

CNS Gene Regulation Platform

2018



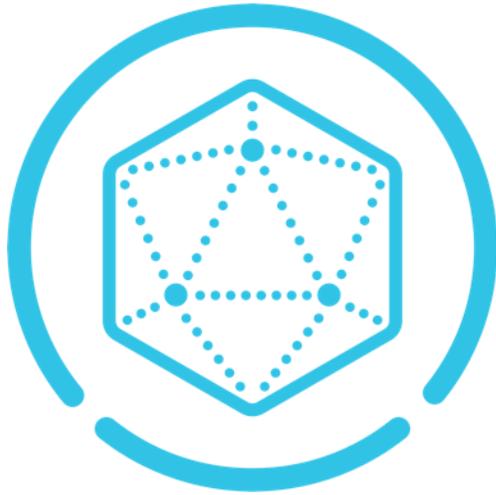
Forward Looking Statements

This presentation contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, as amended. These forward-looking statements include, but are not limited to, financial guidance for full year 2017 as it relates to revenues, operating expenses, and year end cash balances; the design of clinical trials and expected timing for release of data; the anticipated clinical development milestones and other potential value drivers in the future; the expected benefits of the collaboration with Pfizer, the expanded capability of Sangamo's technologies; the benefits of rebranding and reorganization, the research and development of novel gene-based therapies and the application Sangamo's ZFP technology platform to specific human diseases; corporate partnerships; and the potential of Sangamo's genome editing technology to treat genetic diseases. These statements are based upon our current expectations and speak only as of the date hereof. Our actual results may differ materially and adversely from those expressed in any forward-looking statements as a result of various factors and uncertainties. Factors that could cause actual results to differ include, but are not limited to, the dependence on the success of clinical trials of lead programs, the lengthy and uncertain regulatory approval process, uncertainties related to the timing of initiation and completion of clinical trials, whether clinical trial results will validate and support the safety and efficacy of Sangamo's therapeutics, the ability to establish strategic partnerships and our ability to control expenses and achieve our milestones that generate revenues under our agreements. Further, there can be no assurance that the necessary regulatory approvals will be obtained or that Sangamo and its partners will be able to develop commercially viable gene-based therapeutics. Actual results may differ from those projected in forward-looking statements due to risks and uncertainties that exist in Sangamo's operations and business environments. These risks and uncertainties are described more fully in Sangamo's Annual Reports on Form 10-K and Quarterly Reports on Form 10-Q as filed with the Securities and Exchange Commission. Forward-looking statements contained in this presentation are made as of the date hereof, and Sangamo undertakes no duty to update such information except as required under applicable law.



We are committed to translating ground-breaking science into genomic therapies that transform patients' lives

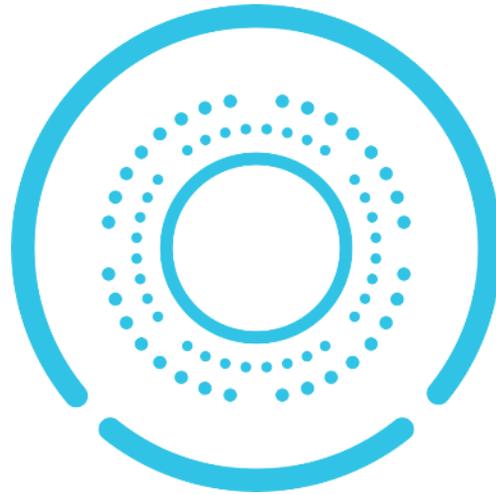
Sangamo is investing across four technological platforms for genomic medicines



