Sangamo THERAPEUTICS

Corporate Presentation

May 2019

Forward-Looking Statements

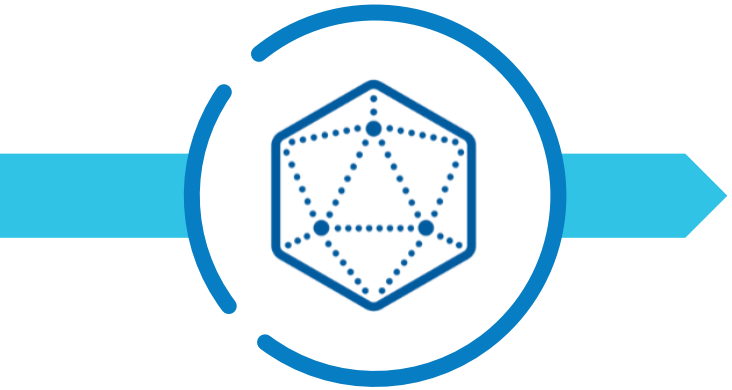
This presentation contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, as amended. These forward-looking statements include, but are not limited to, statements relating to the design of clinical trials and expected timing for enrollment and presentation of data; the anticipated clinical development milestones and other potential value drivers in the future; the expected benefits of our collaborations, the expanded capability 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 our 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; and the potential for CAR-T and CAR-Tregs to effectively treat 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, enrollment and completion of clinical trials, whether clinical trial results will validate and support the safety and efficacy of Sangamo's therapeutics, risks and uncertainties related to preliminary data, whether the preliminary data from ongoing clinical trials and will be representative of final results, whether the final results from ongoing clinical trials will validate and support the safety and efficacy of SB-525, ST-400 and our other product candidates, and the reliance on partners and other third-parties to meet their obligations. 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. These risks and uncertainties are described more fully in Sangamo's Quarterly Report on Form 10-Q for the three months ended March 31, 2019 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 obligation to update such information except as required under applicable law.

Sangamo THERAPEUTICS

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

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

Gene Therapy



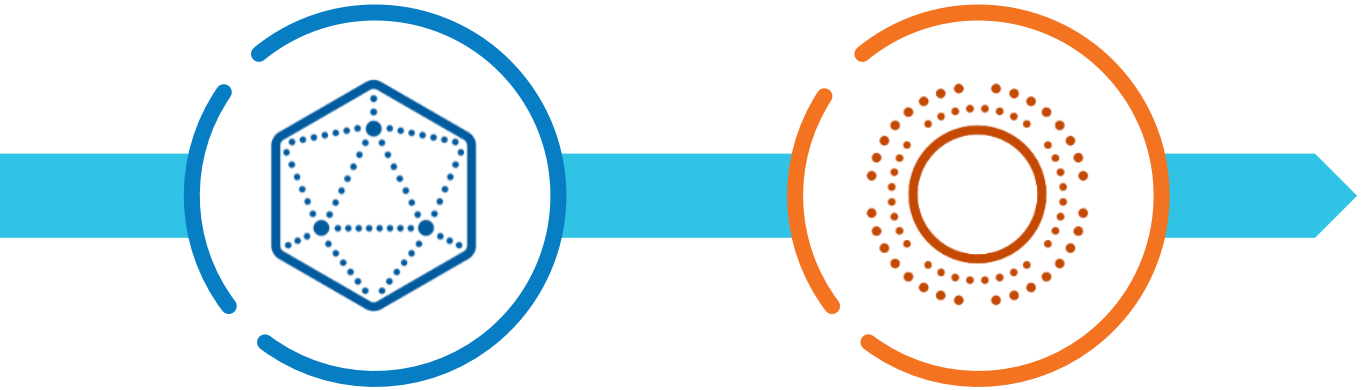
Gene therapy provides tractable, valuable near-term opportunities

