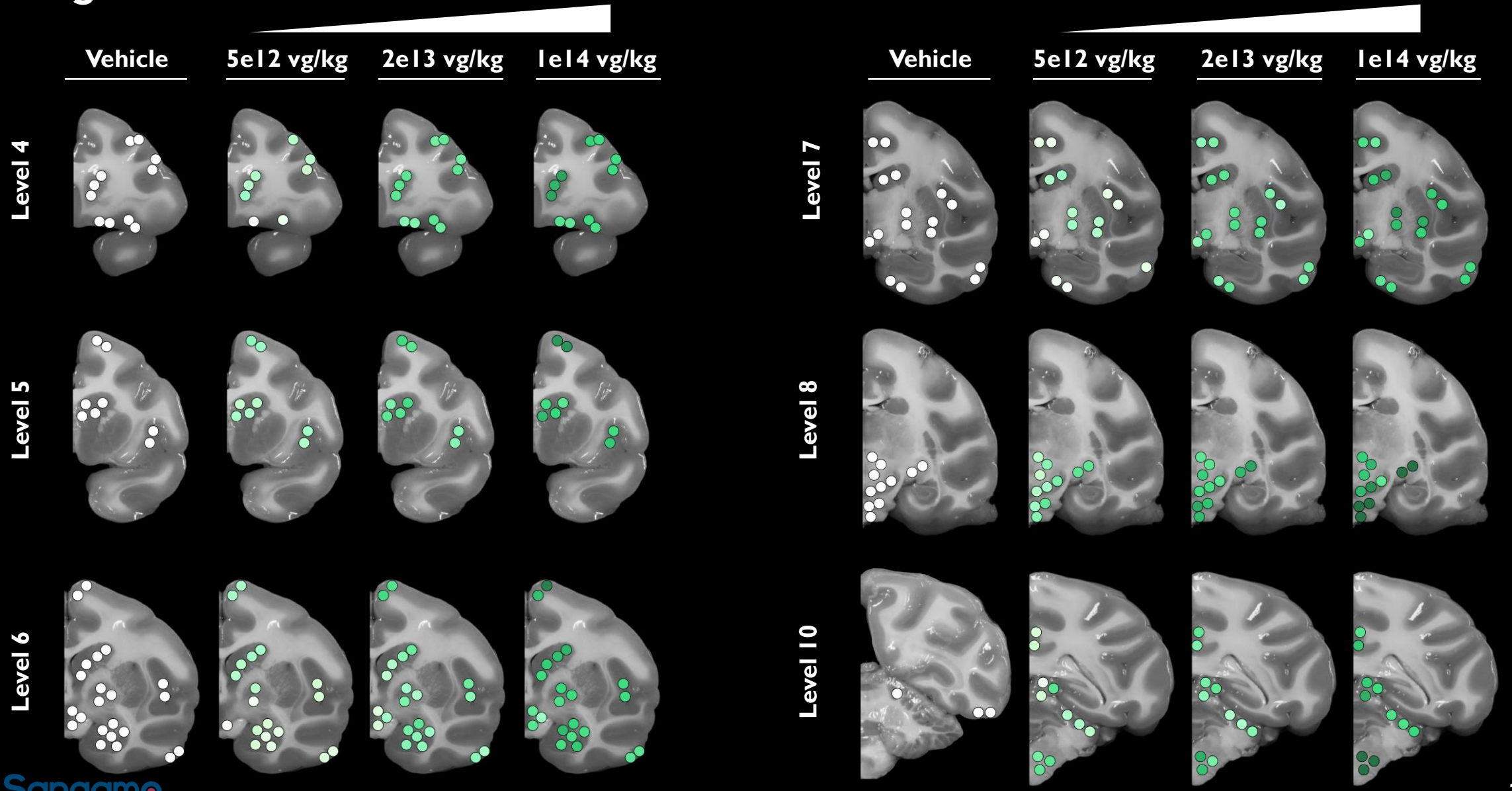


Sangamo's approach is differentiated in several important ways

	ZFR	ASO
All tau forms targeted at the source, inside neurons	✓	✓
One-time, IV administration	✓	✗
All brain regions = all tauopathy indications	✓	✗
Cell-type specificity, restricted to CNS cell types	✓	✗
Rapid pharmacokinetics, 100% single-cell potency	✓	✗

* *Biogen, Clinical Trials in Alzheimer's Disease (CTAD) 2023*
** *Ionis October 2023 Innovation Day*

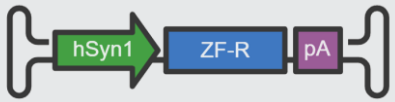
STAC-BBB mediates a clear dose response curve for tau ZFR expression throughout NHP brain



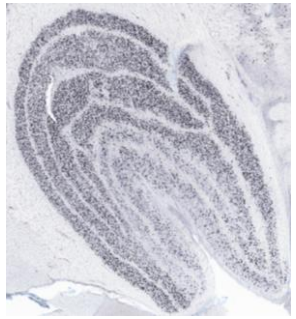
One NHP from each dose group shown, 28 days post administration, RT-qPCR bulk analysis

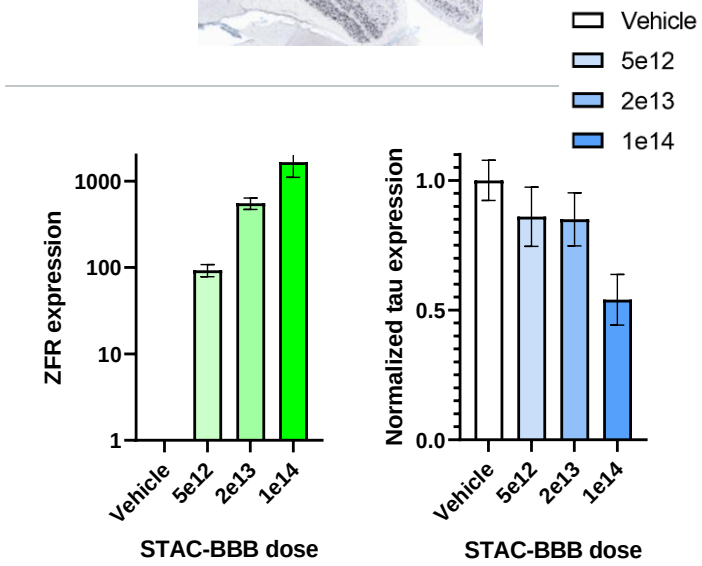
ZFR expression results in dose-dependent tau mRNA repression in bulk analysis of key brain regions

