Sangamo THERAPEUTICS

Corporate Presentation

January 2020

Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the "safe harbor" provisions of United States securities law. These forward-looking statements include, but are not limited to, the therapeutic potential of Sangamo's product candidates; the design of clinical trials and expected timing for milestones, such as enrollment and presentation of data, the expected timing of release of additional data, plans to initiate additional studies for product candidates and timing and design of these studies; the expected benefits of Sangamo's collaborations; the anticipated capabilities of Sangamo's technologies; the research and development of novel gene-based therapies and the application of Sangamo's ZFP technology platform to specific human diseases; successful manufacturing of Sangamo's product candidates; the potential of Sangamo's genome editing technology to safely treat genetic diseases; the potential for ZFNs to be effectively designed to treat diseases through genome editing; the potential for cell therapies to effectively treat diseases; and other statements that are not historical fact. These statements are based upon Sangamo's current expectations and speak only as of the date hereof. Sangamo's actual results may differ materially and adversely from those expressed in any forward-looking statements. Factors that could cause actual results to differ include, but are not limited to, risks and uncertainties related to dependence on the success of clinical trials; the uncertain regulatory approval process; the costly and research and development process, including the uncertain timing of clinical trials; whether interim, preliminary or initial data from ongoing clinical trials will be representative of the final results from such clinical trials; whether the final results from ongoing clinical trials will validate and support the safety and efficacy of product candidates; the risk that clinical trial data are subject to differing interpretations by regulatory authorities; Sangamo's limited experience in conducting later stage clinical trials and the potential inability of Sangamo and its partners to advance product candidates into registrational studies; Sangamo's reliance on itself, partners and other third-parties to meet clinical and manufacturing obligations; Sangamo's ability to maintain strategic partnerships; competing drugs and product candidates that may be superior to Sangamo's product candidates; and the potential for technological developments by Sangamo's competitors that will obviate Sangamo's gene therapy technology. Actual results may differ from those projected in forward -looking statements due to risks and uncertainties that exist in Sangamo's operations. This presentation concerns investigational drugs 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 effectiveness 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. These risks and uncertainties are described more fully in Sangamo's Annual Report on Form 10-K for the year ended December 31, 2018 as filed with the Securities and Exchange Commission on March 1, 2019 and Sangamo's Quarterly Report on Form 10-Q for the quarter ended September 30, 2019 that it filed on or about November 6, 2019. Except as required by law, we assume no obligation, and we disclaim any intent, to update these statements to reflect actual results.

Sangamo THERAPEUTICS

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

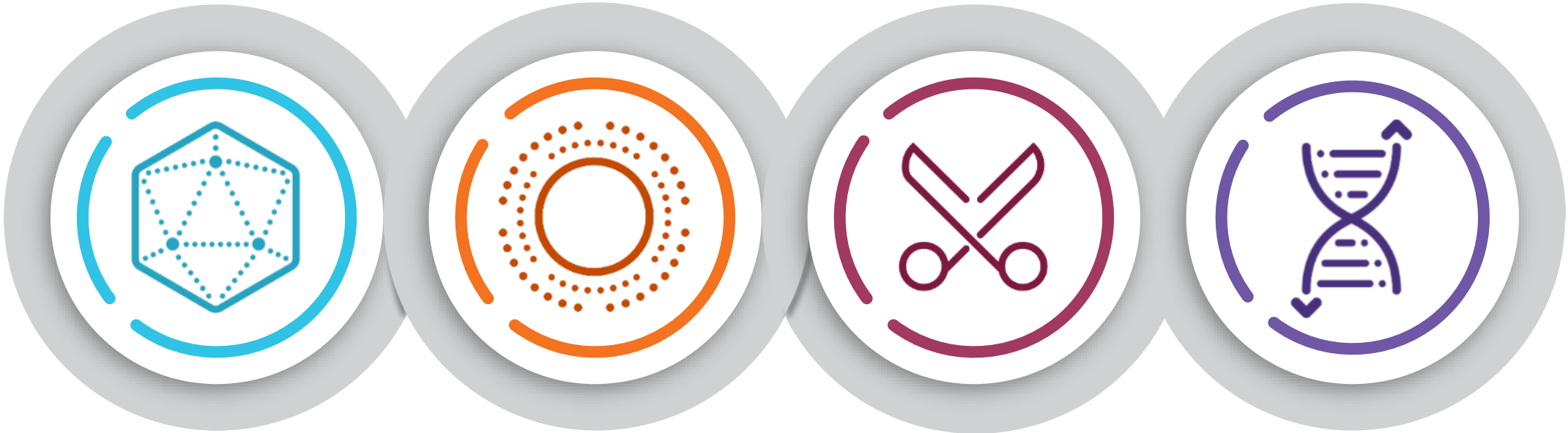
Our proprietary suite of genomic medicine technologies

Gene Therapy
AAV

Gene-Edited Cell Therapy
ZFN; AAV; LV

Genome Editing
AAV; ZFN

Genome Regulation
AAV; ZFP-TF



Gene therapy provides tractable, valuable near-term opportunities

Continue to advance *ex vivo* editing to create cell therapies

Sustain momentum toward the long-term goal with *in vivo* genome editing and genome regulation

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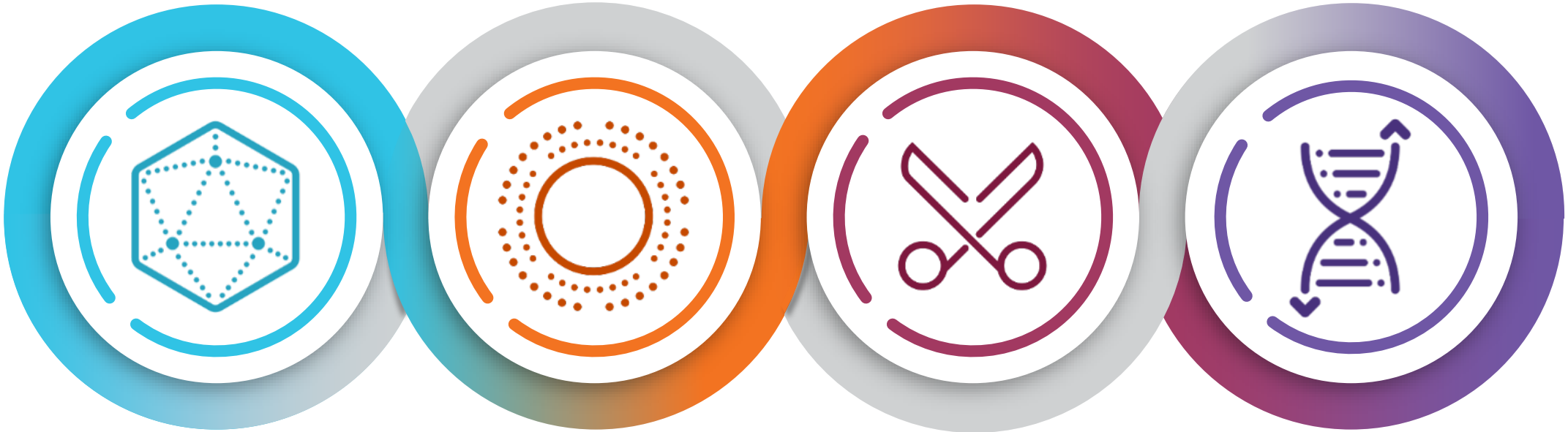
Our capabilities allow us to design therapeutic approaches targeting the underlying genetic causes of disease



Gene Therapy
AAV

SB-525: Hemophilia A
ST-920: Fabry disease
ST-101: PKU

Gene-Edited Cell Therapy
ZFN; AAV; LV

ST-400: Beta thalassemia
BIVV003: Sickle cell disease
TX200: Solid organ transplant
KITE-037: Allo-CD19 CAR-T
Undisclosed targets

Genome Editing
AAV; ZFN

SB-913: MPS II

Genome Regulation
AAV; ZFP-TF

ST-501: Tauopathies
ST-502: α-synuclein
C9ORF72-linked ALS/FTLD
Huntington's disease
Prion

Projected pipeline progress in 2020: SB-525 to Phase 3, TX200 and KITE-037 to Phase 1/2

Preclinical

- PKU (ST-101) — SANGAMO WHOLLY OWNED
- IBD — SANGAMO WHOLLY OWNED
- MS — SANGAMO WHOLLY OWNED
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- α-Synuclein (ST-502) — SANGAMO WHOLLY OWNED
- ALS/FTD — PARTNER Pfizer
- Huntington's Disease (TAK-686) — PARTNER Takeda
- Prion — SANGAMO WHOLLY OWNED
- Tauopathies (ST-501) — SANGAMO WHOLLY OWNED

Phase 1/2

- Fabry Disease (ST-920) — SANGAMO WHOLLY OWNED
- Beta Thalassemia (ST-400) — PARTNER SANOFI
- Oncology (KITE-037) — PARTNER Kite
- Sickle Cell Disease (BIVV003) — PARTNER SANOFI
- Solid Organ Transplant (TX200) — SANGAMO WHOLLY OWNED
- MPS II (SB-913) — SANGAMO WHOLLY OWNED

Phase 3

- Hemophilia A (SB-525) — PARTNER Pfizer

(Pfizer initiated Ph3 lead-in study Oct. '19)

Gene Therapy | *Ex Vivo* Gene-Edited Cell Therapy | *In Vivo* Genome Editing | *In Vivo* Genome Regulation

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Gene therapy in 2020: Building on recent success in hemophilia A

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(Pfizer initiated Ph3 lead-in study Oct. '19)

Gene Therapy | *Ex Vivo* Gene-Edited Cell Therapy | *In Vivo* Genome Editing | *In Vivo* Genome Regulation

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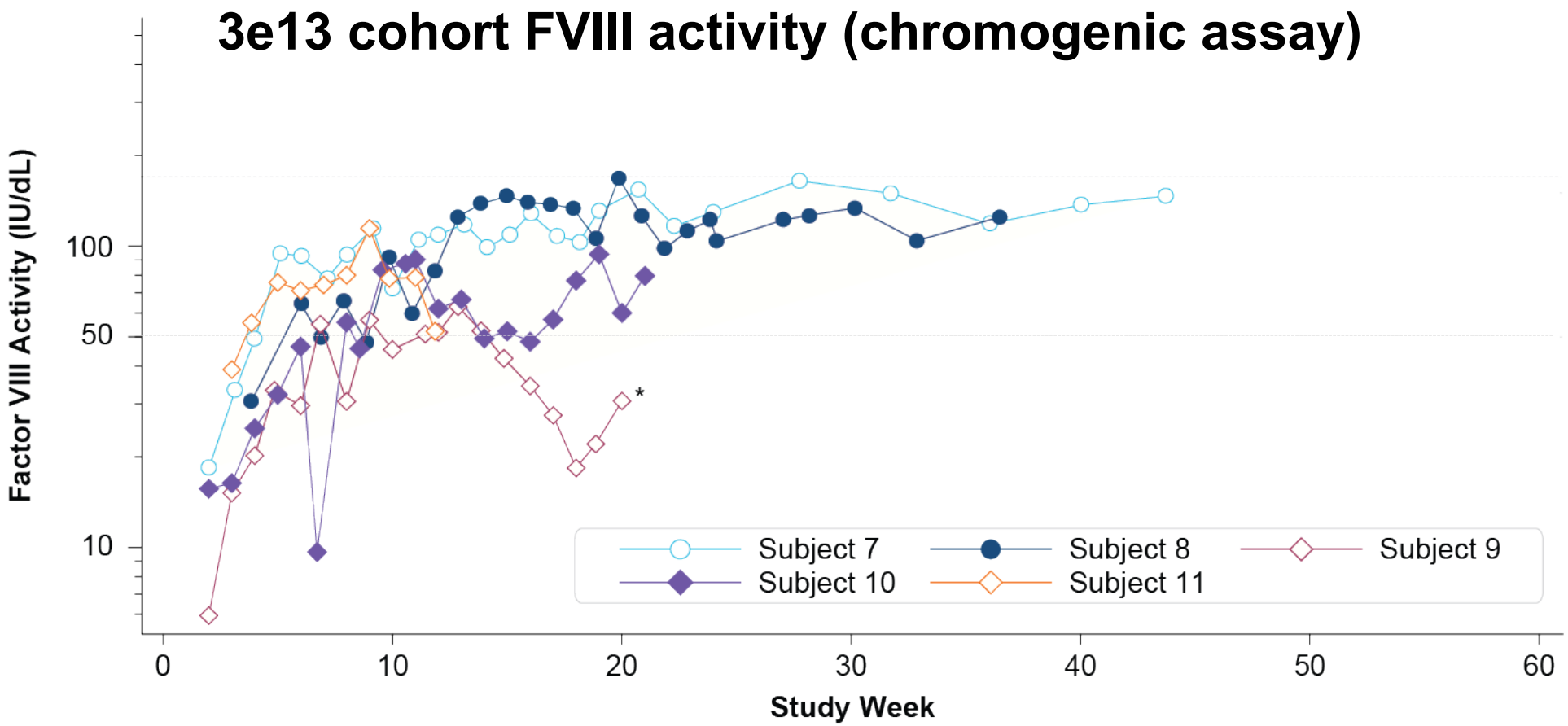
Presented at the 2019 American Society of Hematology Annual Meeting; Orlando, Florida; December 7, 2019