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

Ex Vivo

Gene Therapy

Gene-Edited Cell Therapy



Gene therapy provides tractable, valuable near-term opportunities

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

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

Ex Vivo

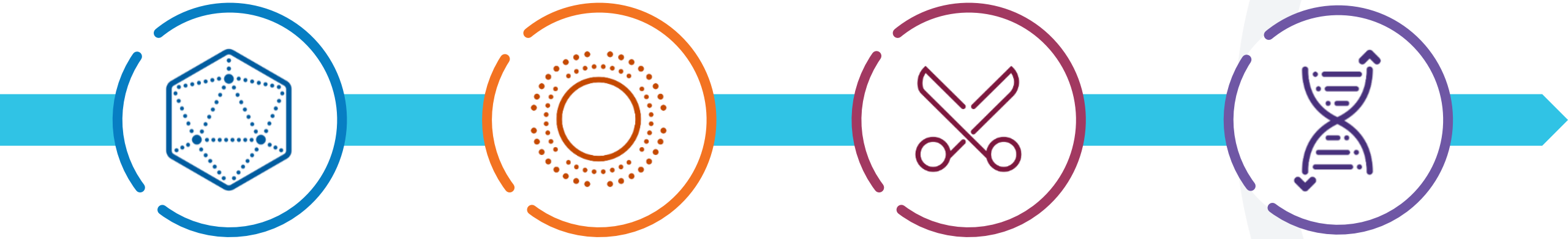
In Vivo

Gene Therapy

Gene-Edited Cell Therapy

Genome Editing

Gene Regulation



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* gene editing and gene regulation

Sangamo's genomic medicines encompass a breadth of technical approaches and diverse pipeline assets