- Mean expression levels show a dose response for ZFR expression and tau mRNA repression in neurons
  - Bulk analysis includes all cell types and all punches for that region
- Neuronal tau is key to disease progression in tauopathies
- Tau ZFR is expressed only in neurons (Synapsin promoter)

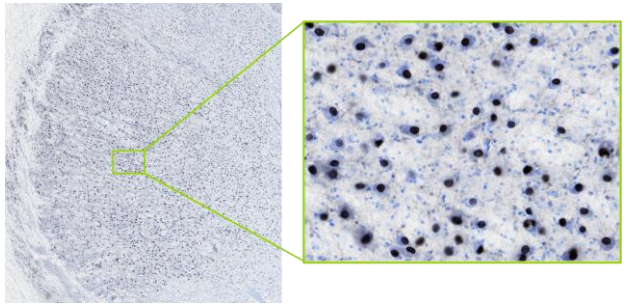


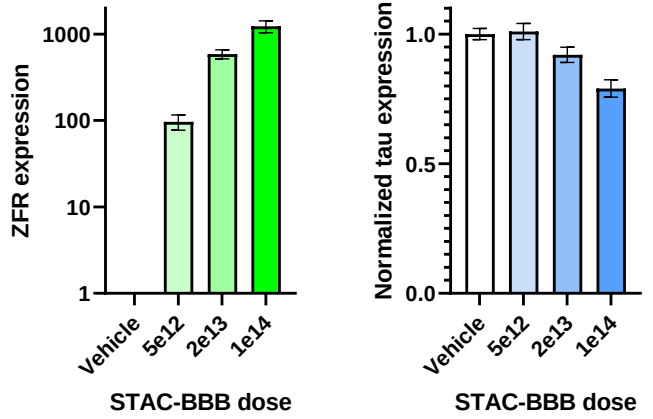
Lateral geniculate nucleus





Thalamus



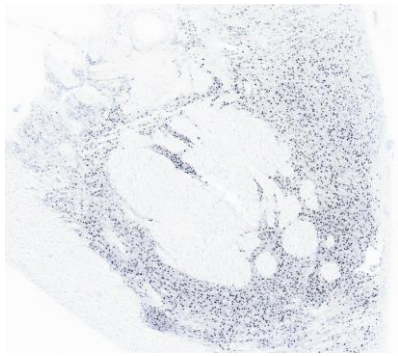


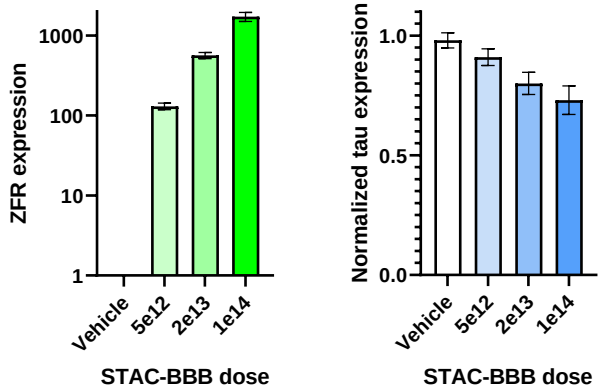
Chromogenic IHC images from reporter arm

Bulk analysis of brain punches, normalized to vehicle

STAC-BBB mediated bulk tau repression translates to potent neuronal suppression at the single cell level