Updated Follow-up of the Alta Study, a Phase 1/2, Open Label, Adaptive, Dose-Ranging Study to Assess the Safety and Tolerability of SB-525 Gene Therapy in Adult Subjects With Hemophilia A

Barbara A. Konkle,[1] Kimo Stine,[2] Nathan Visweshwar,[3] Thomas Harrington,[4] Andrew D. Leavitt,[5] Adam Giermasz,[6] Steven Arkin,[7] Gregory Di Russo,[7] Ashley Snyder,[8] Adrian Woolfson,[8] and Didier Rouy[8]

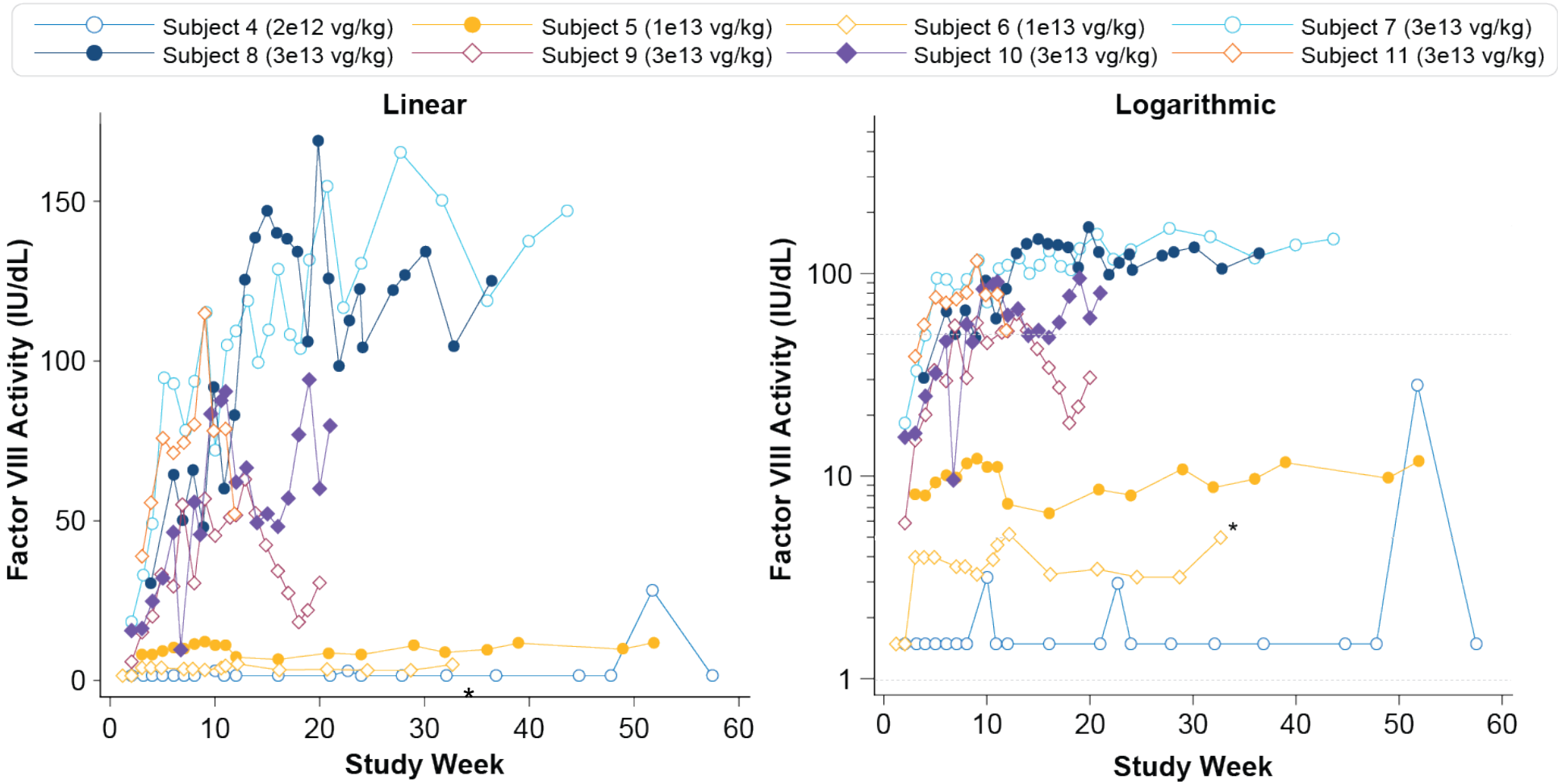
[1]Bloodworks Northwest and the University of Washington, Seattle, WA; [2]Arkansas Children's Hospital, Little Rock, AR; [3]Department of Internal Medicine, Division of Hematology and Medical Oncology, University of South Florida, Tampa, FL; [4]University of Miami Miller School of Medicine, Miami, FL; [5]Department of Laboratory Medicine and Department of Medicine, University of California, San Francisco, CA; [6]University of California, Davis, CA; [7]Pfizer Inc., Cambridge, MA.; [8]Sangamo Therapeutics, Brisbane, CA

High dose cohort FVIII durability up to 11 months



*von Willebrand factor levels for that subject dropped from 118% at week 1 to 48% at week 16
FVIII values with sample dates prior to treatment and up to 1 week after the treatment date or with sample dates within 3 days after an FVIII infusion are excluded.
Data cutoff date: October 17, 2019.

FVIII activity shows dose response between cohorts



Chromogenic Assay. FVIII values with sample dates prior to treatment and up to 1 week after the treatment date or with sample dates within 3 days after a Factor VIII infusion are excluded.
Data cutoff date: October 17, 2019.
*Subject missed follow-up visits and is no longer in contact with the site.

Zero bleeding events in high dose cohort

Dose Cohort (dose vg/kg)	Subject	Follow-up (weeks)	Bleeding Episodes ≥3 Weeks Post Treatment
9e11	1	112	7
9e11	2	103	5
2e12	3	93	8
2e12	4	86	5
1e13	5	70	10
1e13	6	61	0
3e13	7	44	0
3e13	8	37	0
3e13	9	24	0
3e13	10	22	0
3e13	11	12	0

Bleeding episodes are being counted 21 days post dosing.
Days post dosing = October 17, 2019 - dosing day.

Eliminated FVIII replacement use in high dose cohort

Factor VIII Replacement Usage

Dose Cohort (dose vg/kg)	Subject	Follow-up (weeks)	Factor VIII Prophylactic Regimen Prior to Dosing	Factor VIII Infusions ≥3 Weeks Following SB-525 Treatment
9e11	1	112	2/week	115
9e11	2	103	2/week	26
2e12	3	93	2/week	13
2e12	4	86	3/week	9
1e13	5	70	Every other day	17
1e13	6	61	Every other day	0
3e13	7	44	Every 4 days	0
3e13	8	37	Every other day	1*
3e13	9	24	Every 3 days	0
3e13	10	22	Every 3 days	0
3e13	11	12	2/week	0

*Prophylactic coverage stopped 3 weeks and 2 days after SB-525 administration.
Factor VIII infusions are being counted 21 days post dosing.
Days post dosing = October 17, 2019 - dosing day.

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ALT elevation did not result in loss of FVIII expression

4 out of 5 subjects in the high dose cohort had an ALT elevation

Subject number	Time of first ALT elevation (week)	Maximum ALT value (U/L / grade)	Steroids high dose (weeks)	Steroids taper (weeks)	FVIII levels (Chromo, IU/dl) at start of steroids	FVIII levels (Chromo, IU/dl) at end of taper	Time of second ALT elevation (week)	Weeks of steroids after second elevation
7	4.5	98 (Gr 1)	5	7.5	94.8	108.2	28.5	1.5*
8	12	66 (Gr 1)	2	9	83.1	112.6	N/A	N/A
10	5.5	63 (Gr 1)	5	6	46.4	57.1	20	4#
11	8	192 (Gr 2)	2.5	4.5	80.2	Pending	N/A	N/A

*After the end of the second course of steroids, the FVIII level was 150.4 IU/dL.
#Ongoing.

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Safety Summary: SB-525 was generally well tolerated

Treatment-Related Adverse Event Summary

MedDRA Preferred Term	Cohort 1 9e11 vg/kg (N=2) n (%) [T]	Cohort 2 2e12 vg/kg (N=2) n (%) [T]	Cohort 3 1e13 vg/kg (N=2) n (%) [T]	Cohort 4 3e13 vg/kg (N=5) n (%) [T]	All Subjects (N=11) n (%) [T]
Any treatment-related event	0	2 (100) [4]	0	4 (80.0) [12]	6 (54.5) [16]
Alanine aminotransferase increased	0	2 (100) [3]	0	2 (40.0) [3]	4 (36.4) [6]
Pyrexia	0	0	0	3 (60.0) [3]	3 (27.3) [3]
Aspartate aminotransferase increased	0	1 (50) [1]	0	1 (20.0) [1]	2 (18.2) [2]
Tachycardia	0	0	0	2 (40.0) [2]	2 (18.2) [2]
Fatigue	0	0	0	1 (20.0) [1]	1 (9.1) [1]
Hypotension	0	0	0	1 (20.0) [1]	1 (9.1) [1]
Myalgia	0	0	0	1 (20.0) [1]	1 (9.1) [1]

N=Total number of subjects in each treatment group, n=number of subjects in each system organ class (SOC), [T]=total number of treatment-related adverse events. Each subject is counted only once for each applicable specific adverse event. A subject with multiple adverse events within a system organ class is counted only once for that system organ class.
Table is sorted in descending order. Data cutoff date: October 17, 2019.

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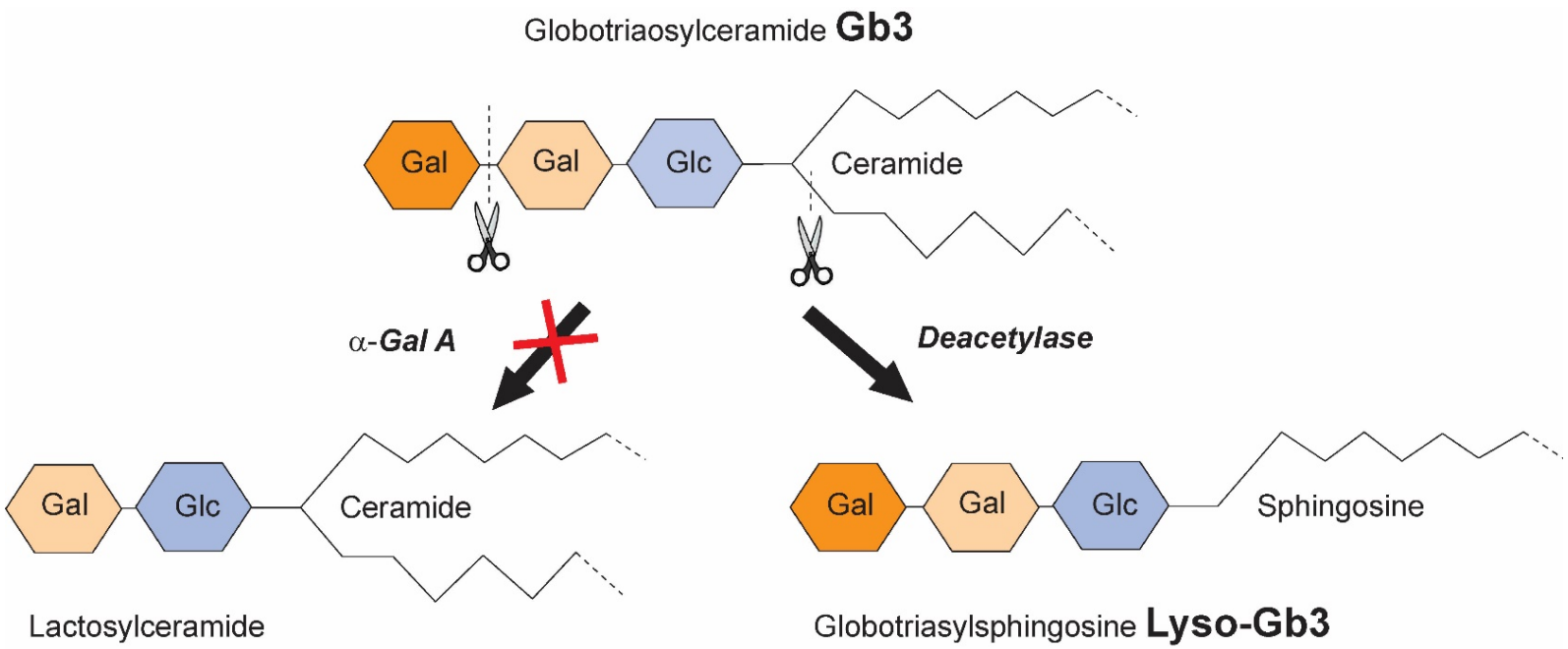
SB-525 (PF-07055480) program transitioned to Pfizer for Phase 3 development