Gene Therapy



Genome Editing

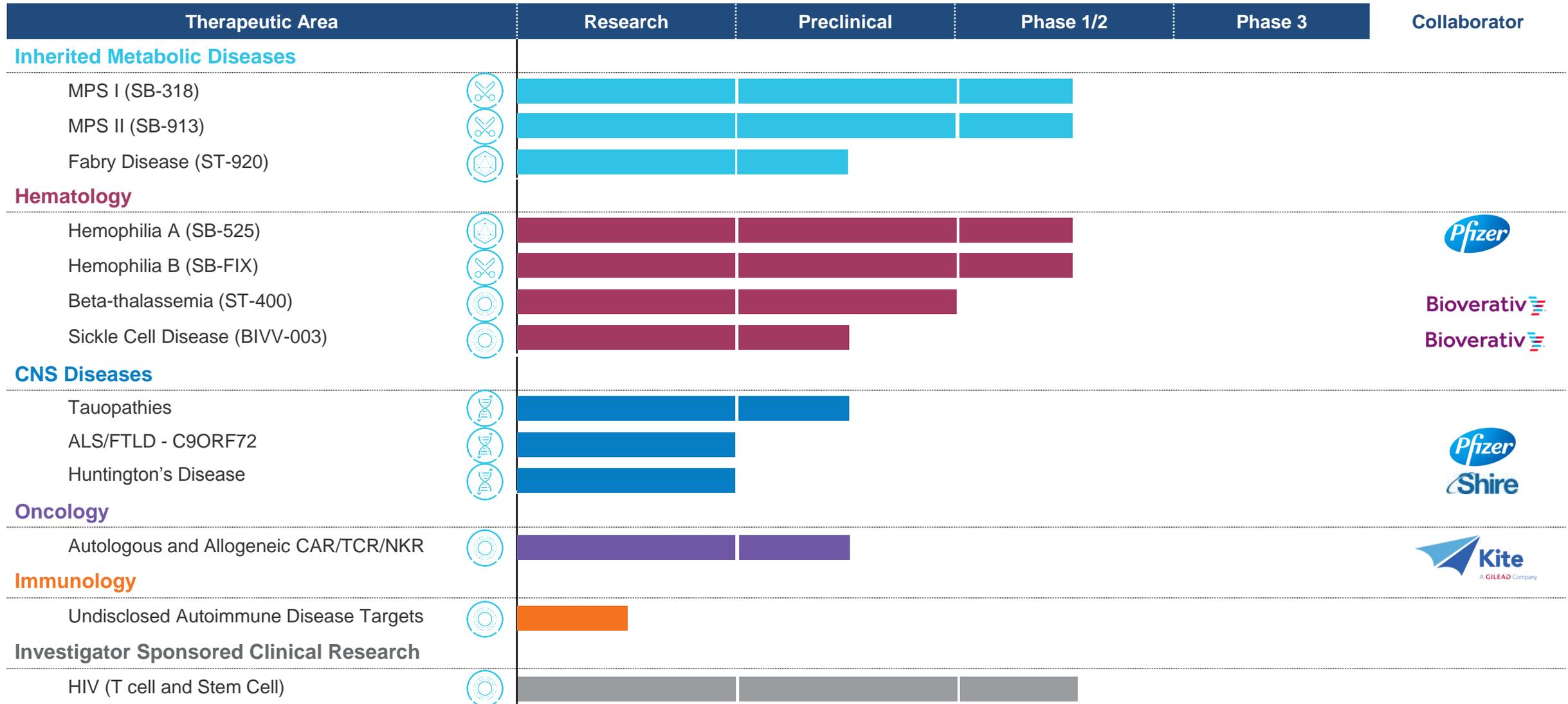


Cell Therapy

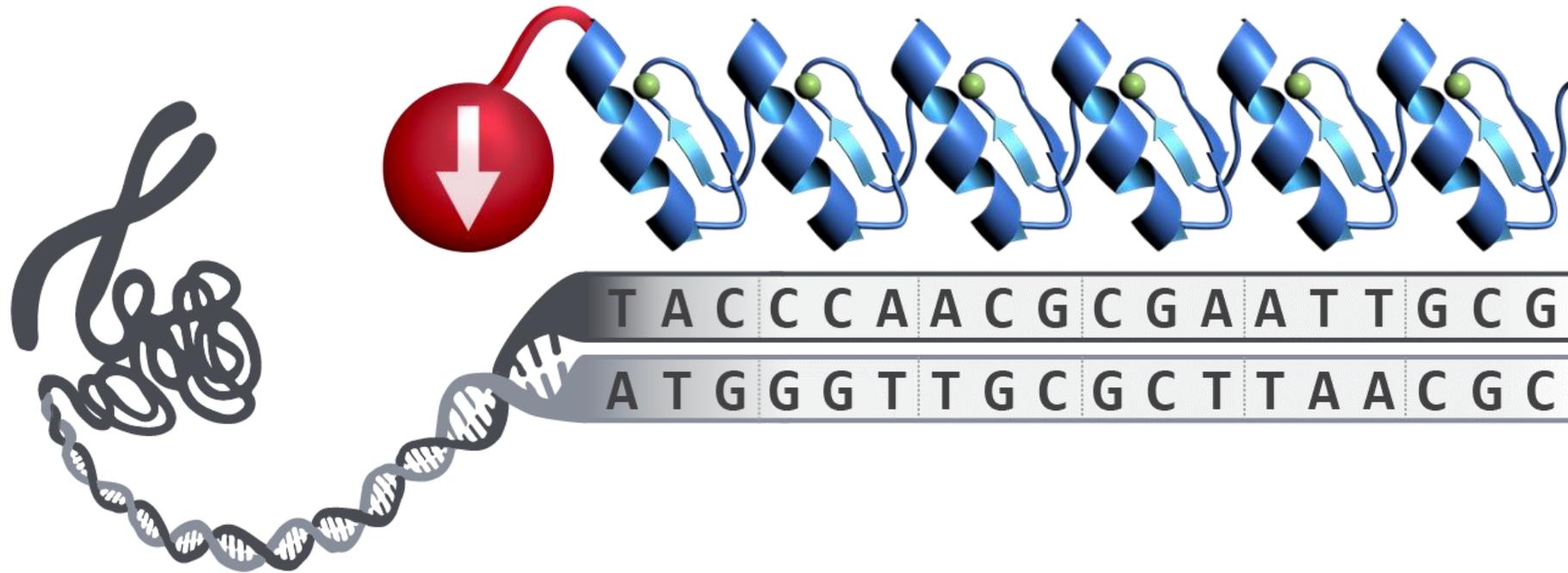


Gene Regulation

Product portfolio diversified across therapeutic area and technology