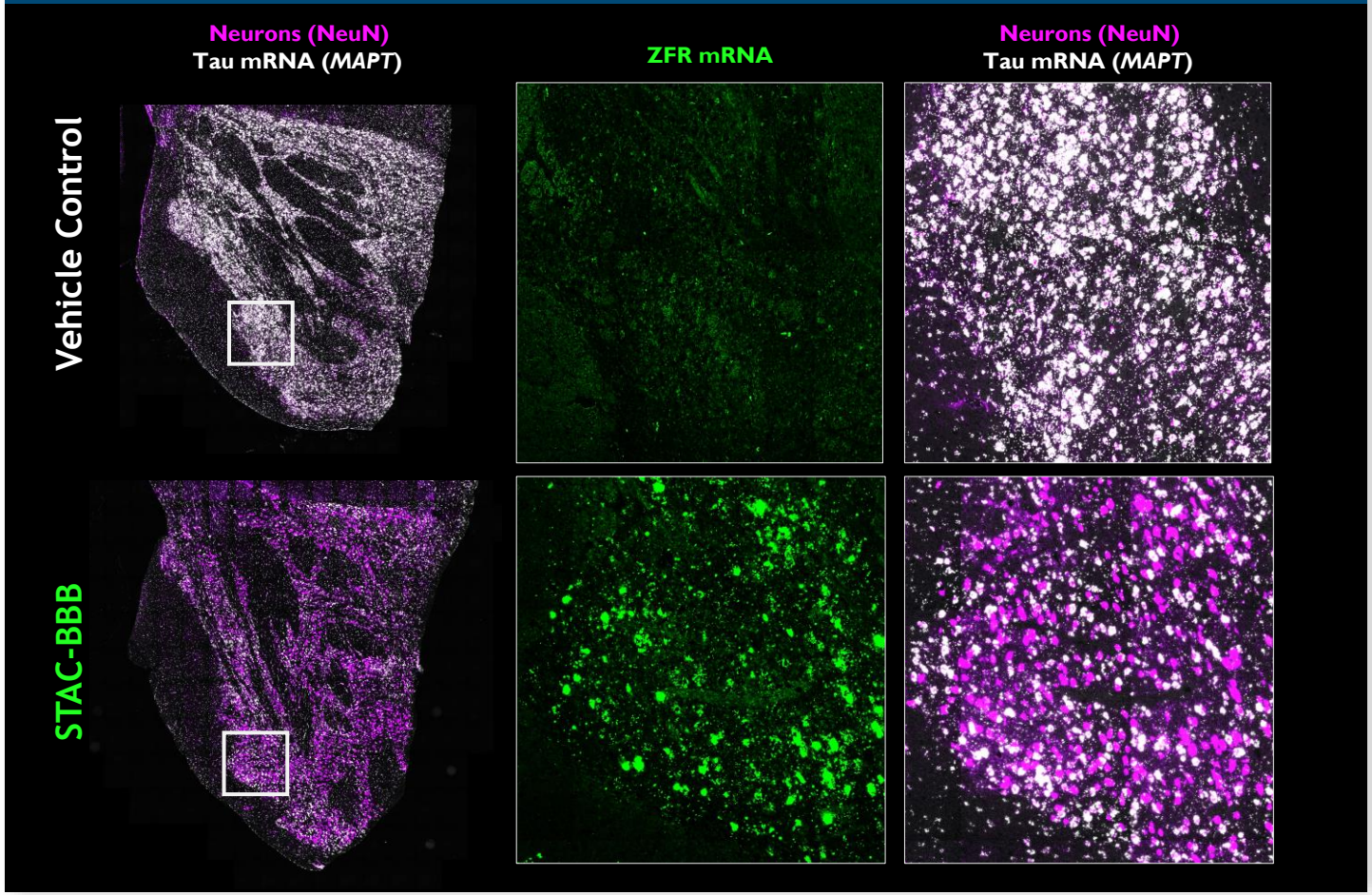
Pons: Bulk ZFR and tau mRNA





Chromogenic IHC image from reporter arm
Bulk analysis of brain punches, normalized to vehicle

Pons: Single-cell ZFR and tau mRNA



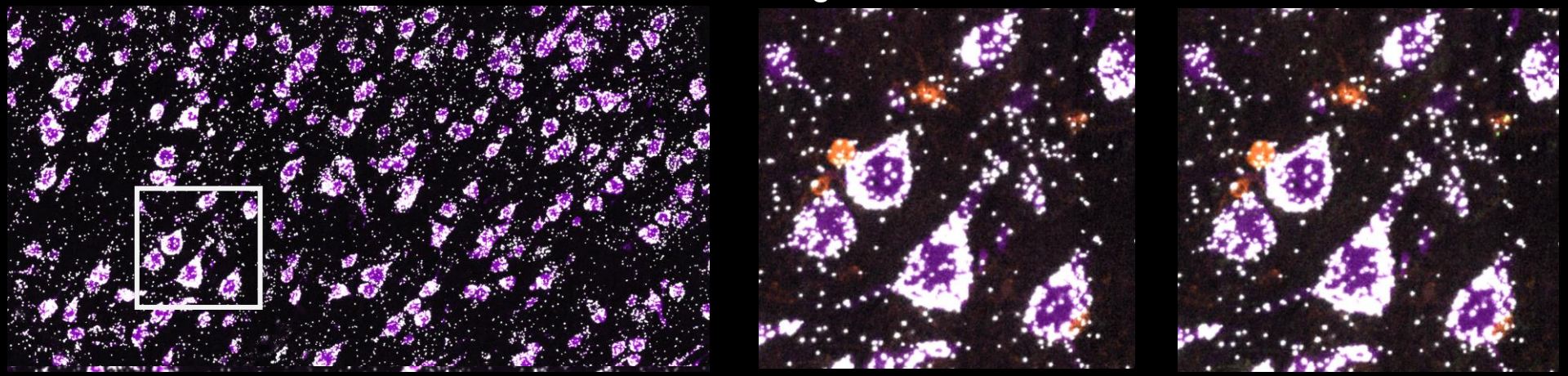
Multiplexed RNAscope ISH / IHC assay for NeuN, MAPT mRNA, and ZFR mRNA
1e14 vg/kg dose, 28 days post administration

Sangamo THERAPEUTICS

Single cell analysis also shows potent and selective repression of neuronal tau in the motor cortex

In control animals, tau mRNA is detected in neurons and glia. No ZFR is detected.

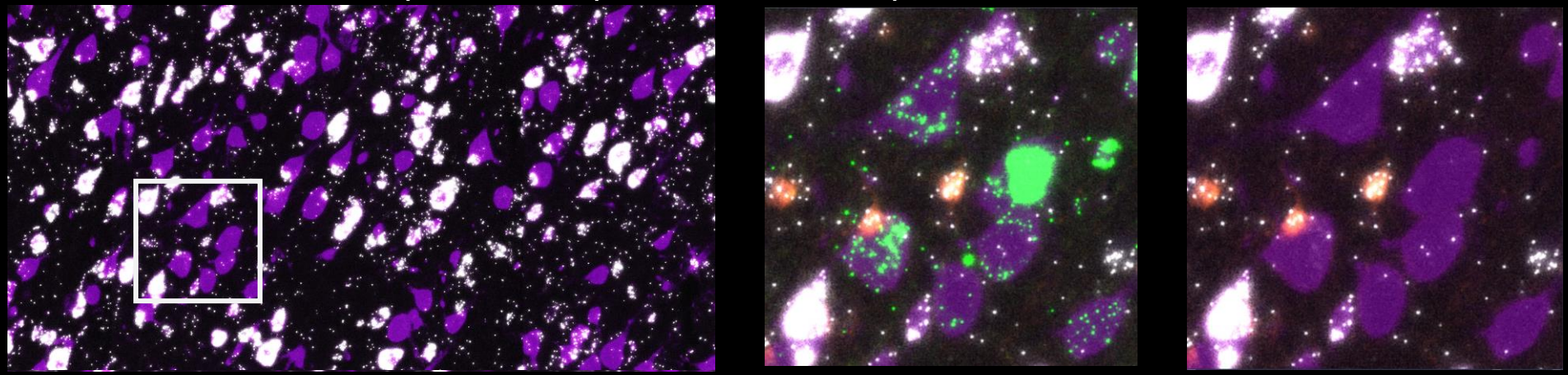
Vehicle Control



Glia (S100β)
ZFR mRNA
Neurons (NeuN)
Tau mRNA (MAPT)