- Pfizer advancing SB-525 to Phase 3 in 2020
- Enrollment in Pfizer's Phase 3 lead-in study commenced in October
  - Objective: To establish ≥ 6 months of prospective efficacy data of current FVIII prophylaxis replacement therapy in the usual care setting of hemophilia A subjects, who are negative for nAb to SB-525 capsid (AAV6), prior to the Phase 3 gene therapy study

Sangamo THERAPEUTICS + Pfizer

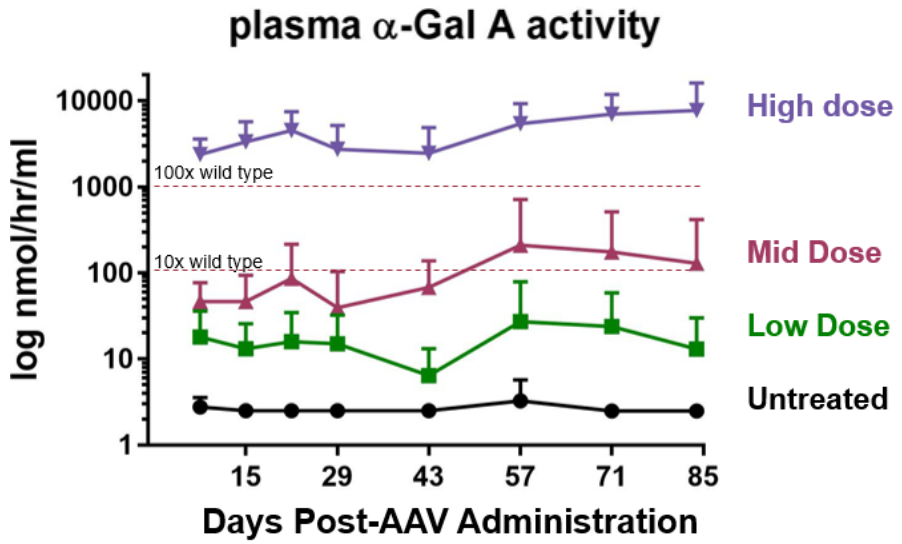
Fabry disease: A lysosomal storage disorder

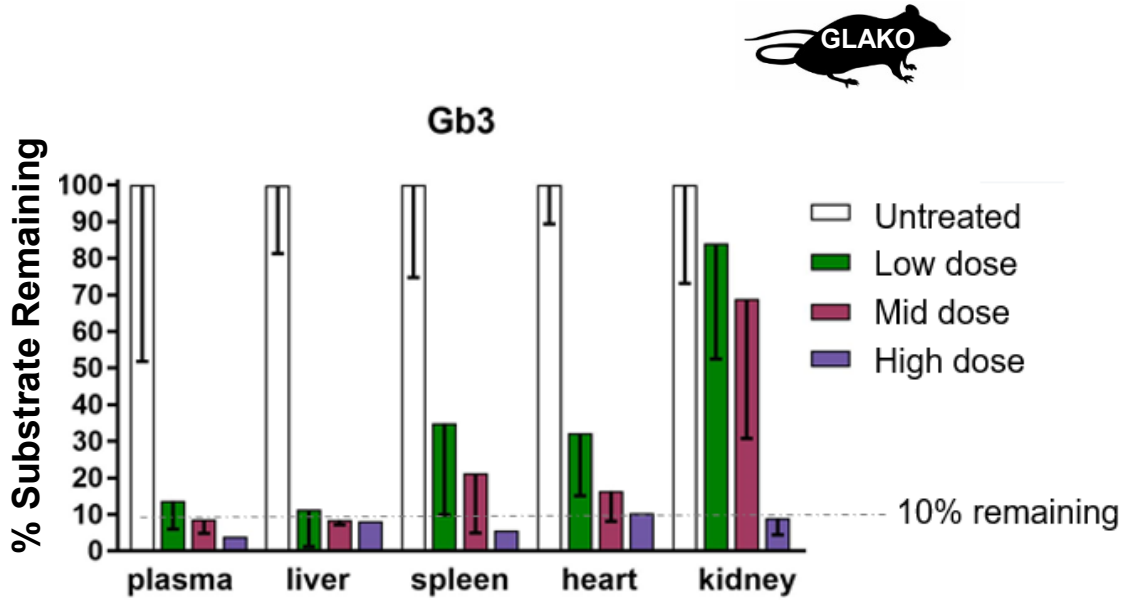


- Fabry disease is an **X-linked** monogenic disease caused by mutations in GLA gene encoding the enzyme alpha-galactosidase A **(α-Gal A**)
- **α-Gal A** plays a role in degradation of glycolipids in the lysosome
- The lack of functioning enzyme results in the accumulation of **Gb3** and its soluble form **lyso-Gb3**.

ST-920 preclinical models indicate promising potential

- ✓ US FDA orphan drug designation granted; UK approval granted for CTA
- ✓ AAV produced using clinical scale manufacturing methods





Sangamo's gene therapy demonstrated strong expression of α-Gal A and Gb3 substrate reduction across tissue types in GLAKO murine model

Phase 1/2 study evaluating ST-920

Primary Objective

- Assess safety & tolerability of ST-920

Secondary Objectives

- Assess the pharmacodynamics of α-Gal A and the presence of its substrates in plasma over time
- Assess impact of ST-920 on ERT administration required for subjects on ERT
- Assess the impact of ST-920 on renal function
- Evaluate AAV2/6 vector DNA shedding over time

Patient Population

- Male subjects ≥ 18 years of age with classic Fabry disease
- On ERT regimen; or ERT-naïve; or ERT-pseudo-naïve and has not received ERT treatment in the prior 6 months

The goal is to abrogate the need for ERT with a recombinant AAV2/6 vector encoding cDNA for human α-Gal A, resulting in long-term expression of α-Gal A

ST-920 offers a potentially differentiated treatment for Fabry

- In a single IV infusion, ST-920 may provide continuous, potentially life-long expression of endogenously expressed α-Gal A
- No preconditioning regimen
- Potential to deliver efficacy with preserved renal function and reduced cardiac morbidity
- FDA draft guidance may considerably shorten time to approval and allow ST-920 to be among the first gene therapy treatments on the market

Ex vivo gene-edited cell therapy in 2020

Preclinical

- PKU (ST-101) — SANGAMO WHOLLY OWNED
- IBD — SANGAMO WHOLLY OWNED
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- α-Synuclein (ST-502) — SANGAMO WHOLLY OWNED
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- Tauopathies (ST-501) — SANGAMO WHOLLY OWNED

Phase 1/2

- Fabry Disease (ST-920) — SANGAMO WHOLLY OWNED
- Beta Thalassemia (ST-400) — PARTNER SANOFI
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- Solid Organ Transplant (TX200) — SANGAMO WHOLLY OWNED
- MPS II (SB-913) — SANGAMO WHOLLY OWNED

Phase 3

- Hemophilia A (SB-525) — PARTNER Pfizer

(Pfizer initiated Ph3 lead-in study Oct. '19)

Gene Therapy | *Ex Vivo* Gene-Edited Cell Therapy | *In Vivo* Genome Editing | *In Vivo* Genome Regulation

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Presented at the 2019 American Society of Hematology Annual Meeting; Orlando, Florida; December 9, 2019

Preliminary Results of a Phase 1/2 Clinical Study of Zinc Finger Nuclease-Mediated Editing of *BCL11A* in Autologous Hematopoietic Stem Cells for Transfusion-Dependent β-Thalassemia

Angela R. Smith, MD, MS[1]; Gary J. Schiller, MD[2]; Gregory M Vercellotti, MD[3]; Janet L. Kwiatkowski, MD, MSCE[4]; Lakshmanan Krishnamurti, MD[5]; Erica B. Esrick, MD[6]; David A. Williams, MD[7]; Weston P. Miller, MD[8]; Adrian Woolfson, MD, PhD[8] and Mark C. Walters, MD[9]

[1]Pediatric Blood and Marrow Transplantation, University of Minnesota, Minneapolis, MN; [2]Division of Hematology and Oncology, Department of Medicine, David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA; [3]Division of Hematology, Oncology and Transplantation, Department of Medicine, University of Minnesota Medical School, Minneapolis, MN; [4]The Children's Hospital of Philadelphia, Philadelphia, PA; [5]Aflac Cancer and Blood Disorders Center, Department of Pediatrics, Children's Healthcare of Atlanta, Emory University, Atlanta, GA; [6]Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Harvard Medical School, Boston, MA; [7]Boston Children's Hospital, Harvard Medical School, Boston, MA; [8]Sangamo Therapeutics, Brisbane, CA; [9]USCF Benioff Children's Hospital Oakland, Oakland, CA

ST-400: Patient demographics and disease characteristics

Patient	Age at Consent (Years)	Genotype	Annualized PRBC Events Pre-Enrollment	Most Recent Study Visit
1	36	β^0 β^0	27	39 weeks
2	30	β^+ (severe IVS-I-5: G>C) β^+ (severe IVS-I-5: G>C)	18	26 weeks
3	23	β^0 β^+ (severe IVS-II-654 C>T)	15	12 weeks
4	18	β^{WT} ($\alpha\alpha$) β^0 ($\alpha\alpha\alpha\alpha$)	13	Recently Dosed
5	35	β^0 β^+ (severe IVS-I-110 G>A)	15	Recently Dosed

- β^0, absence of β–globin production; β^+, decreased β–globin production; β^{WT}, wild type (normal β–globin production); PRBC events, packed red blood cell transfusion

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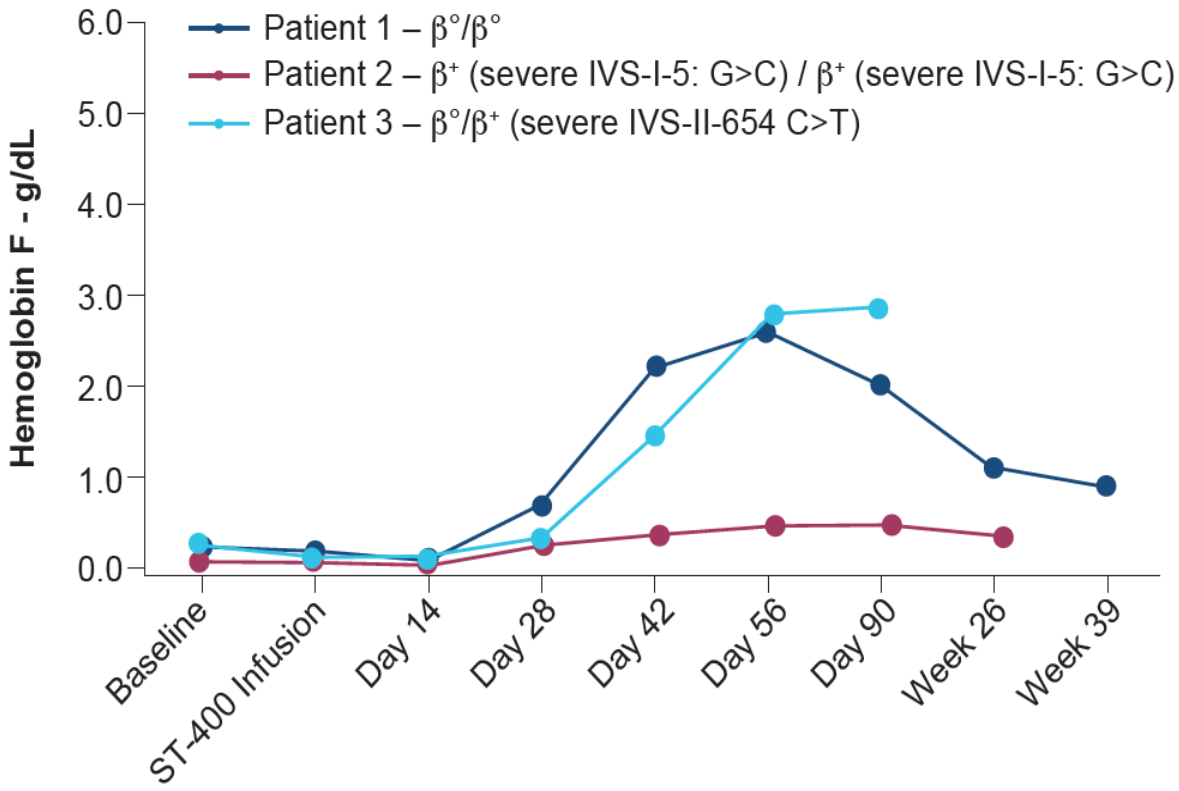
Data cuts: clinical, October 10, 2019; laboratory, November 8, 2019