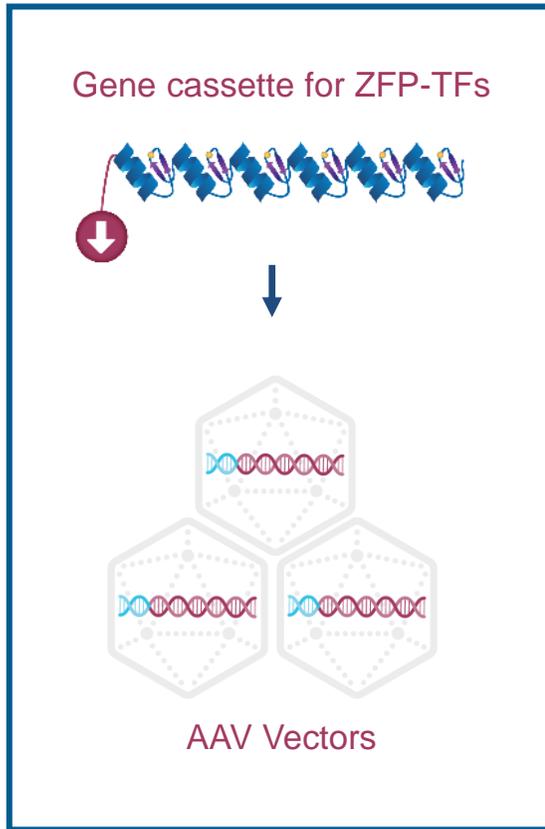


ZFP-Transcriptions Factors can be engineered to regulate any gene

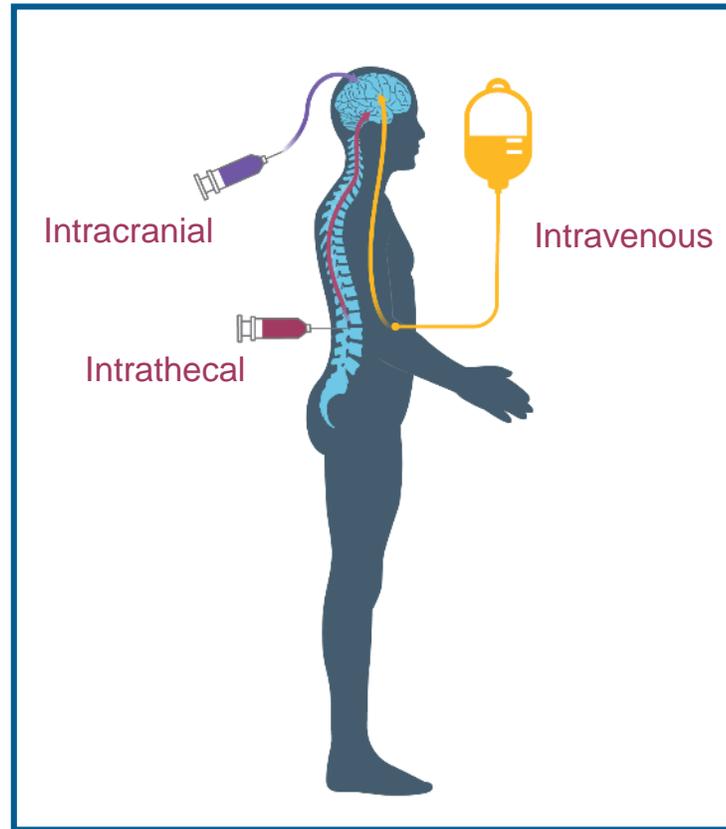


Sangamo's ZFP-TF platform: precise and specific gene regulation to treat CNS diseases