STAC-BBB mediates ZFR expression and potent tau mRNA repression in neurons

STAC-BBB



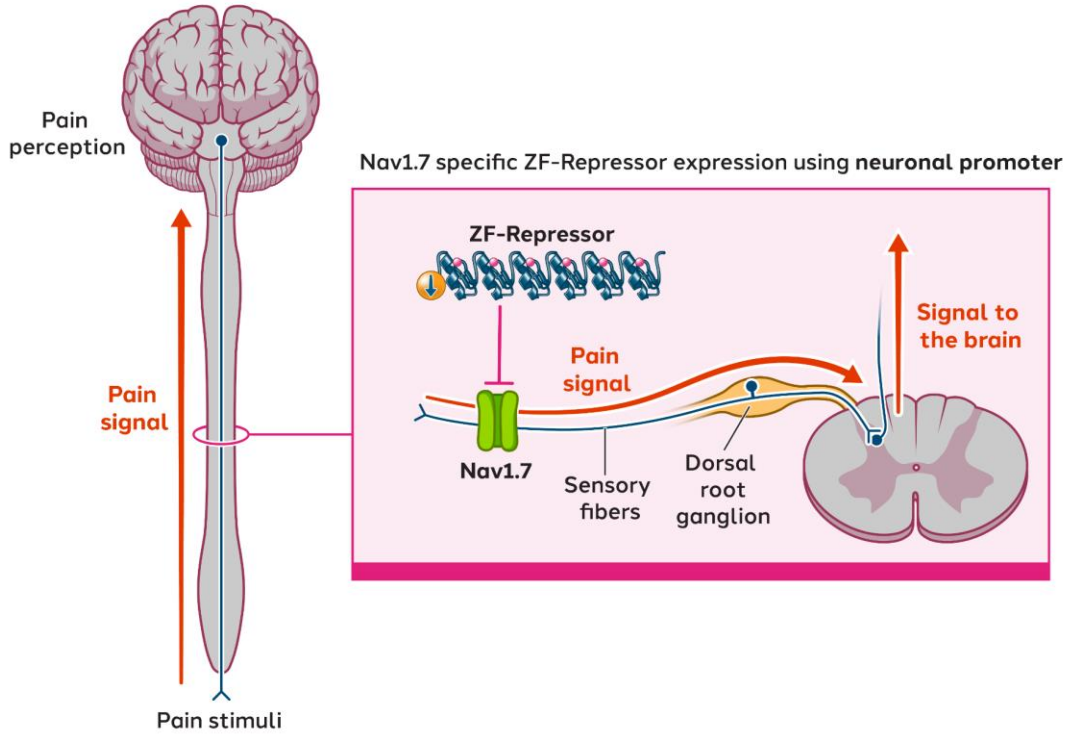
Multiplexed RNAscope ISH / IHC assay for NeuN, S100β, MAPT mRNA, and ZFR mRNA
1e14 vg/kg dose, 28 days post administration

Sangamo THERAPEUTICS

Balancing Risk Through a Diversified Delivery Approach

Urgent need for novel chronic neuropathic pain therapeutics

Leverages an AAV delivery capsid already in the clinic. Targets a gene validated by human genetics. Targets a patient population with high unmet medical need. Gateway to additional indications.



- Nav1.7 is a voltage gated sodium channel expressed in the Dorsal Root Ganglion (DRG)
- Alterations in Nav1.7 activity **directly regulate pain levels** in several genetic disorders
- 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**

Zinc finger repressors potently reduce Nav1.7 in human neurons with exquisite and maximal specificity

iPSC-derived neurons

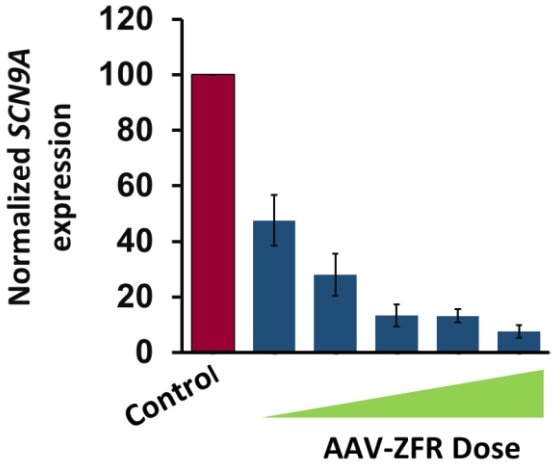
+

AAV + ZFR

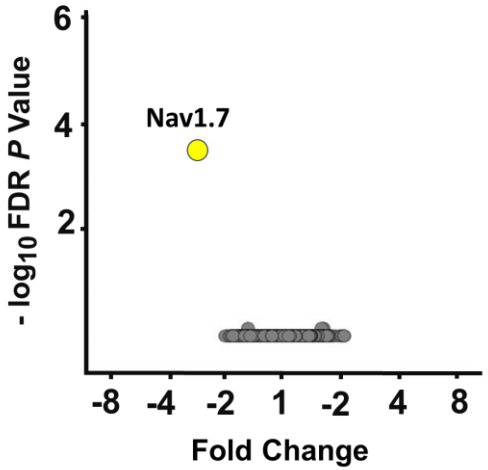
↓ 30d

Nav1.7 expression,
Off-target assessment

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

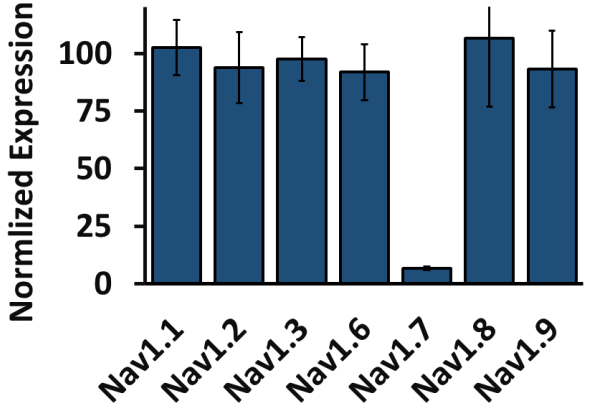


Selective repression of *SNC9A* as shown by global genomic analysis



Differential expression of 20,000 genes was evaluated

Specific repression of Nav1.7 without impacting other sodium channels

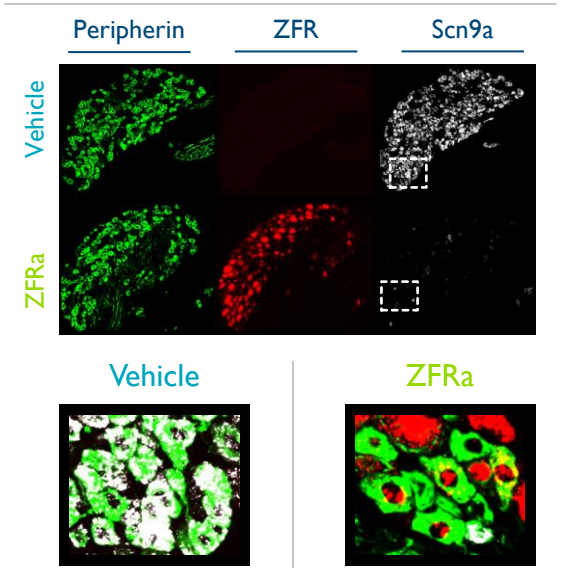


Nav1.7 repressors reverse neuropathic pain in preclinical models

IND-enabling activities continue to advance in the Nav1.7 program to treat chronic neuropathic pain.