ST-400: Fetal hemoglobin response

HSC Transplant Variable	Patients				
	1	2	3	4	5
Cell Dose	◑	○	●	◔	◕
Lot Potency	◔	○	●	◑	◕
Editing	○	◑	◔	●	◕
BThal Genotype	○	◔	◑	●	◑
Age (Youth)	○	◑	◕	●	◔

○ ◔ ◑ ◕ ●

Potentially more favorable



Sangamo THERAPEUTICS | SANOFI

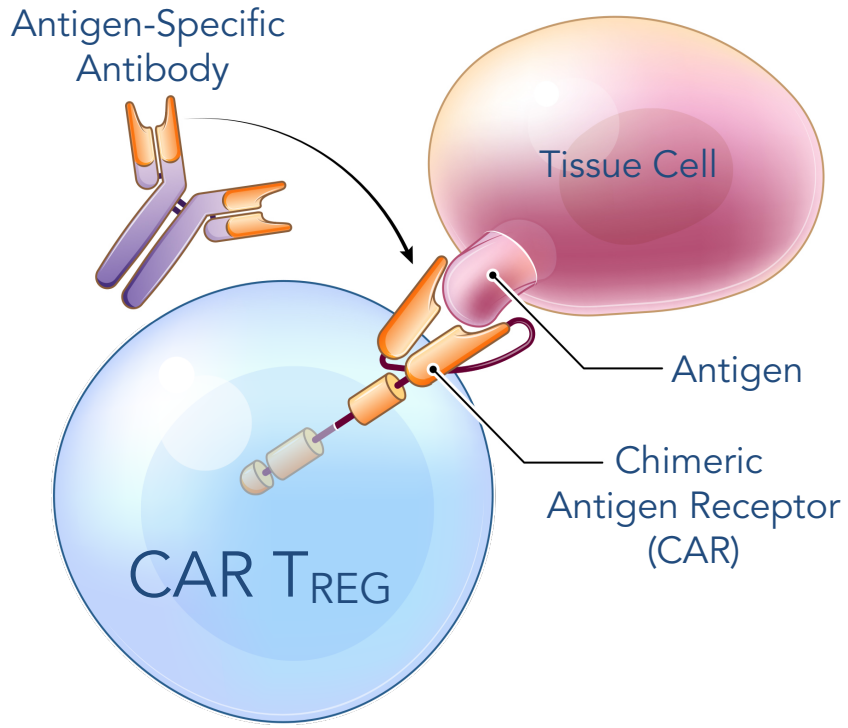
Data cuts: clinical, October 10, 2019; laboratory, November 8, 2019

ST-400: Safety profile

- Reported adverse events (AEs) have been consistent with those expected with myeloablative autologous HCT
- Two serious AEs have been reported
  - #1: assessed as likely related to DMSO, the cryoprotectant excipient
  - #2: not related to ST-400
- No emerging clonal hematopoiesis observed by indel pattern monitoring

Harnessing T_{REG} Function with CAR-T_{REG} Therapy

CAR-T_{REGS} overcome limitations of polyclonal T_{REG} Therapy

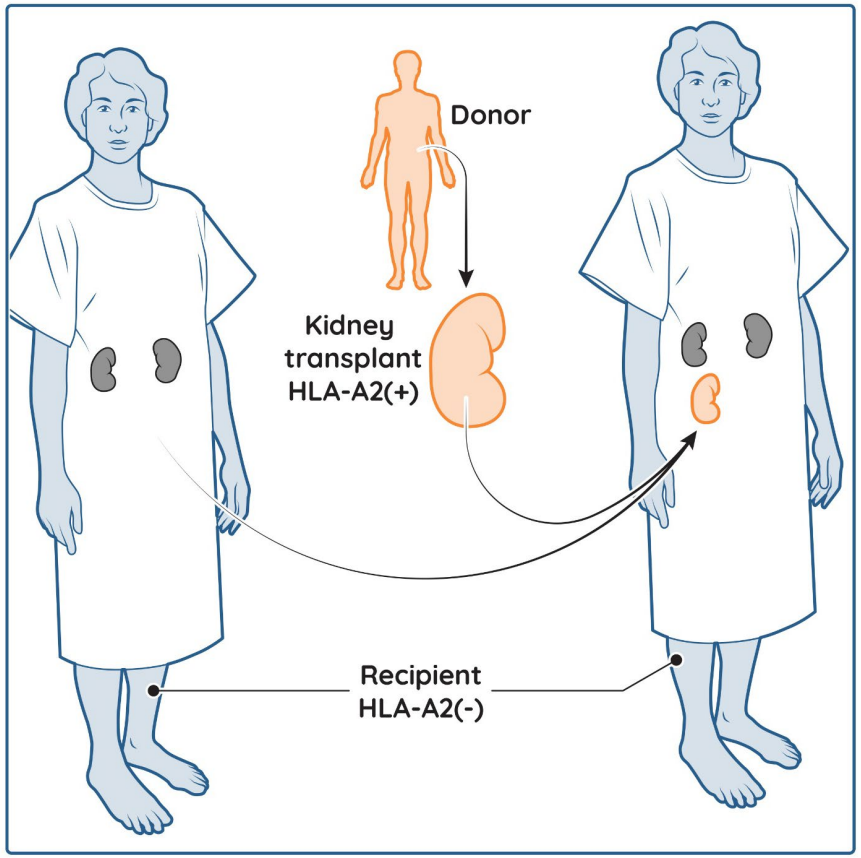


- *Ex vivo* engineered and expanded
- Tissue targeted
- Antigen activated & expanded
- Multiple mechanisms of immune regulation

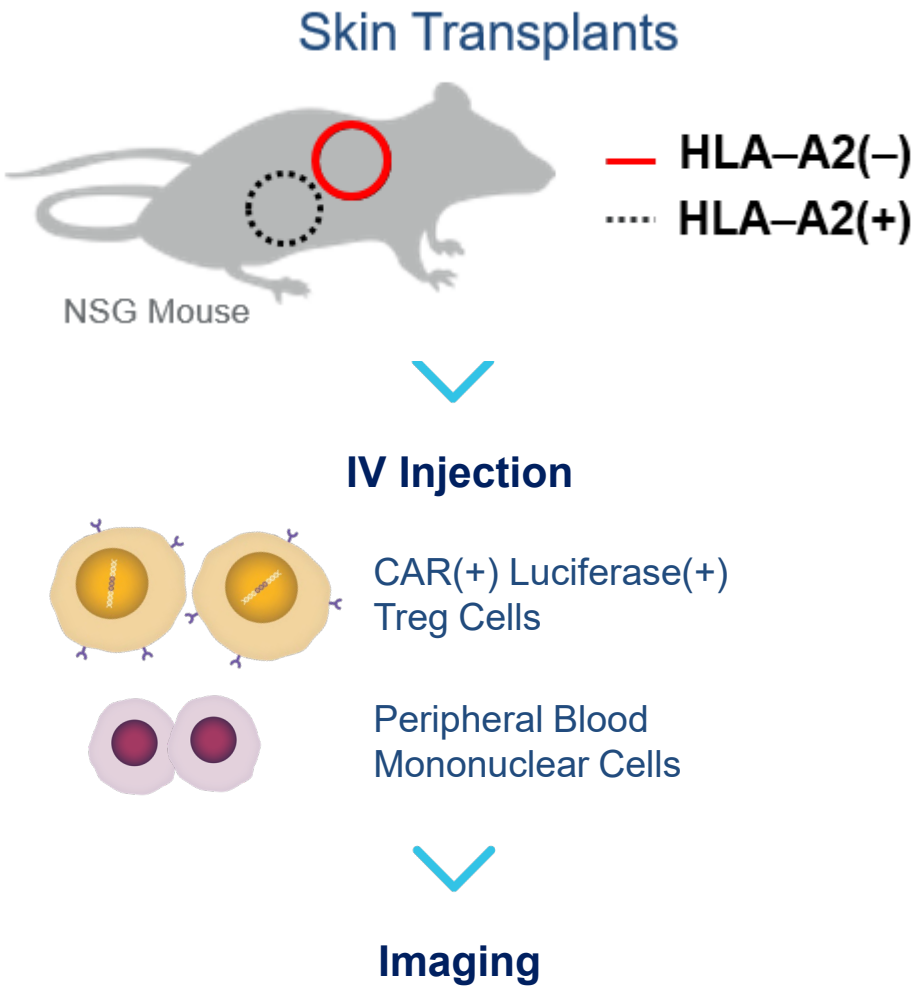
Sangamo is pioneering this new frontier with TX200 for solid organ transplantation

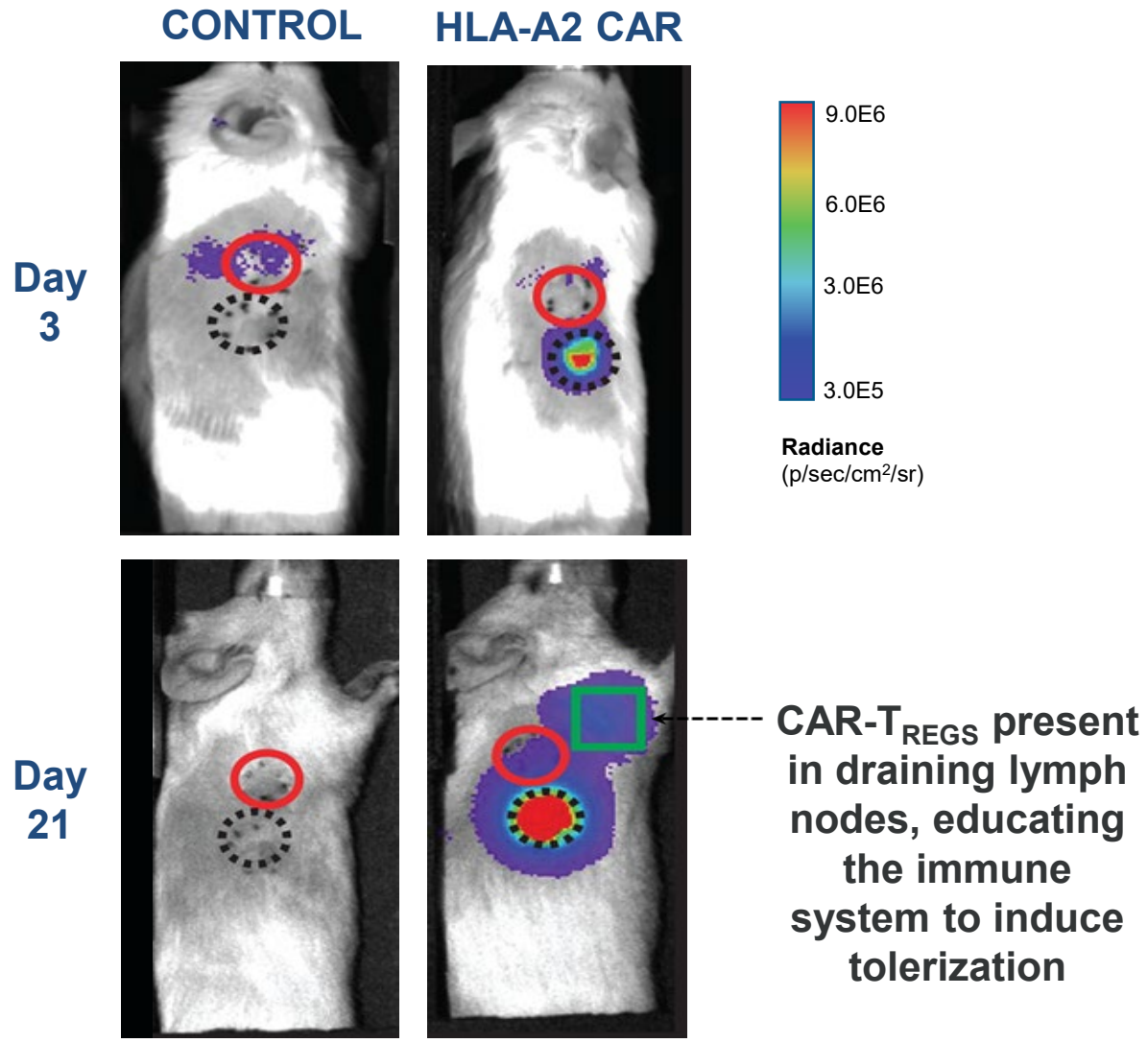
Autologous HLA-A2 specific CAR-T_{REG} cell therapy