Ex Vivo

In Vivo

Gene Therapy

SB-525: Hemophilia A
ST-920: Fabry disease
Undisclosed targets

Gene-Edited Cell Therapy

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

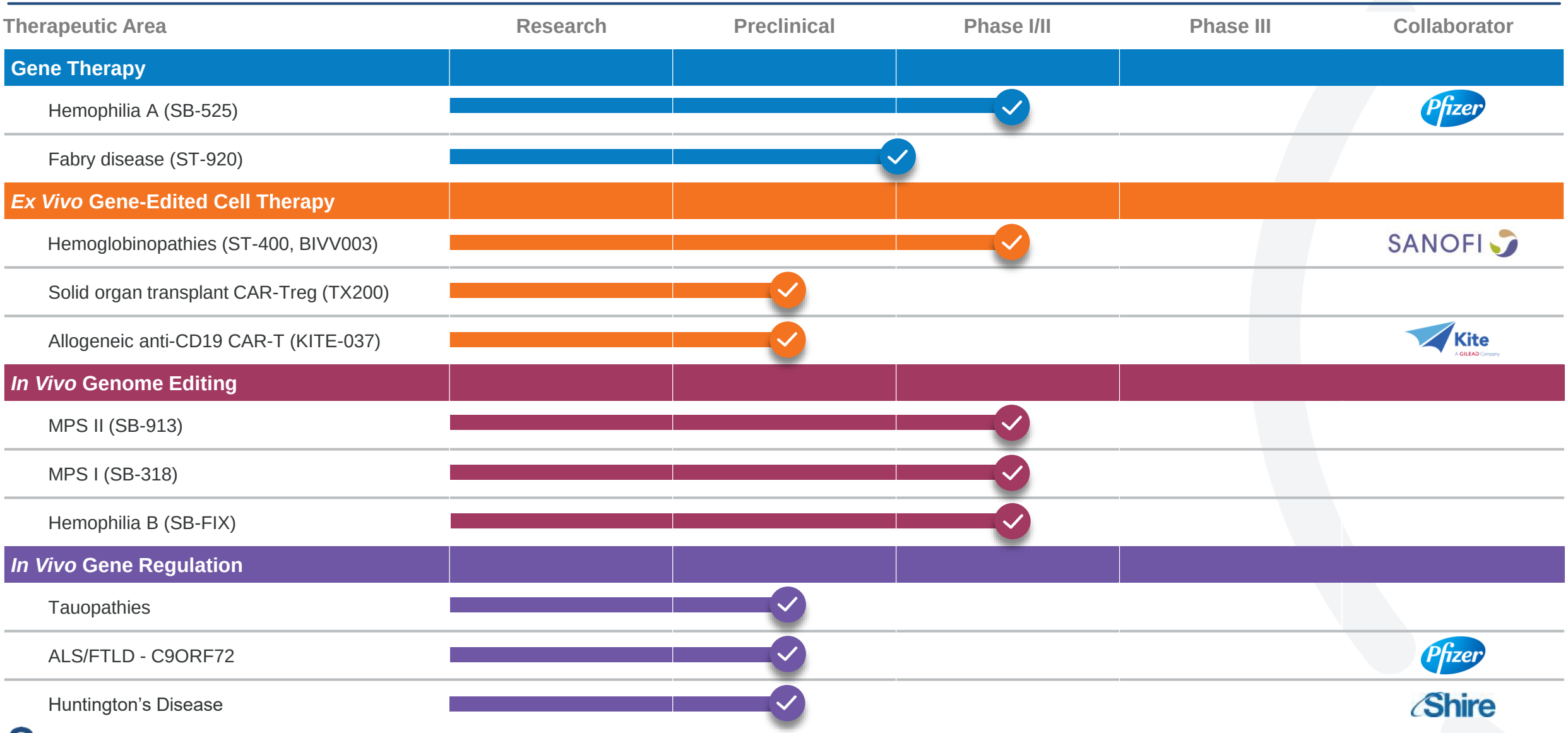
Genome Editing

SB-913: MPS II
SB-318: MPS I
SB-FIX: Hemophilia B
Undisclosed targets

Gene Regulation

Tauopathies
C9ORF72-linked ALS/FTLD
Huntington's disease
Undisclosed targets

Robust pipeline of genomic medicines in clinical and preclinical stages of development



Sangamo THERAPEUTICS

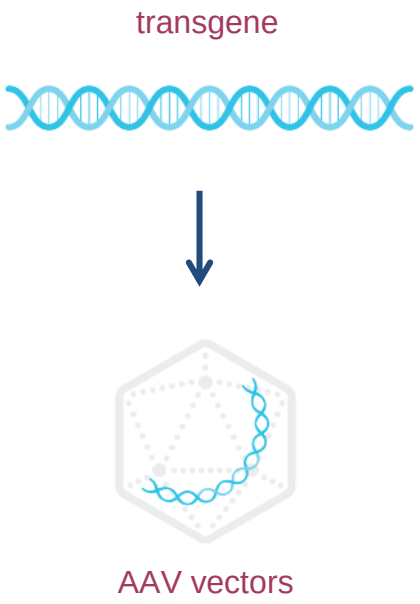
Gene Therapy

SB-525: Hemophilia A

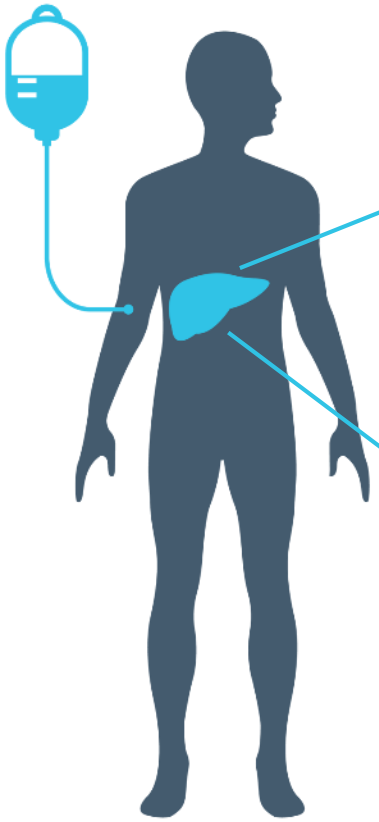
ST-920: Fabry disease

Sangamo's gene therapy platform: potential for potent therapeutic solutions for monogenic diseases