Potent Scn9a mRNA repression in mouse DRG neurons

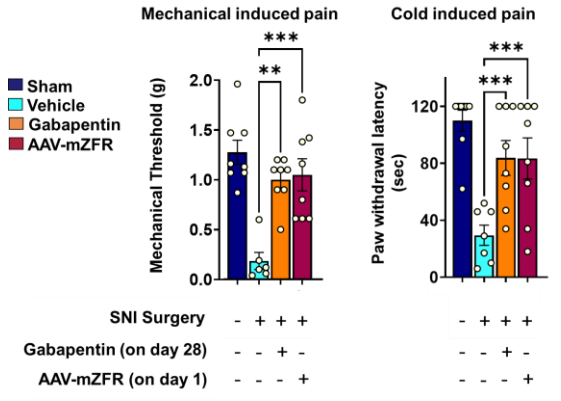
Intrathecal injection,
4 weeks



Full restoration of mechanical and cold induced pain responses in mZFR-treated mice

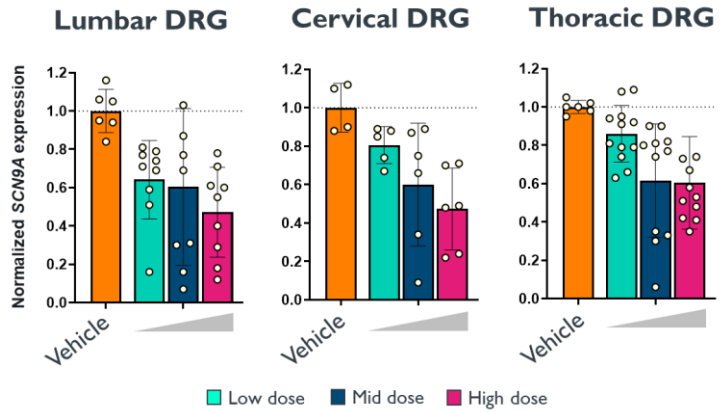
Intrathecal injection

Mechanical pain measurement



hZFR repressed SCN9A by up to 40-60% at the bulk tissue level across a 100-fold dose range

AAV/ZFRs
IT Injection



- Well tolerated across a 100x dose range
- No clinical signs of toxicity or clinical pathology findings
- No adverse macroscopic findings; minimal-mild DRG findings, not considered dose-limiting

Gabapentin was administered one hour before measurement
***p<0.01, ***p<0.001 vs Vehicle group*

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The Nav1.7 program activities continue to advance

Summary

- Clinical lead ZFR with >95% Nav1.7 reduction per cell, no off-targets, and exceptional potency *in vitro* and *in vivo*
- Target engagement, efficacy, durability, and safety and rescue of pain hypersensitivity in a mouse model of neuropathic pain
- Clinical candidate ZFR repressed Nav1.7 mRNA by up to 40-60% at the bulk DRG level across a 100-fold dose range in the NHPs
- Clinical lead ZFR was well tolerated at all doses tested and not associated with any in-life clinical or neurological observations, with minimal adverse microscopic findings
- IND-enabling studies continue to advance.

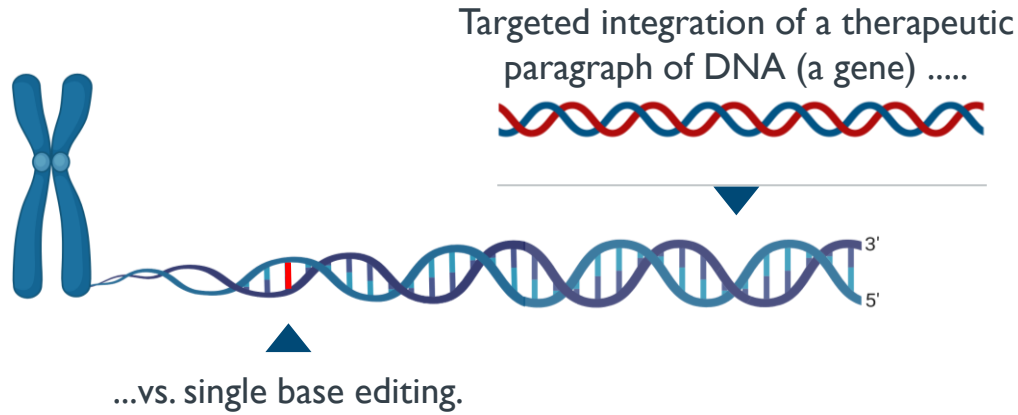
	ZFR design, screening	In vitro validation	Rodent TE, safety	Rodent efficacy	NHP dose, TE, safety	NHP GLP/TOX	IND
Activity, Status							
Models	Human cell line Mouse cell line	Human iPSC neurons Mouse neurons	Wildtype mice	SNI pain model - 4 weeks post dosing	1-month Cynomolgus NHP	3- and 6- month Cynomolgus NHP	
Endpoints	Nav1.7 mRNA Transcriptomics	• Nav1.7, ZFR, and other Nav channel mRNA • Transcriptomics • Nav1.7 function	• Nav1.7 mRNA Transcriptomics • Tolerability	• Mechanical and cold induced pain • Nav1.7, ZFR mRNA • Single-cell ISH/IHC • Safety and behavior	• Nav1.7, ZFR and other Nav mRNA • Single-cell ISH/IHC • Biodistribution • Immunogenicity • Safety/pathology	• Nav1.7, ZFR mRNA • Biodistribution • Toxicokinetics • Immunogenicity • Safety/pathology	