- Initial target indication: Prevention of immune mediated rejection in living donor renal transplantation
  - The STEADFAST Study will evaluate the safety and mechanism of action of TX200 in renal transplant recipients
  - 80,000 renal transplantations per year (US and EU)
  - 20-25% of transplanted organs are HLA-A2 mismatched
- Therapeutic hypothesis and goals
  - Regulate the immune system in a targeted manner
  - Promote immunological tolerance to the renal transplant
  - Help preserve graft function and reduce graft loss



HLA-A2 CAR-T_{REGS} achieve precise and durable targeting of skin graft in a mouse model





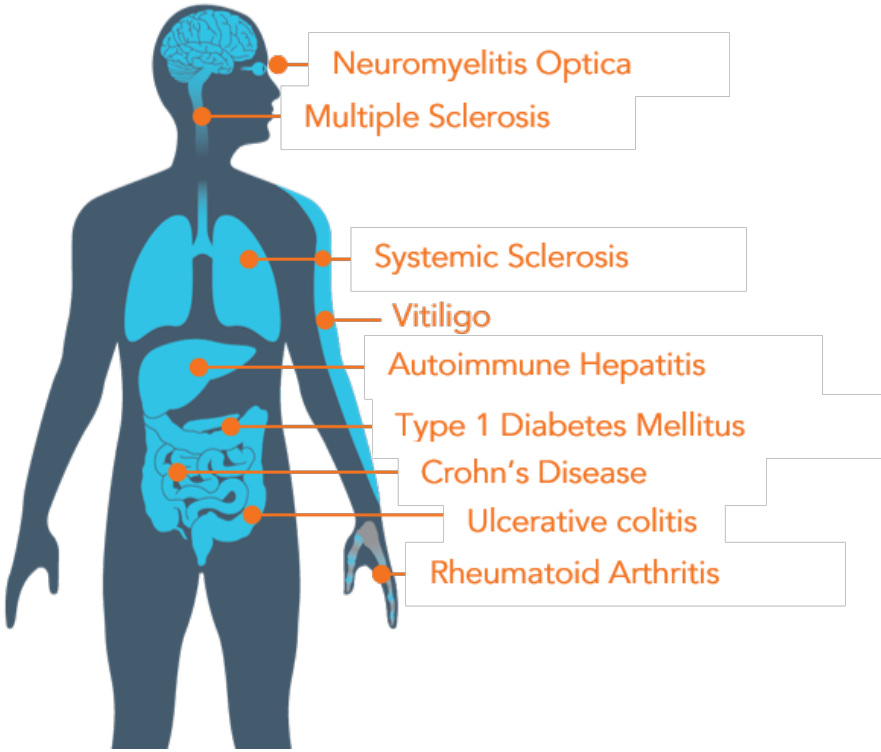
CAR-T_{REGS} present in draining lymph nodes, educating the immune system to induce tolerization

Dawson NA, Lamarche C et al. JCI Insight 2019;4(6):e123672.

TX200: Gateway to major autoimmune indications

Key outcomes from TX200 CAR-T_{REG} program

- Provides data on safety and proof of concept
- Answers critical questions on CAR-T_{REG} pharmacology and biology in patients
- Establishes CAR-T_{REG} cell therapy process development know how and manufacturing infrastructure
- Gateway to multiple autoimmune indications with large patient populations and high unmet need



Sangamo plans to develop next generation CAR-T_{REG} products with ZFN multiplex editing

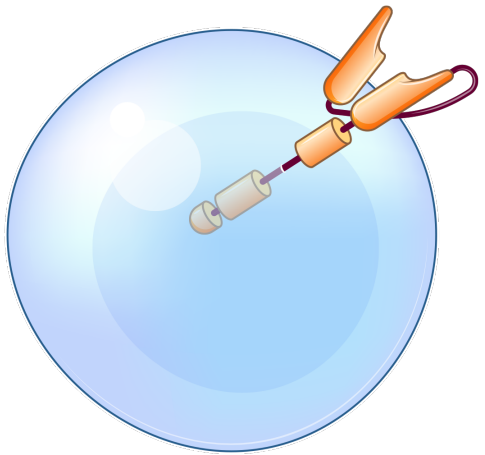
Sangamo ZFN Multiplexed Genomic Engineering

Allogeneic Off-the-Shelf

- Healthy donor-derived allogeneic T_{REG}
- iPSC-derived allogeneic T_{REG}
- Hypoimmunogeneic editing

Improved Function

- Increased Persistence
- Enhanced localization
- Improved potency



Sangamo T_{REG} Platform Investments

- T_{REG} Manufacturing
- scFv T_{REG} CAR screening platform

Optimize and diversify *in vivo* genome editing

Preclinical				Phase 1/2			Phase 3
PKU (ST-101)	IBD	MS	Oncology	Fabry Disease (ST-920)	Beta Thalassemia (ST-400)	Oncology (KITE-037)	Hemophilia A (SB-525)
SANGAMO WHOLLY OWNED	SANGAMO WHOLLY OWNED	SANGAMO WHOLLY OWNED	PARTNER Kite	SANGAMO WHOLLY OWNED	PARTNER SANOFI	PARTNER Kite	PARTNER Pfizer
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SANGAMO WHOLLY OWNED	PARTNER Pfizer	PARTNER Takeda	SANGAMO WHOLLY OWNED	PARTNER SANOFI	SANGAMO WHOLLY OWNED	SANGAMO WHOLLY OWNED	
Tauopathies (ST-501)							
SANGAMO WHOLLY OWNED							

Gene Therapy | *Ex Vivo* Gene-Edited Cell Therapy | *In Vivo* Genome Editing | *In Vivo* Genome Regulation

Sangamo THERAPEUTICS

Five potential levers for optimizing *in vivo* editing

Enhanced efficiency of ZFN delivery to hepatocytes is critical

HemA data suggests targeting > 3e13 is necessary

1) Dose

2) AAV2.0

3) Second-generation ZFNs (phosphate contact residue modifications, etc.)

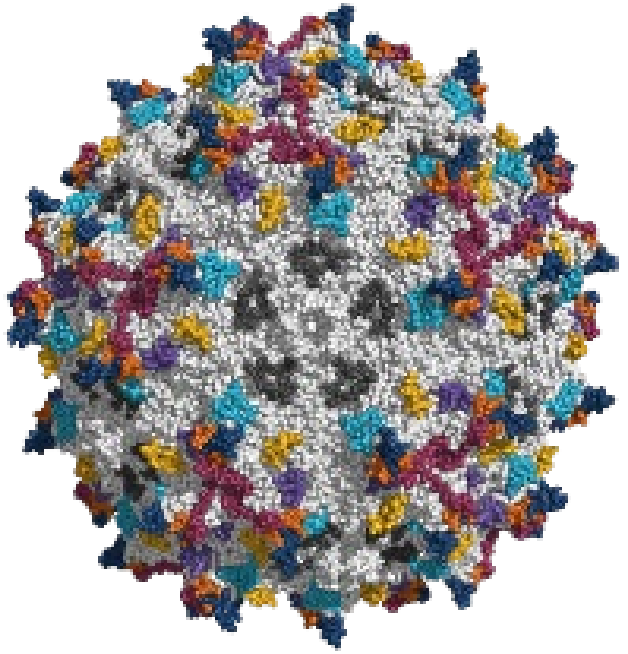
4) Donor 2.0

5) 2 in 1 ZFNs (co-package left and right ZFNs)

New delivery capabilities offer new possibilities

Exploring new delivery modalities

- Engineered AAV6
- Other AAV serotypes
- Lipid Nanoparticles (LNPs)
- Other modalities



AAV

In vivo genome regulation for CNS diseases

Preclinical

- PKU (ST-101) — SANGAMO WHOLLY OWNED
- IBD — SANGAMO WHOLLY OWNED
- MS — SANGAMO WHOLLY OWNED
- Oncology — PARTNER Kite
- α-Synuclein (ST-502) — SANGAMO WHOLLY OWNED
- ALS/FTD — PARTNER Pfizer
- Huntington's Disease (TAK-686) — PARTNER Takeda
- Prion — SANGAMO WHOLLY OWNED
- Tauopathies (ST-501) — SANGAMO WHOLLY OWNED

Phase 1/2

- Fabry Disease (ST-920) — SANGAMO WHOLLY OWNED
- Beta Thalassemia (ST-400) — PARTNER SANOFI
- Oncology (KITE-037) — PARTNER Kite
- Sickle Cell Disease (BIVV003) — PARTNER SANOFI
- Solid Organ Transplant (TX200) — SANGAMO WHOLLY OWNED
- MPS II (SB-913) — SANGAMO WHOLLY OWNED

Phase 3

- Hemophilia A (SB-525) — PARTNER Pfizer

(Pfizer initiated Ph3 lead-in study Oct. '19)

Gene Therapy | *Ex Vivo* Gene-Edited Cell Therapy | *In Vivo* Genome Editing | *In Vivo* Genome Regulation

Sangamo THERAPEUTICS

Potential CNS applications for Sangamo's zinc finger protein transcription factors (ZFP-TFs) and ZFNs

ZFP-TF genome regulation

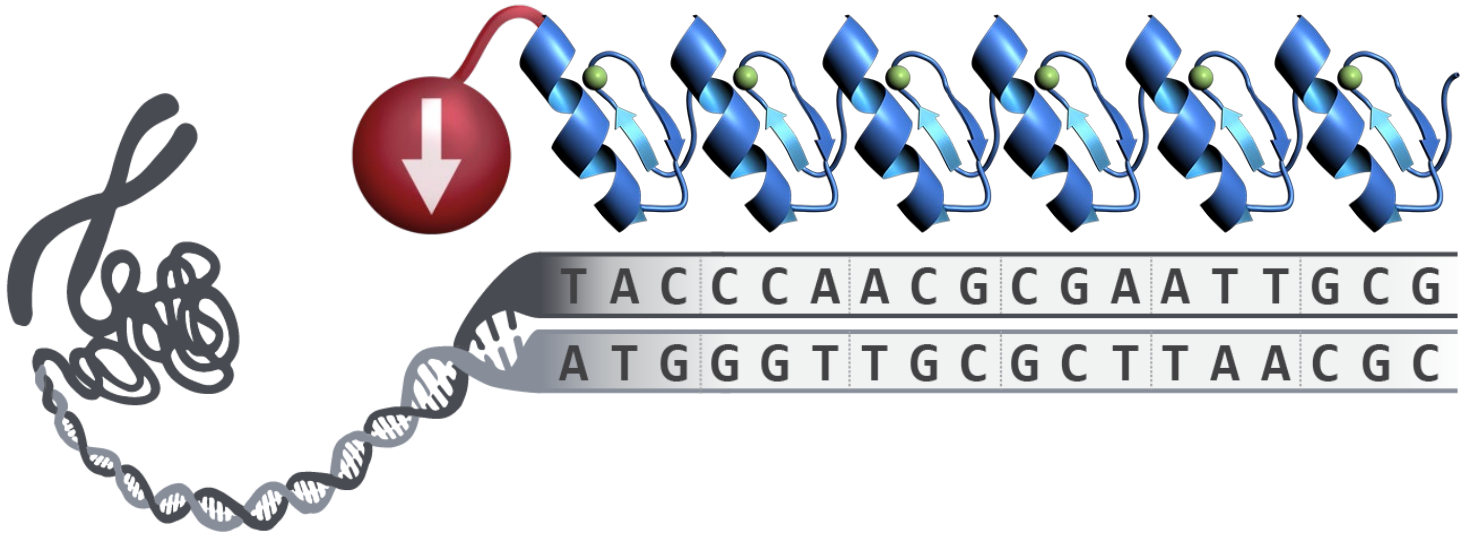
Pan-Allele	ZFP-TFs for single gene repression	• Tauopathies (IND 2021) • α-synuclein (IND 2022) • Prion
Allele-Selective	ZFPs target disease allele repeats selectively	• Huntington's Disease • C9ORF72-linked ALS
Epigenetic editing	ZFP-Epi to demethylate select sites	• Rett Syndrome • Fragile X