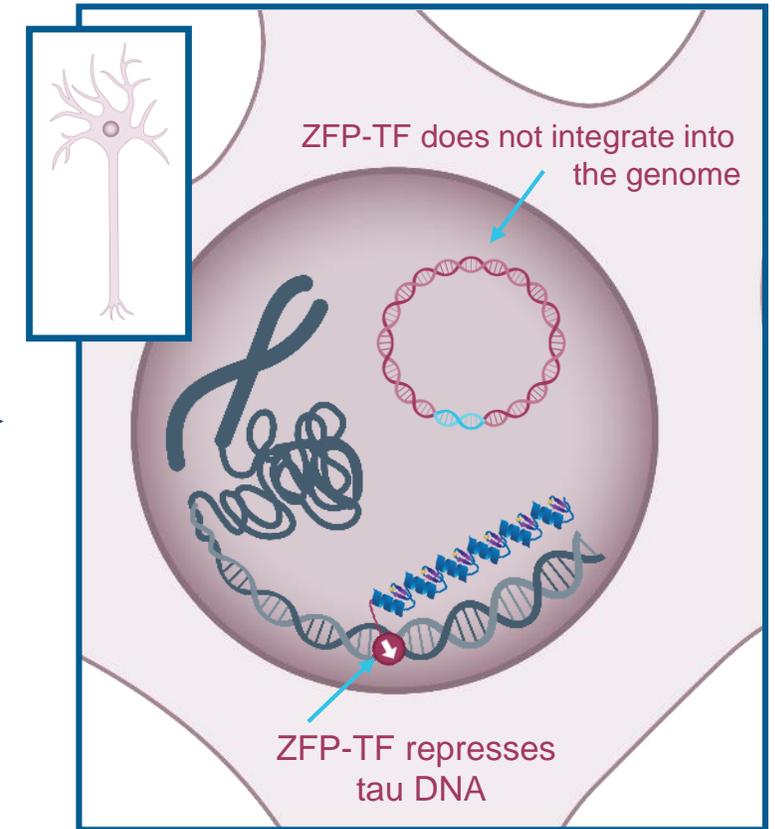
Packaging into AAV vectors



Potential Routes of Administration



In Neurons

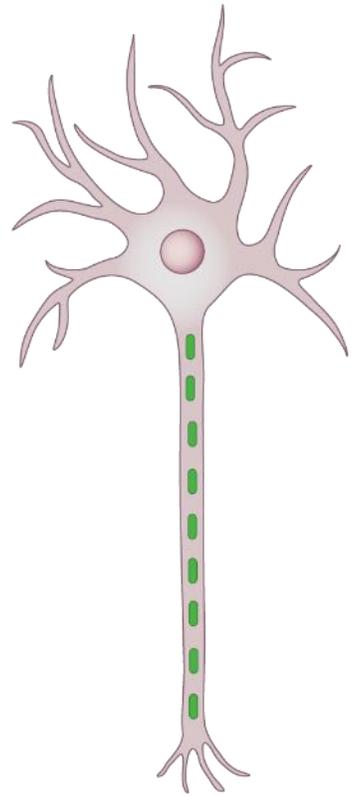




CNS diseases

- Tauopathies and Alzheimer's disease
- C9ORF72-linked ALS and FTLD

Neuronal loss in tauopathies can be blocked by reducing tau expression



Healthy neuron
Axonal tau

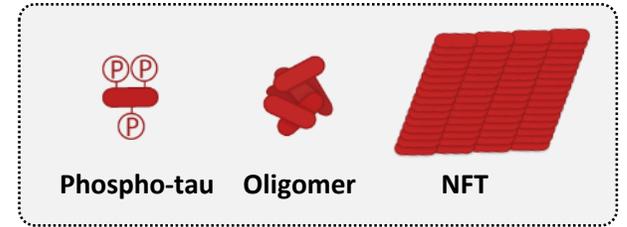
Disease →
Alzheimer's Disease
Frontal Temporal Dementia
Progressive Supranuclear Palsy
Corticobasal Degeneration
Chronic Traumatic Encephalopathy

→
Preventative T
tau KO or tau Het (mice)
H2 haplotype (human)

←
Reversal
Turn off mutant tau (mice)
ASOs (mice)