Advancing Next-Generation Genome Engineering

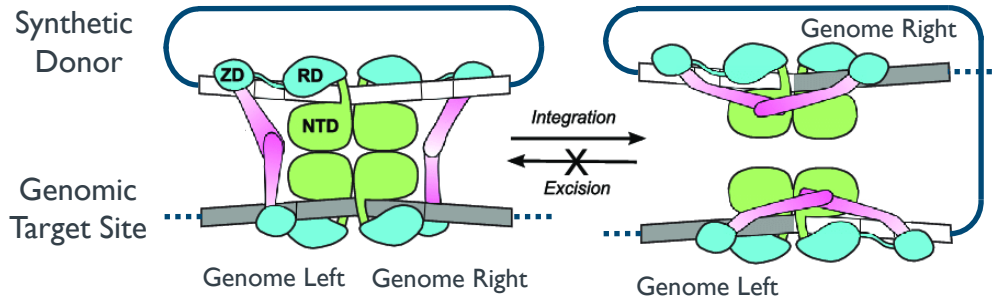
What is an integrase and why is it important?

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



Bxb1 Integration Mechanism



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

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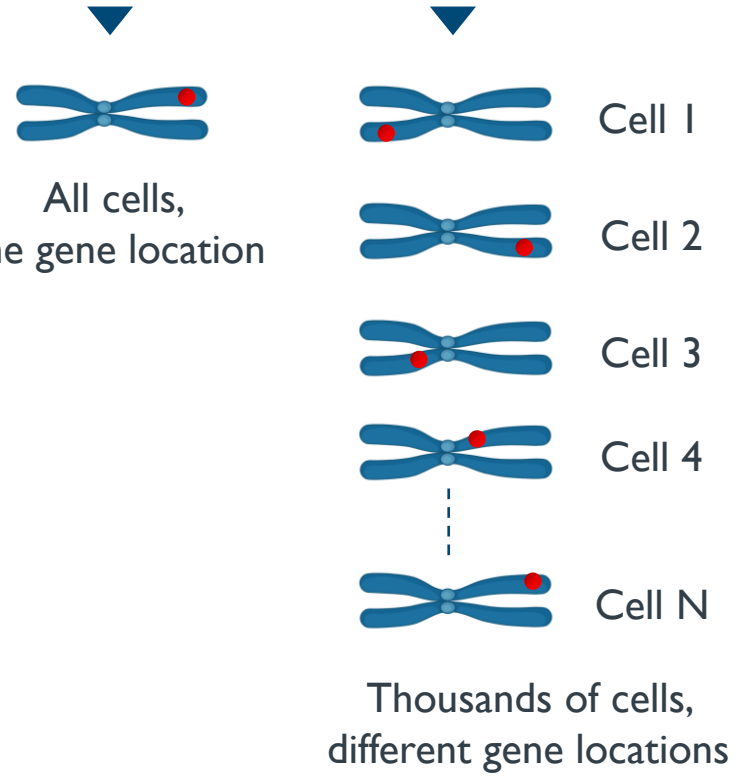
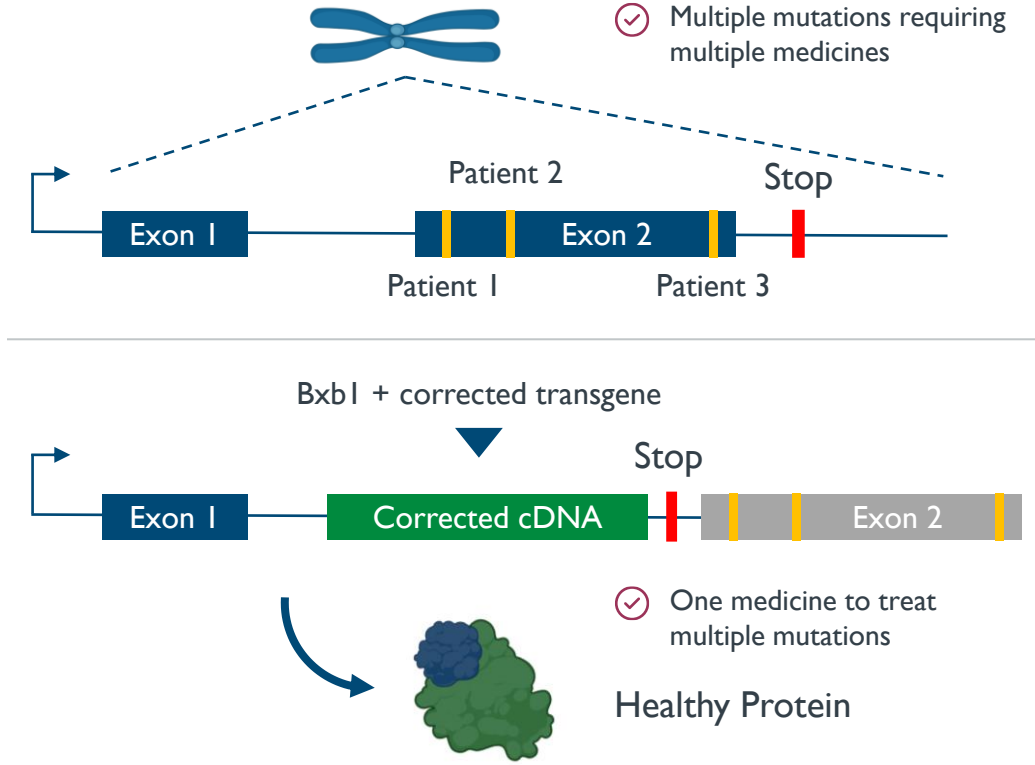
Targeted integration improves existing therapies, and enables new therapies