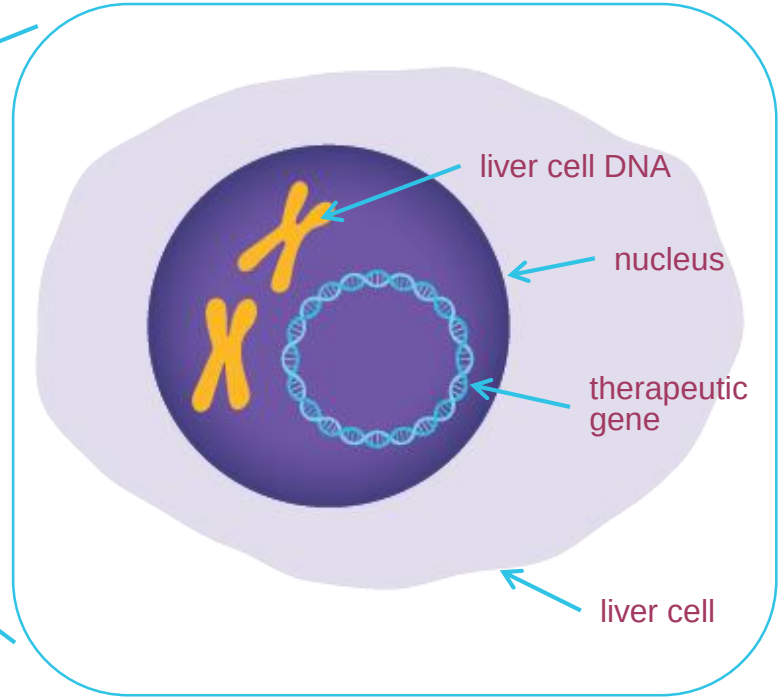
Packaging into AAV vectors



Delivery



To the liver



SB-525, gene therapy for hemophilia A

Phase I/II Open Label Study

Dose Escalation Complete

Cohort 1	Cohort 2	Cohort 3	Cohort 4
9e11 vg/kg	2e12 vg/kg	1e13 vg/kg	3e13 vg/kg

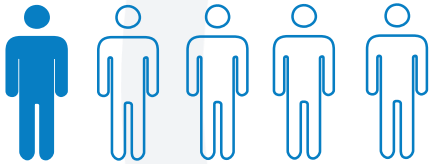
(Patients did not receive prophylactic steroids)

March 2019 SMC Review

- Expand 3e13 vg/kg cohort

Next steps

- Enroll up to 5 additional patients



3e13 vg/kg

FDA
- Orphan Drug
- Fast Track

- Orphan Medicinal Product

IND open

Goals

Patient safety | FVIII activity | Reduction of bleeding events | Reduction of factor replacement use