Diseased neuron
Pathological, mislocalized tau
Aggregates and tangles



Multiple tau species
Pathogenic form(s) unclear

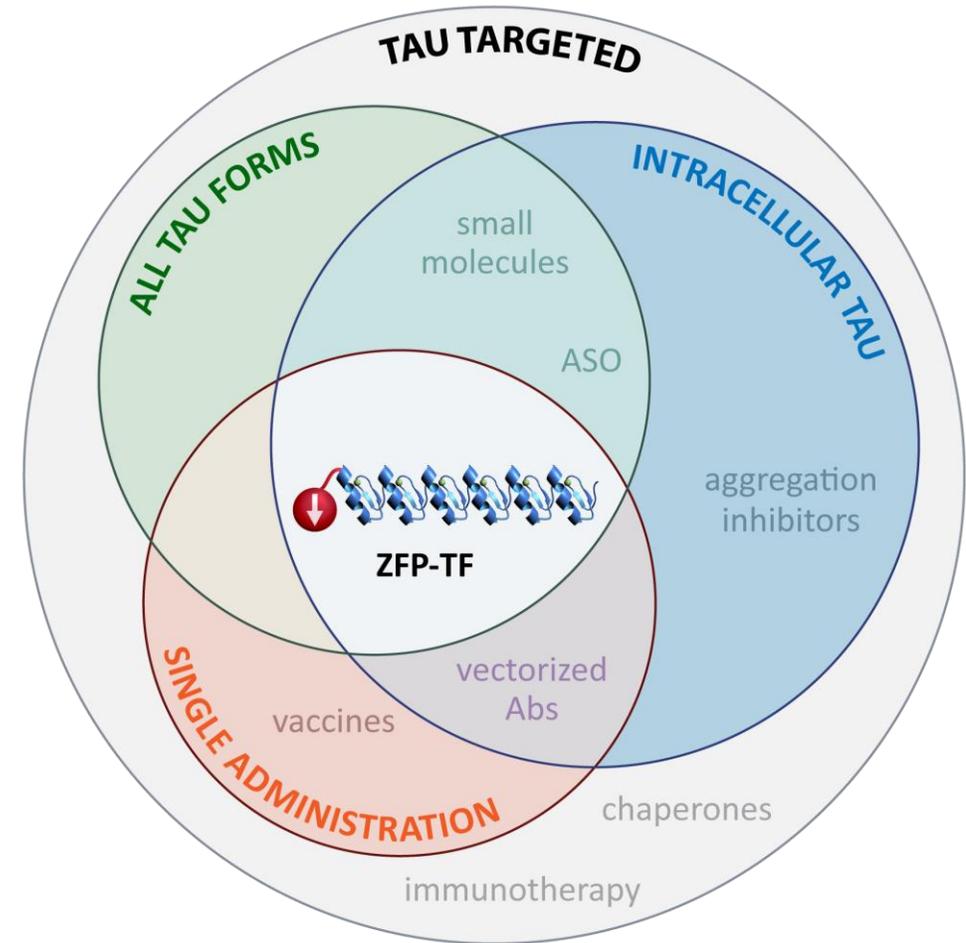


Dying neuron
Consumed by NFTs
Atrophied

Sangamo's ZFP-TFs: A differentiated platform for tau targeting

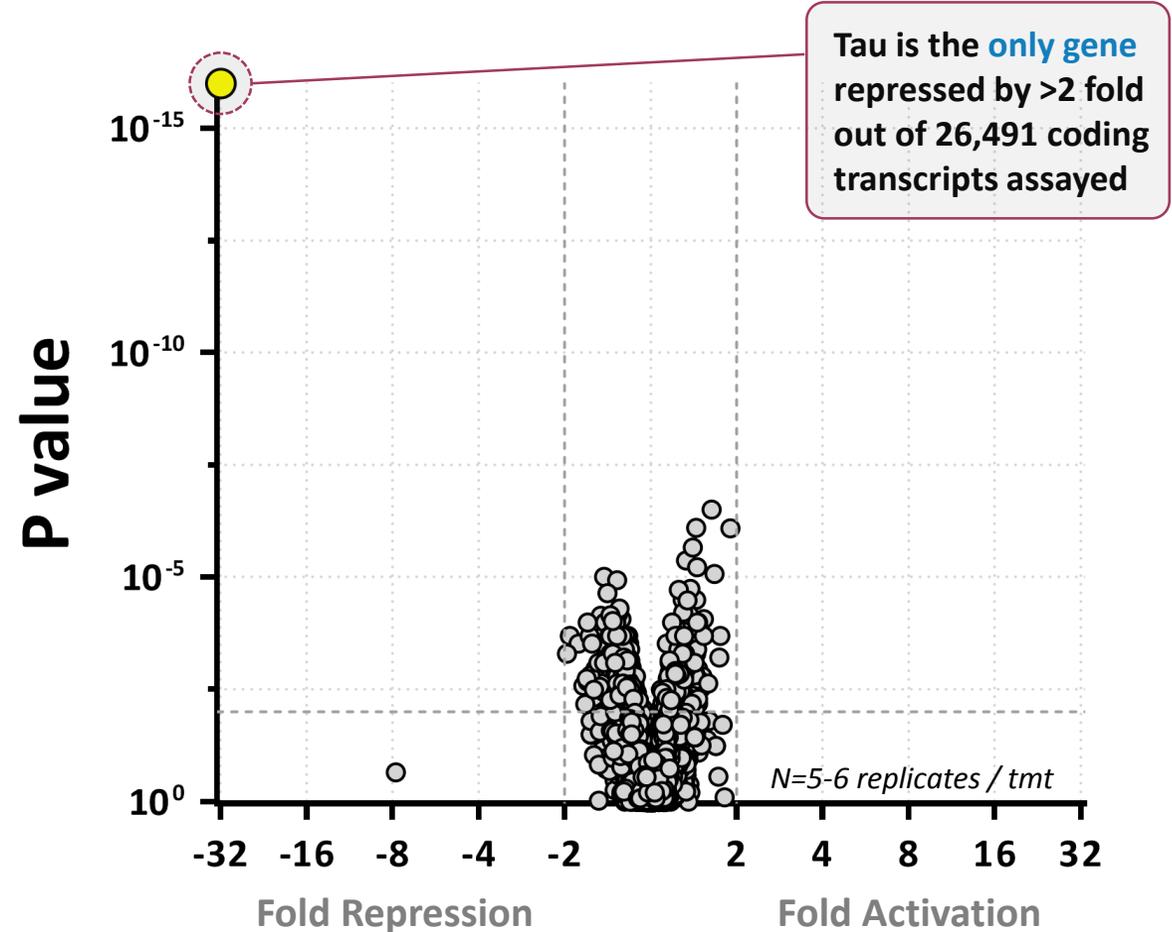
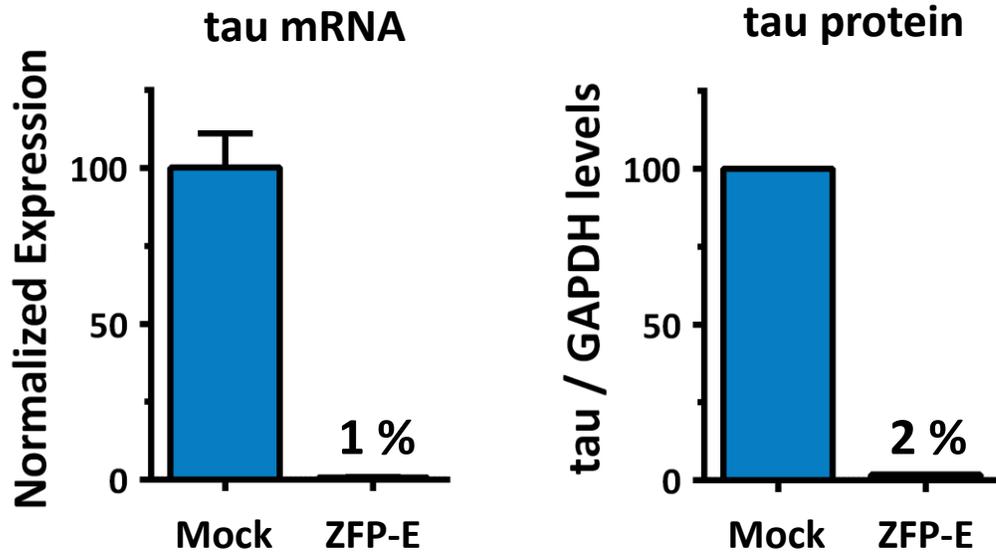
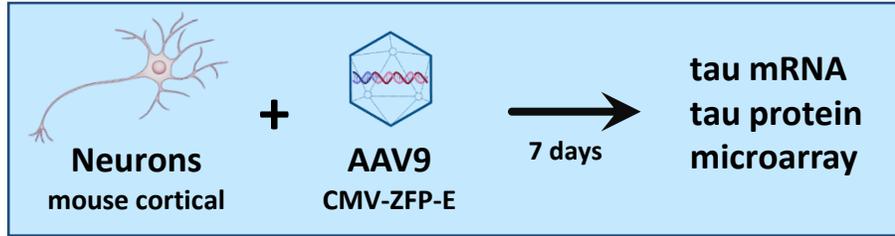
"Of the many approaches to reduce tau expression that we've studied, zinc finger protein gene regulation technology is especially promising for its exquisite specificity, its potent reduction of tau protein expression, and its potential to provide a durable, long-lasting effect with only a single administration."

Bradley Hyman, M.D., Ph.D.
Director, Massachusetts Alzheimer's Disease Research Center
Alzheimer's Unit Director, MassGeneral Institute for Neurodegenerative Disease
Professor of Neurology, Harvard Medical School.