Targeted vs. Random Integration



One medicine vs. multiple variants for each mutation

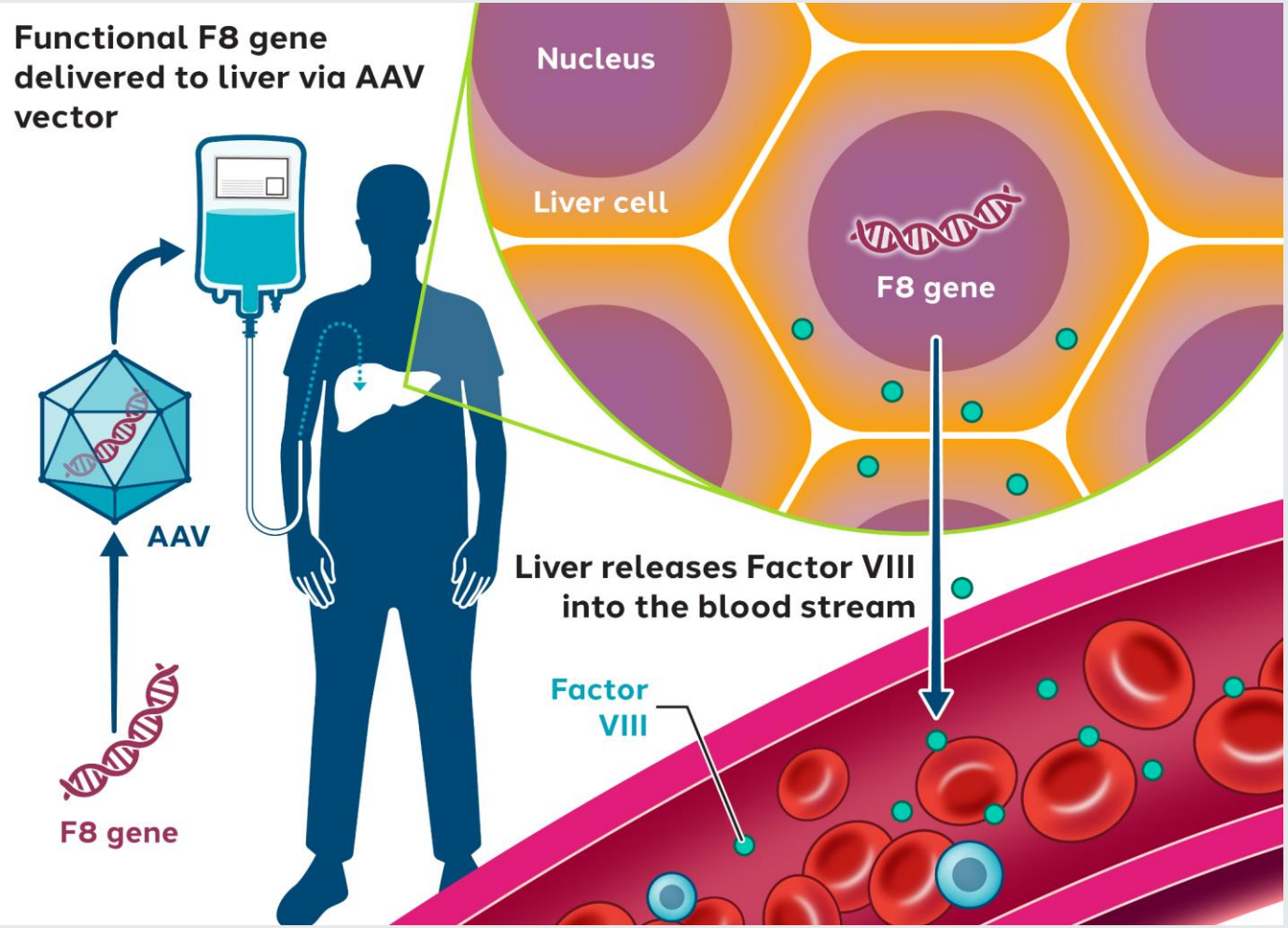


Images by Biorender

Optimizing Value of Clinical Programs

Hemophilia A: giroctocogene fitelparvovec (Pfizer)