ZFN genome editing

Inflammation	T_{REGS} for inhibition of neuroinflammation and remyelination	• Multiple Sclerosis • ALS
Mitochondrial	ZFNs for selective clearance of mutant mitochondrial genomes	• Cerebellar Ataxia • Leigh Syndrome

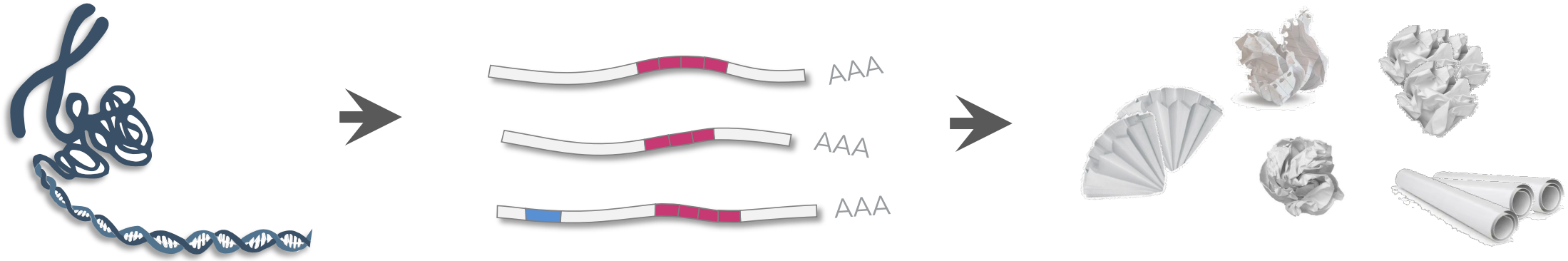
Sangamo THERAPEUTICS

ZFP-TFs can be engineered to regulate any gene



- **Compact**
  Easily packaged into AAV
- **High potency**
  2 targets per cell
- **Human origin**
  ZFP and KRAB come from human genes

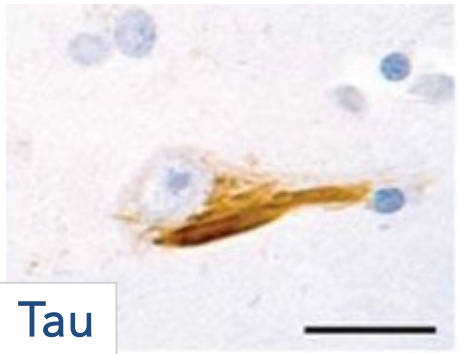
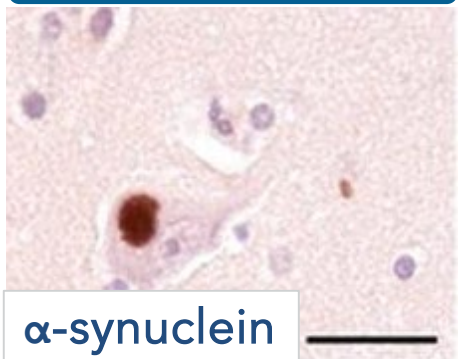
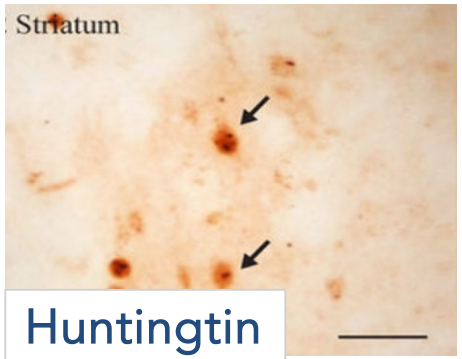
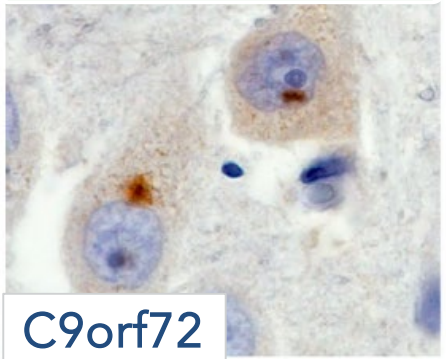
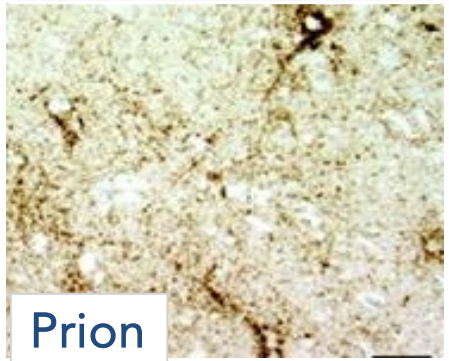
ZFP-TFs target upstream at the source of mutant DNA



DNA
1 mutant allele

RNA
Sense, antisense, mis-spliced

Protein
Varied and complex

ALZHEIMER'S DISEASE	PARKINSON'S DISEASE	HUNTINGTON'S DISEASE	ALS	PRION DISEASE
				
Tau	α-synuclein	Huntingtin	C9orf72	Prion

Hill et al., 2003
Irwin et al., 2015
Jucker & Walker 2013
Waldvogel et al., 2014

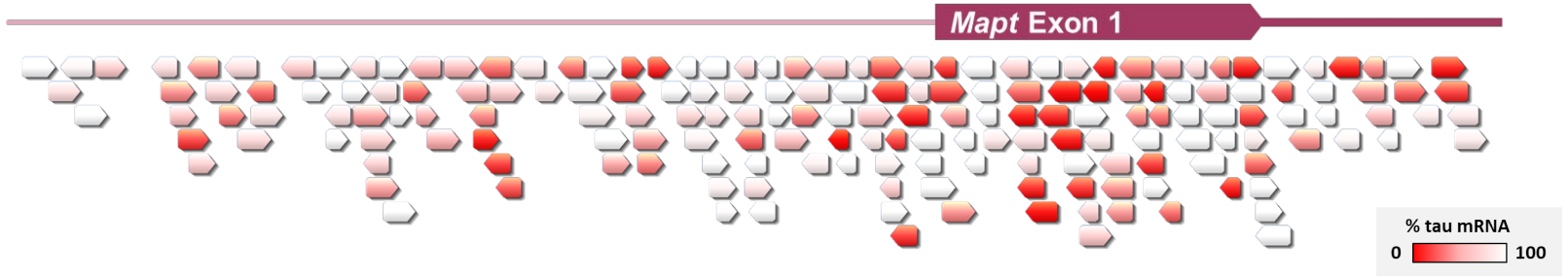
Potent, long-lasting, specific repression of tau by ZFP-TFs

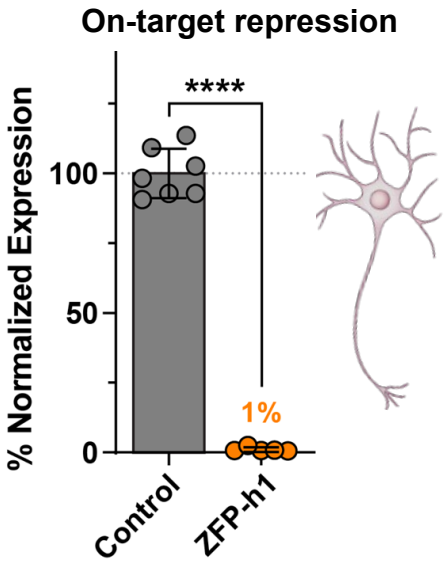
Pan-Allele

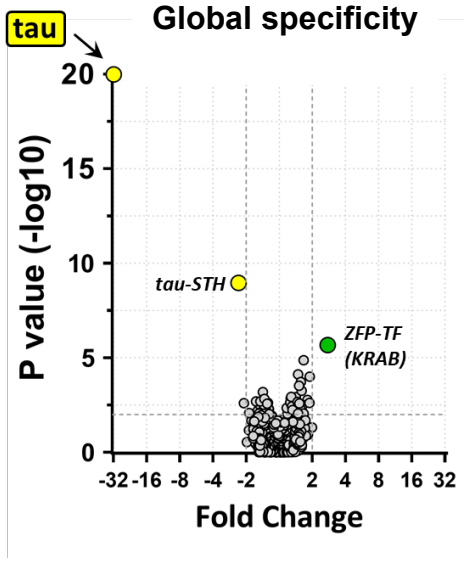
ST-501 – ALZHEIMER'S DISEASE AND OTHER TAUOPATHIES

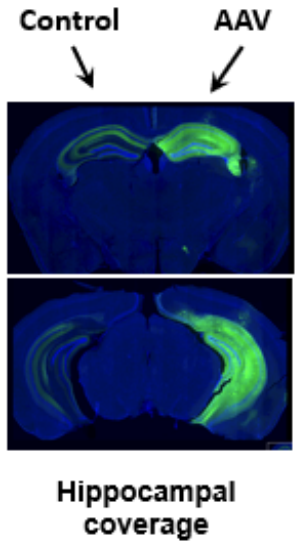
Abnormal tau is toxic to brain cells and leads to neurodegeneration in Alzheimer's disease

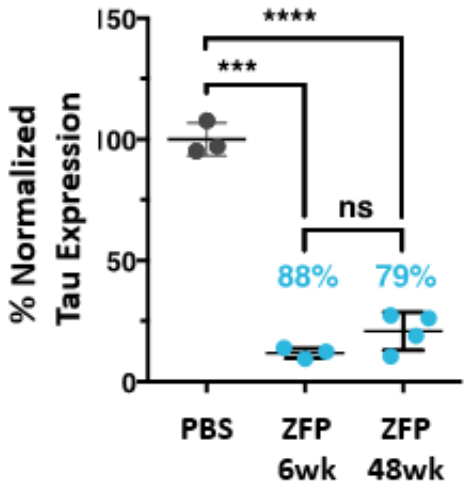
Tau reduction is a therapeutic strategy for targeting these diseases











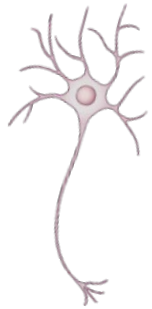
Tuning gene expression with ZFP-TFs to target disease pathology

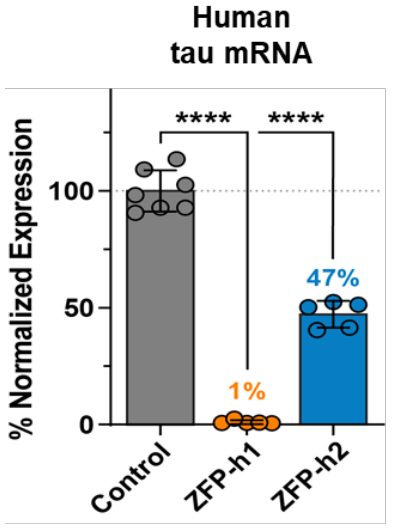
Pan-Allele

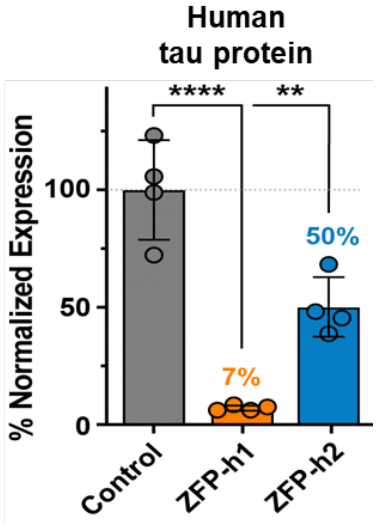
ST-501 – ALZHEIMER'S DISEASE AND OTHER TAUOPATHIES

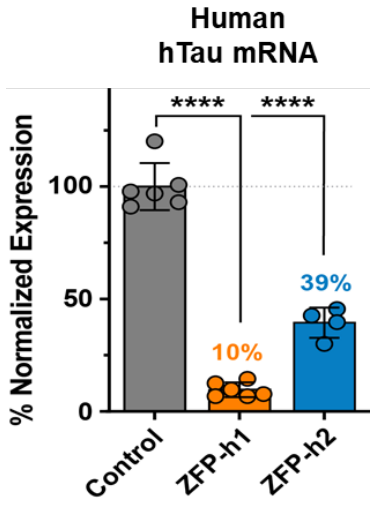
ZFP-TFs reduce expression of tau in a highly specific, tunable manner