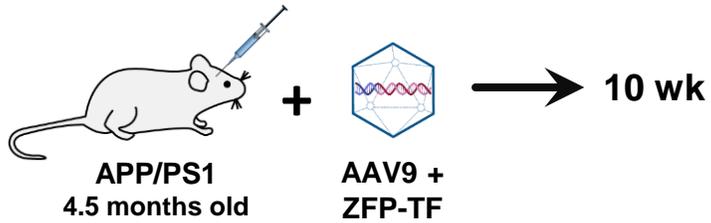
Potential to block **all forms** of **intracellular tau** with a **single administration**

Potent single-gene specific repression of tau in primary neurons



~100-fold reduction in tau levels with no detectable off-targets

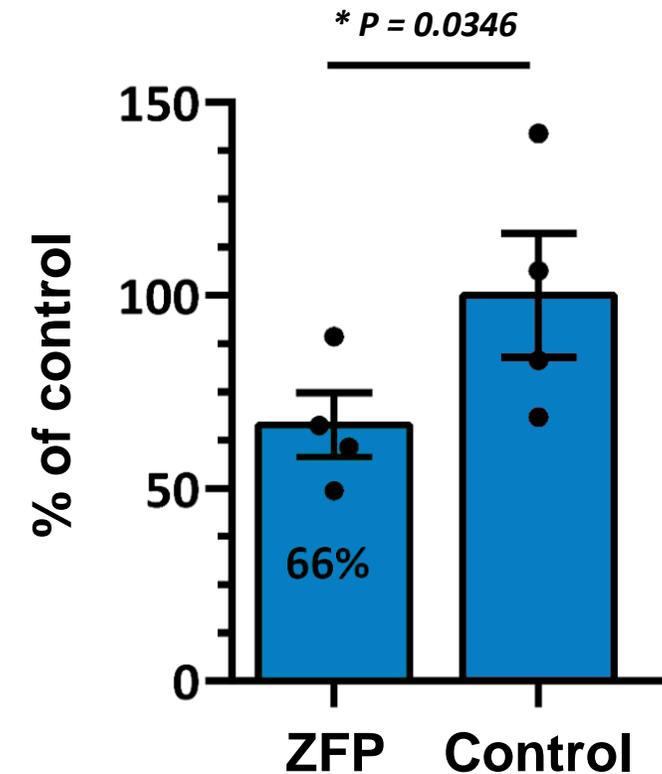
ZFP treatment reduces amyloid-induced dystrophic neurites in mice with established disease



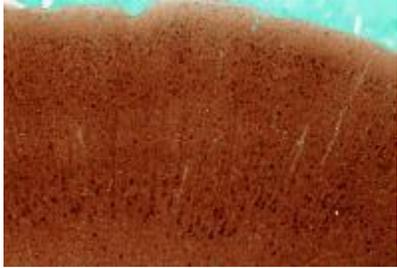
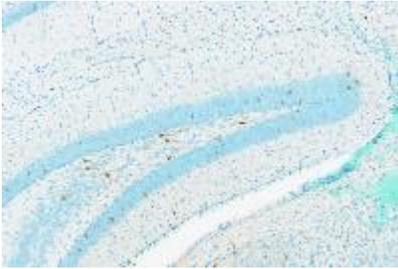
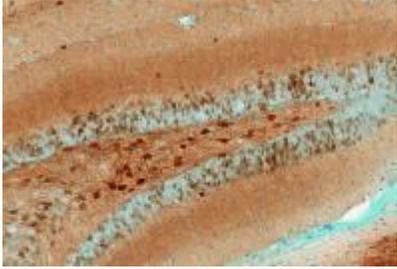
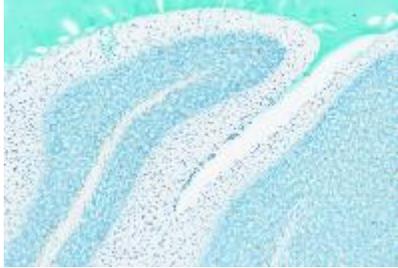
ZFP-treated mice have a **34% reduction** in neuritic dystrophies / amyloid plaque

First demonstration of a tau lowering agent showing efficacy on neuritic dystrophies