Highly compelling readout for Phase 3 AFFINE trial

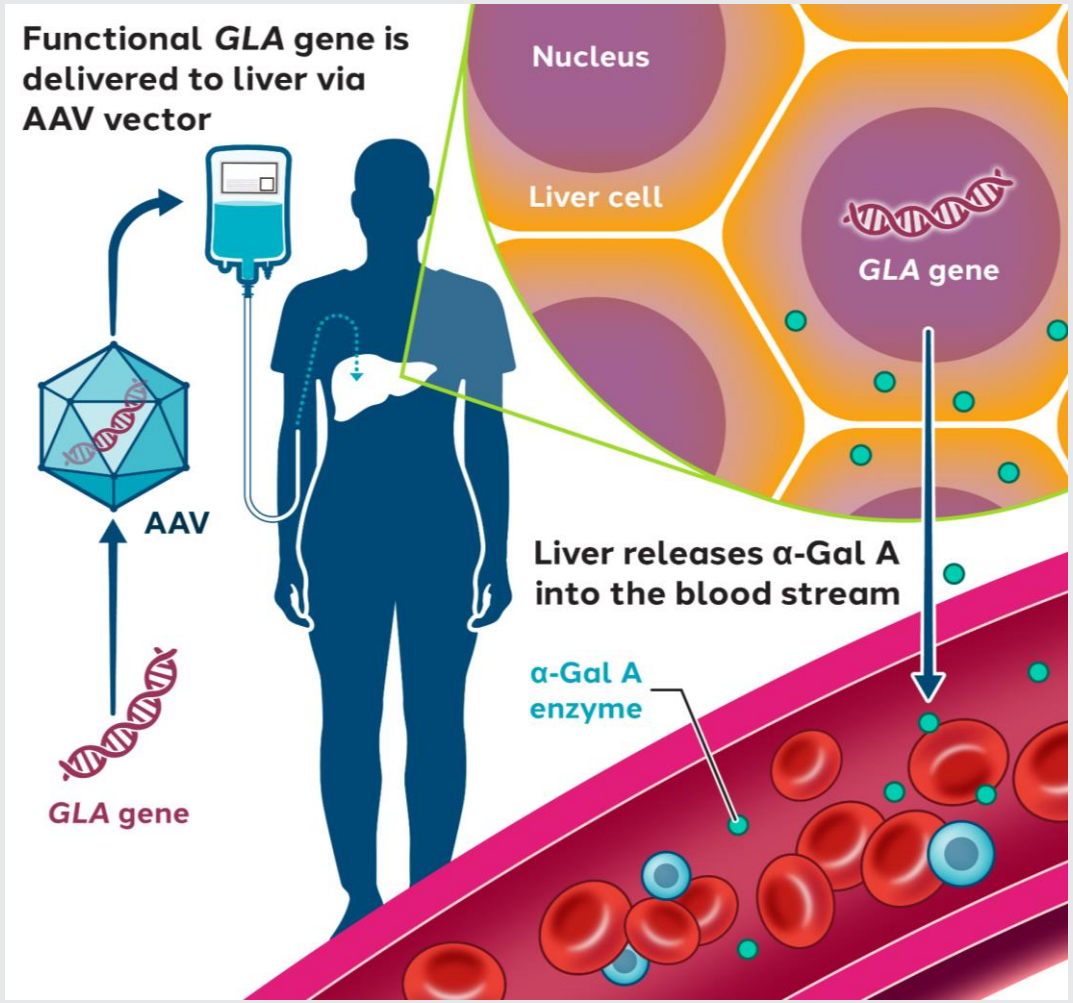


- Program transitioned to Pfizer for Phase 3 development.
- Positive topline results from the Phase 3 AFFINE trial in July 2024, which met primary and key secondary endpoints.
- Pfizer plans to discuss these data with regulatory authorities in the coming months.
- Potential to generate up to **$220 million in remaining milestone** payments* upon the achievement of certain regulatory and commercial milestones and 14-20% royalties on potential sales from this program, if approved and commercialized**

*beginning in 2025. **subject to customary reductions

Fabry Disease: isaralgagene civaparvovec (ST-920)

Abbreviated clinical pathway supports efforts to secure a collaboration partner



- Largest gene therapy program in Fabry disease
  - Enrollment, screening and dosing complete in Phase 1/2 STAAR study – 33 patients total
  - 17 of 18 patients off Enzyme Replacement Therapy (ERT)*
- Compelling clinical data
  - Continue to amass encouraging clinical data, including evidence of improvements in kidney function.
  - In18 patients treated >1yr, observed a statistically significant rise in both mean and median eGFR levels.
  - Updated clinical data expected in the coming months.
- FDA alignment on abbreviated regulatory pathway
  - Aligned on a single-arm study with up to 25 patients, alongside confirmatory evidence, as an acceptable pathway to BLA
- Held productive meeting with EMA on regulatory pathway
- Received EMA PRIME eligibility and UK MHRA ILAP status

*As at August 6, 2024

Fabry Disease: isaralgagene civaparvovec (ST-920)
Summary of updated Phase 1/2 STAAR study data, as presented at WORLD*Symposium* 2024

- ST-920 gene therapy was well-tolerated with an excellent safety profile in this population of adults with symptomatic Fabry disease:
  - No prophylactic steroids/other immunomodulatory agents administered
  - No LFT elevations requiring steroids
- Durable efficacy was demonstrated, with supraphysiological levels of α-Gal A activity maintained for up to 36.2 months
  - Largest plasma lyso-Gb3 reductions seen in naïve/pseudo-naive subjects with highest baseline values
- Compared to baseline, the 13 subjects with ≥12 months of follow-up showed:
  - Renal function remained stable
  - Significant improvement in FOS-MSSI disease severity score, with 38% of subjects on ERT improving in disease severity category
  - Significant improvement in SF-36 QoL and GSRS GI symptom scores
- All 12 subjects who discontinued ERT have remained off ERT for up to 19 months, as of the data cut-off
  - 11/12 have maintained sustained supraphysiological α-Gal A activity (1 with sustained α-Gal A activity in normal physiologic range)
  - 75% (6/8) had an improved disease severity score at 12 months compared to their baseline severity score on ERT
- Total or neutralizing α-Gal A antibodies decreased markedly in 7 subjects and became undetectable in 5 (71%)
- ***ST-920 has potential as a one-time, durable treatment option for Fabry disease that can improve patient outcomes***

Clinical data from WORLD, February 2024

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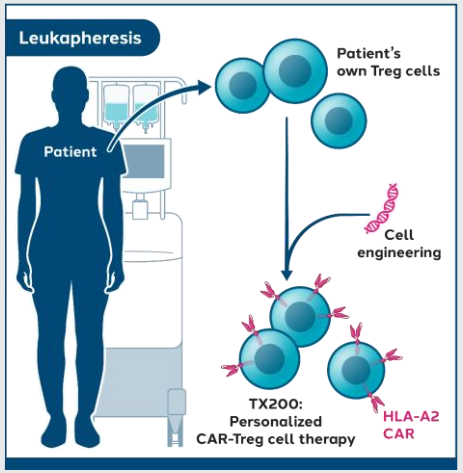
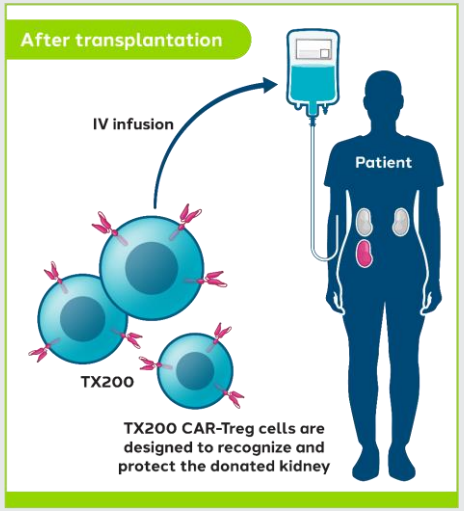
CAR-Treg cell therapy

Seeking collaboration partner or direct investment





- Dosing complete in Phase 1/2 STEADFAST study of TX200 for the prevention of immune mediated rejection in HLA A2 mismatched kidney transplantation, with eight patients dosed in total
- The product candidate continues to be generally well tolerated in all patients dosed*
- Continue seeking a potential collaboration partner or external investment in the autologous CAR-Treg cell therapy programs

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*As at August 6, 2024

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

Sangamo THERAPEUTICS

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

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

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

SHARP STRATEGIC FOCUS IN NEUROLOGY

Successful partnership track record with $50 million in expected near-term payments from Genentech and $220 million in potential milestone payments* from Pfizer. **Fabry partner discussions ongoing, with clear pathway to potential registration.**

OPTIMIZING ASSET VALUE

Sangamo THERAPEUTICS

**beginning in 2025, upon the achievement of certain regulatory and commercial milestones. Subject to customary reductions.*