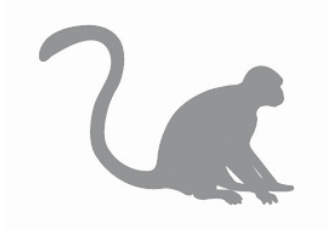
ZFP-TFs therefore represent a *novel therapeutic strategy for treating tauopathies*

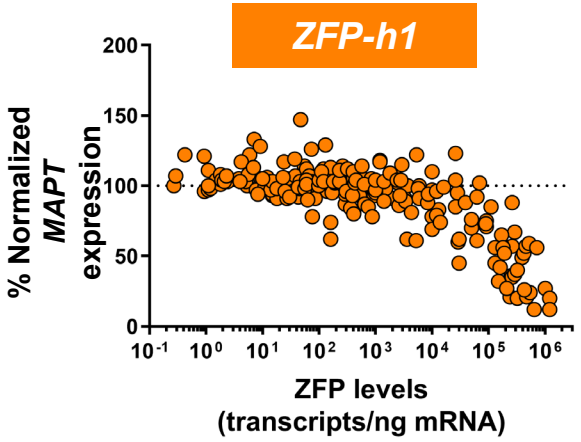


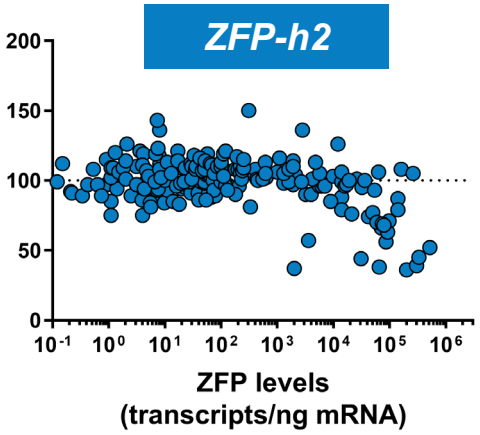












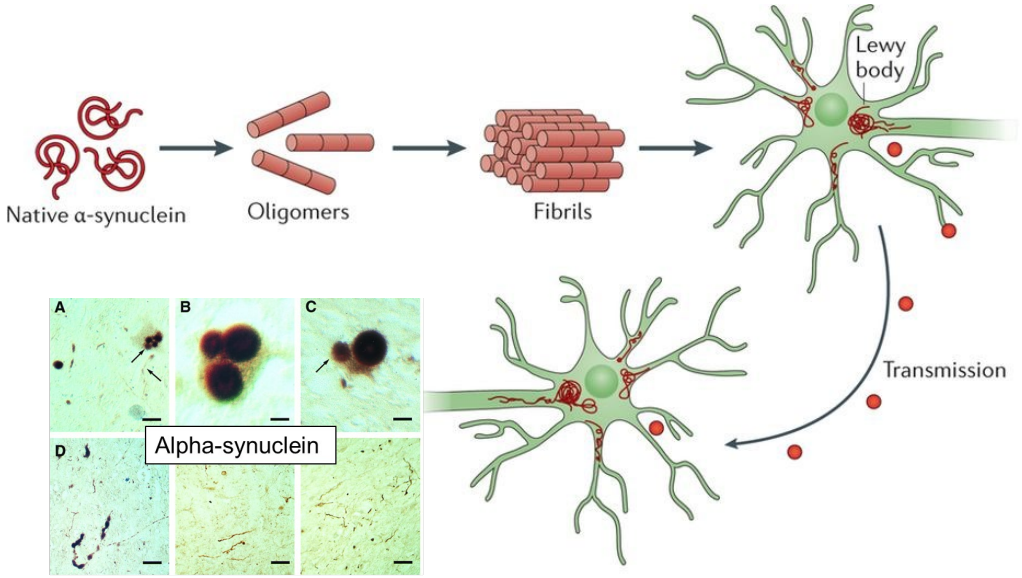
Sangamo THERAPEUTICS

Reducing gene expression with ZFP-TFs to target disease pathology

Pan-Allele

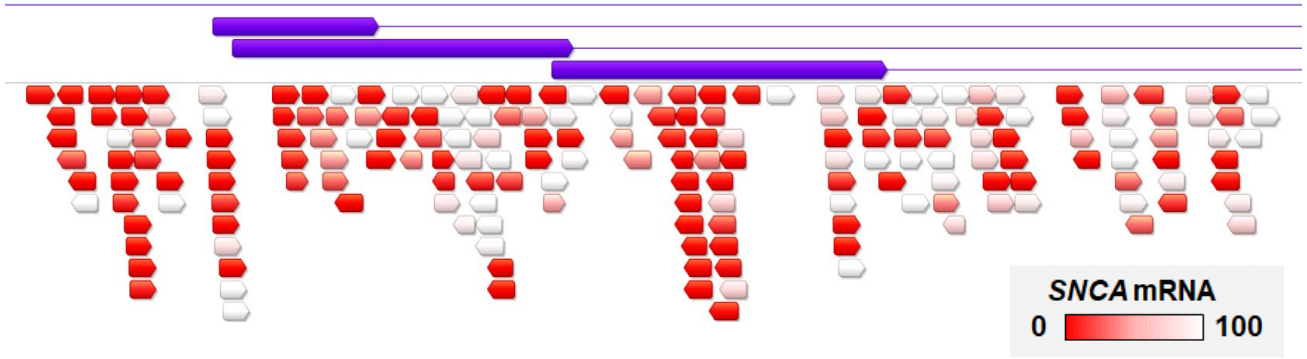
ST-502 – PARKINSON'S DISEASE

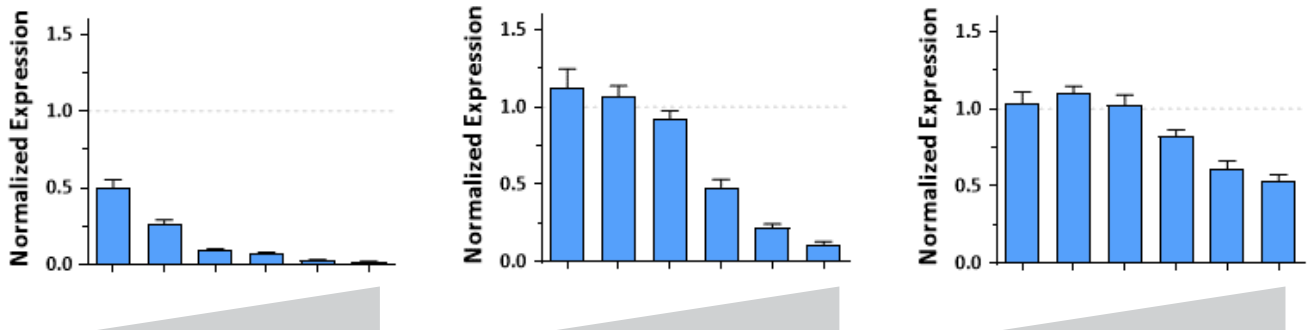
α-synuclein pathology tracks with disease progression in PD



Alpha-synuclein fibrils identified as major components of Lewy bodies and Lewy neurites (Goedert and Spillantini, 1998)

Kingwell 2017





55% of ZFP-TFs reduced total *SNCA* by ≥ 50%

3 / 10 / 30 / 100 / 300 / 1000
ng ZFP mRNA

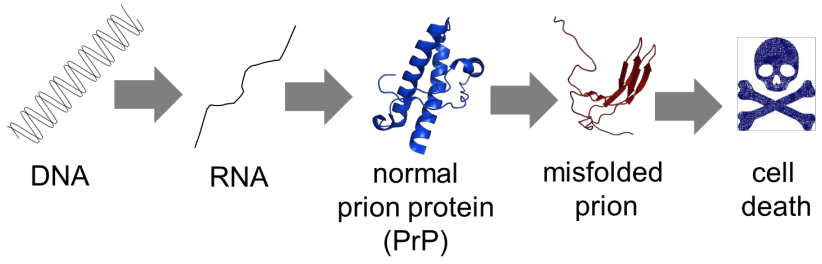
Sangamo THERAPEUTICS

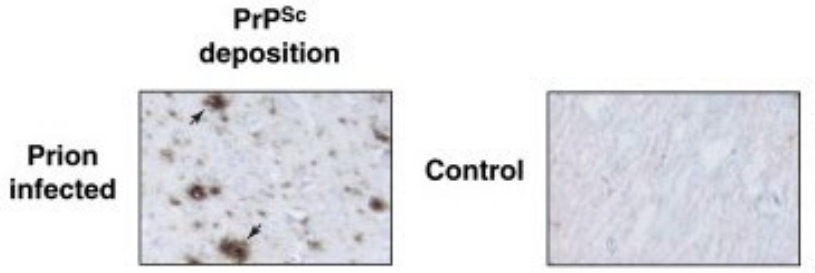
Reducing gene expression with ZFP-TFs to target disease pathology

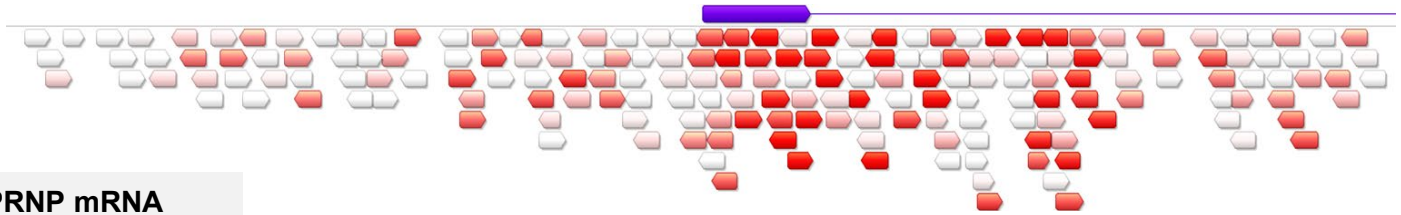
Pan-Allele

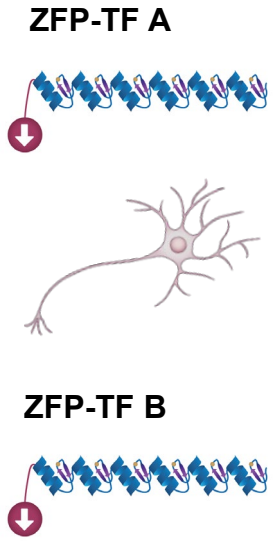
PRION DISEASE

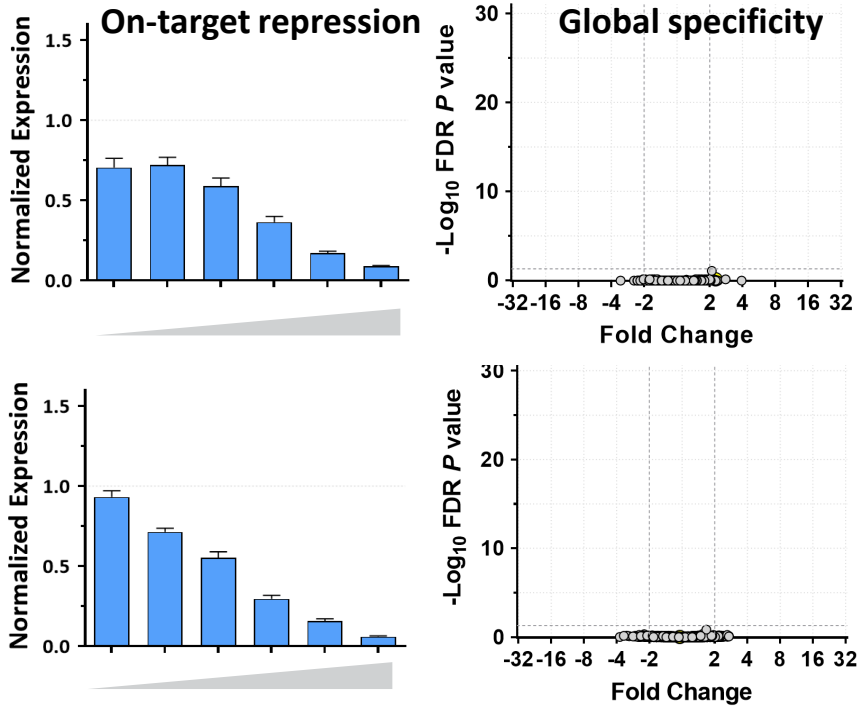
Misfolded prion protein leads to neurodegeneration in familial and sporadic forms of prion disease