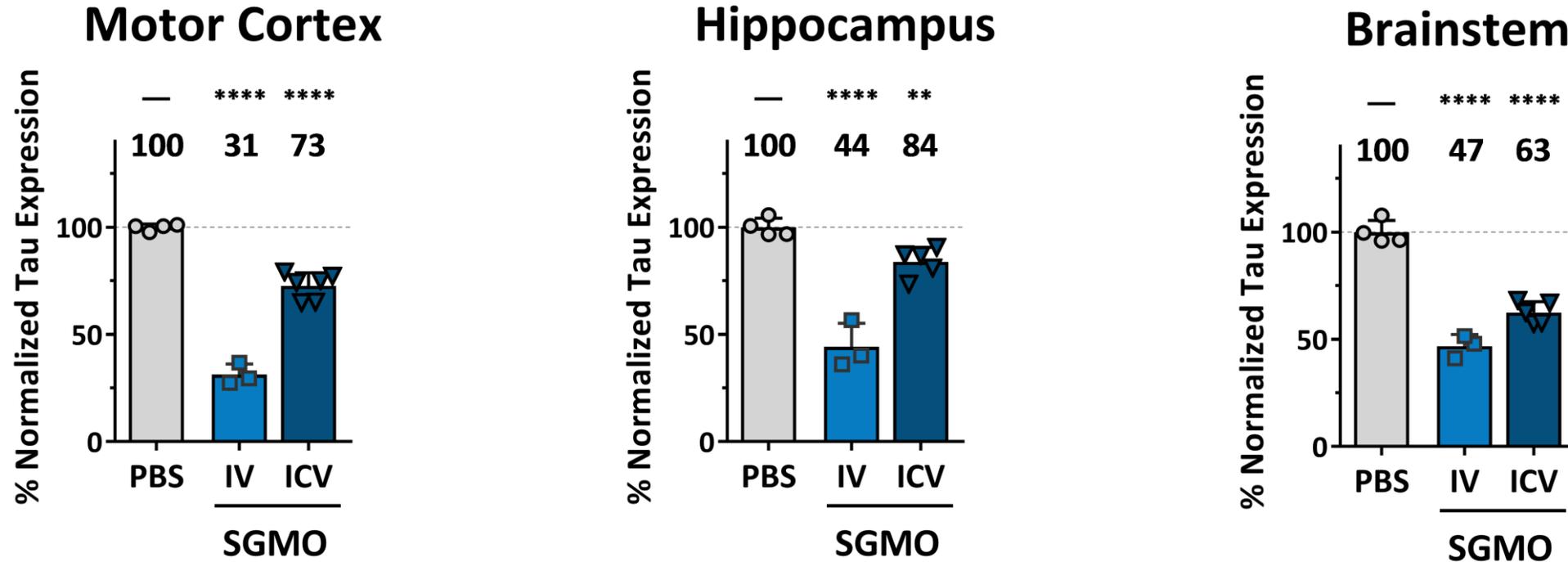
Dystrophies per amyloid plaque



AAV.SGMO delivery via IV or ICV administration results in greater neuronal transduction efficiency compared to AAV9

Route of Admin.	ICV	IV	ICV	IV
Motor Cortex				
Hippocampus				
Cerebellum				
	 AAV9		 AAV.SGMO	

AAV.SGMO ZFP-TF: potent tau reduction via IV / ICV administration



Up to ~50-70% tau reduction in targeted brain regions for tauopathies



CNS diseases

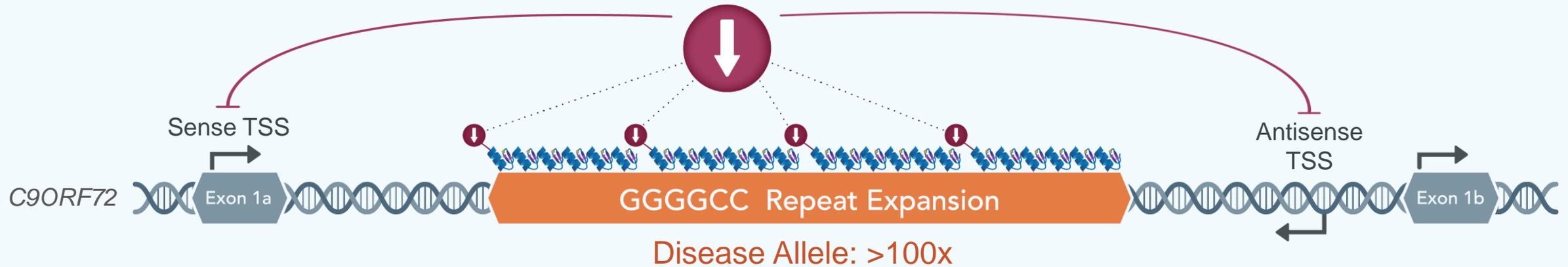
- Tauopathies and Alzheimer's disease
- C9ORF72-linked ALS and FTLD

Allele specific repression of C9ORF72 with ZFP-TFs exemplifies Sangamo's differentiated therapeutic approach to CNS diseases

Expansion of Six Base Pair Repeat Causes Neuronal Degeneration



Cooperative Inhibition by ZFP-TFs Represses Mutant C9 Transcripts



Thank you.