Sangamo THERAPEUTICS

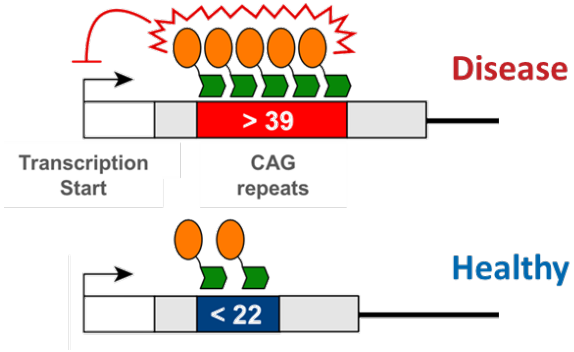
BROAD INSTITUTE

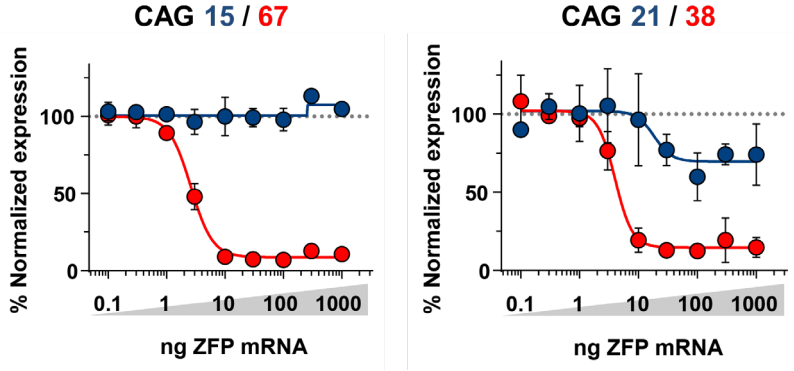
Reducing gene expression with ZFP-TFs to target disease pathology

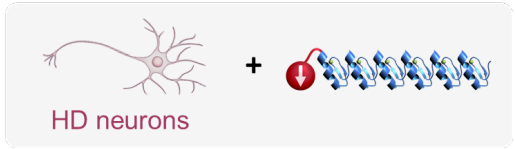
Allele-selective

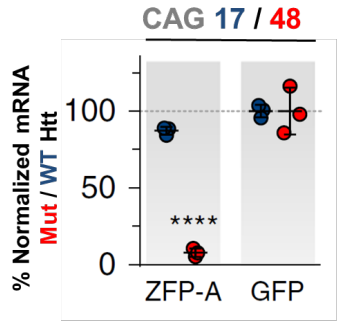
HUNTINGTON'S DISEASE

- Normal huntingtin protein has essential cellular functions
- Ideal therapy: Eliminate mutant, preserve normal
- ~90% of HD patients: **CAG15-22** and **CAG38-48**









Sangamo THERAPEUTICS + Takeda

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

HUNTINGTON'S DISEASE

Astrocyte molecular signatures in Huntington's disease

Blanca Diaz-Castro[1], Mohitkumar R. Gangwani[1], Xinzhu Yu[1], Giovanni Coppola[2,3,4], Baljit S. Khakh[1,5]*

Diaz-Castro *et al., Sci. Transl. Med.* **11**, eaaw8546 (2019) 16 October 2019

Mutant huntingtin enhances activation of dendritic Kv4 K^+ channels in striatal spiny projection neurons

Luis Carrillo-Reid[1,2], Michelle Day[1], Zhong Xie[1], Alexandria E Melendez[1], Jyothisri Kondapalli[1], Joshua L Plotkin[1,3], David L Wokosin[1], Yu Chen[1], Geraldine J Kress[1,4], Michael Kaplitt[5], Ema Ilijic[1], Jaime N Guzman[1], C Savio Chan[1], D James Surmeier[1]*

eLIFE elifesciences.org

Carrillo-Reid *et al.* eLife 2019;8:e40818. DOI: https://doi.org/10.7554/eLife.40818

Faulty neuronal determination and cell polarization are reverted by modulating HD early phenotypes

P. Conforti[a,b], D. Besusso[a,b,1], V. D. Bocchi[a,b,1], A. Faedo[a,b,1,2], E. Cesana[c], G. Rossetti[b], V. Ranzani[b], C. N. Svendsen[d], L. M. Thompson[e,f], M. Toselli[c], G. Biella[c], M. Pagani[b,g], and E. Cattaneo[a,b,3]

www.pnas.org/cgi/doi/10.1073/pnas.1715865115

nature medicine ARTICLES

https://doi.org/10.1038/s41591-019-0478-3

Allele-selective transcriptional repression of mutant *HTT* for the treatment of Huntington's disease

Bryan Zeitler[1]*, Steven Froelich[1], Kimberly Marlen[1], David A Shivak[1], Qi Yu[1], Davis Li[1], Jocelynn R Pearl[1], Jeffrey C Miller[1], Lei Zhang[1], David E Paschon[1], Sarah J Hinkley[1], Irina Ankoudinova[1], Stephen Lam[1], Dmitry Guschin[1,8], Lexi Kopan[1], Jennifer M Cherone[1], Hoang-Oanh B Nguyen[1], Guijuan Qiao[1], Yasaman Ataei[1], Matthew C Mendel[1], Rainier Amora[1], Richard Surosky[1], Josee Laganiere[1,9], B Joseph Vu[1], Anand Narayanan[1], Yalda Sedaghat[2], Karsten Tillack[2], Christina Thiede[2], Annette Gärtner[2], Seung Kwak[3], Jonathan Bard[3], Ladislav Mrzljak[3], Larry Park[3], Taneli Heikkinen[4], Kimmo K Lehtimäki[4], Marie M Svedberg[5], Jenny Häggkvist[5], Lenke Tari[5], Miklós Tóth[5], Andrea Varrone[5], Christer Halldin[5], Andrea E Kudwa[6], Sylvie Ramboz[6], Michelle Day[7], Jyothisri Kondapalli[7], D James Surmeier[7], Fyodor D Urnov[1,10], Philip D Gregory[1], Edward J Rebar[1], Ignacio Muñoz-Sanjuán[3]* and H Steve Zhang[1,11]

NATURE MEDICINE | VOL 25 | JULY 2019 | 1131–1142 | www.nature.com/naturemedicine

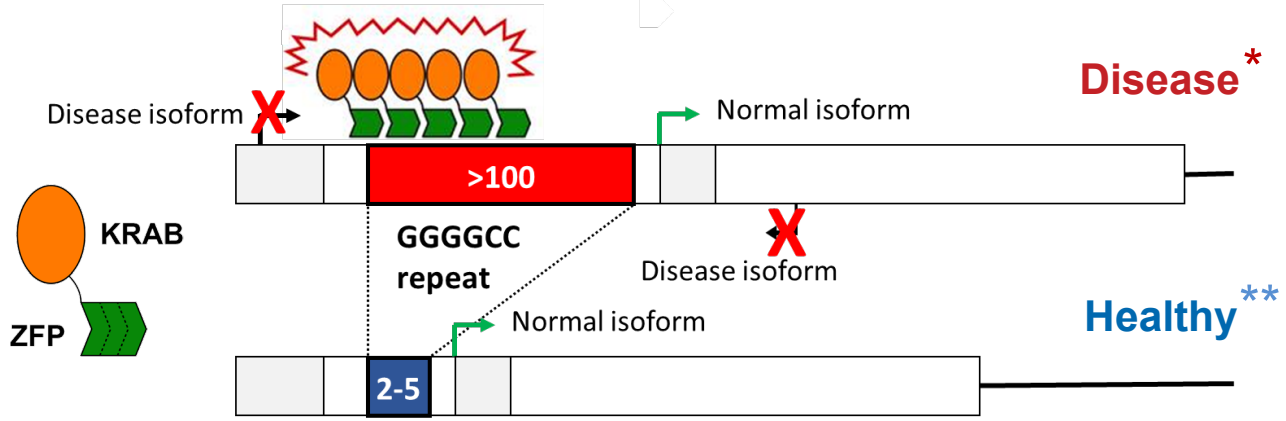
July 2019

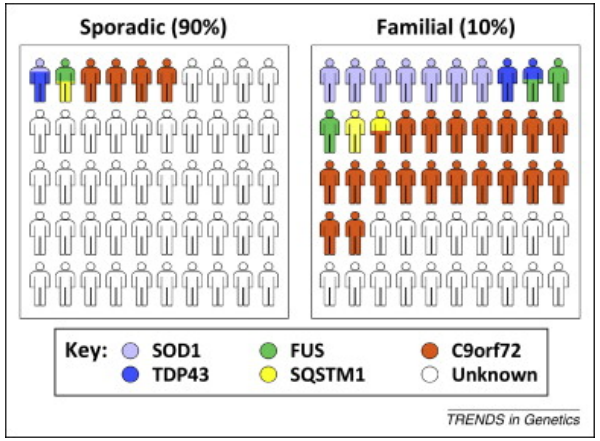
Reducing gene expression with ZFP-TFs to target disease pathology

Allele-selective

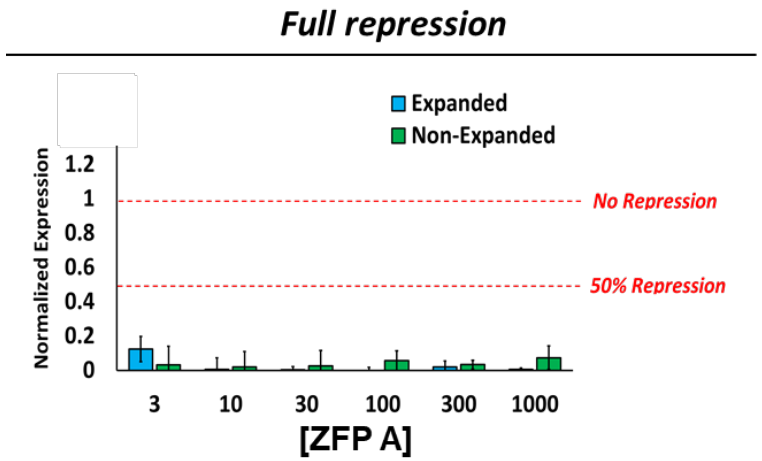
AMYOTROPHIC LATERAL SCLEROSIS (ALS)

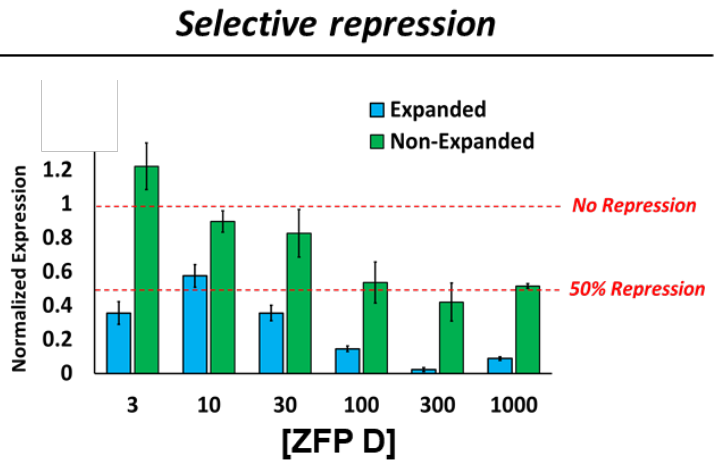
- Expansion of the GGGCC six base pair repeat causes neuronal degeneration in ALS/FTD
- Repeat-targeted ZFP-TFs selectively repress disease isoforms while preserving expression of normal C9ORF72





Lattante et al 2015





Sangamo THERAPEUTICS + Pfizer

*Expanded repeat **Non-expanded

Finance and Operations

Financial results

Manufacturing

In-house cGMP facility and dedicated external manufacturing capacity provide scale for clinical research and commercial supply

Ensuring control of quality, cost and timelines

In-house Phase 1/2 cGMP Facilities

Brisbane, US:
- Cell therapy (late 2020)
- Gene therapy (early 2021)

Valbonne, France:
- Cell therapy (late 2021)

CDMO Thermo Fisher – dedicated access to AAV capacity up to 2000-L bioreactor scale

- Leveraging Thermo Fisher AAV manufacturing know-how
- Enables seamless transition from early to late-stage development
- Provides late-stage clinical and large-scale commercial grade supply

ThermoFisher SCIENTIFIC

Conclusions

Key takeaways

- Genomic medicine company building value with gene therapy, *ex vivo* gene-edited cell therapy, *in vivo* genome editing and genome regulation
- Precise, efficient and specific gene editing technology (ZFNs) backed by a robust patent estate
- Broad portfolio of rare and large indications across inherited metabolic diseases, immunology, CNS, hematology and oncology
- In-house cGMP facility and dedicated CDMO capacity provide manufacturing scale for clinical and commercial supply
- Strong balance sheet, four validating biopharma partnerships (Kite, Pfizer, Sanofi, Takeda)

Sangamo THERAPEUTICS

Sangamo THERAPEUTICS