Sangamo THERAPEUTICS | Pfizer

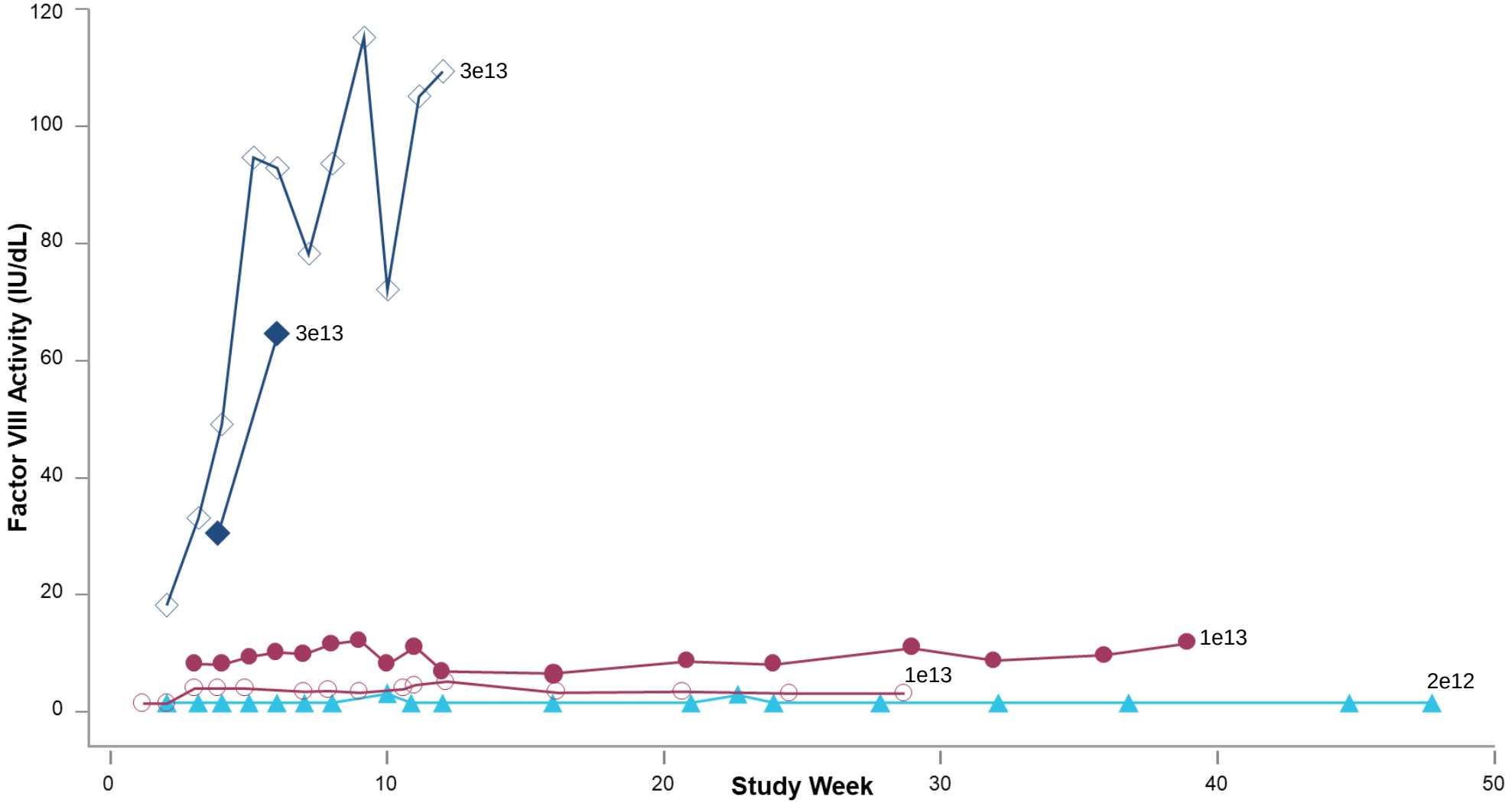
SB-525: Safety summary – adverse events related to study drug*

Event	9x10^11 vg/kg (N=2)	2x10^12 vg/kg (N=2)	1x10^13 vg/kg (N=2)	3x10^13 vg/kg (N=2)	Overall (N=8)
Tachycardia **(Gr 1)**	0	0	0	1	1
Fatigue **(Gr 1)**	0	0	0	1	1
Pyrexia **(Gr 2)**	0	0	0	2	2
ALT increased **(Gr 1)**	0	2	0	1	3
Myalgia **(Gr 1)**	0	0	0	1	1
Hypotension **(Gr 3)**	0	0	0	1	1

number of subjects with each event

*Data were announced April 2, 2019

SB-525: Factor VIII activity – chromogenic, linear scale*



Data for Patients 1, 2 and 3 are not displayed due to their continued use of recombinant FVIII replacement

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

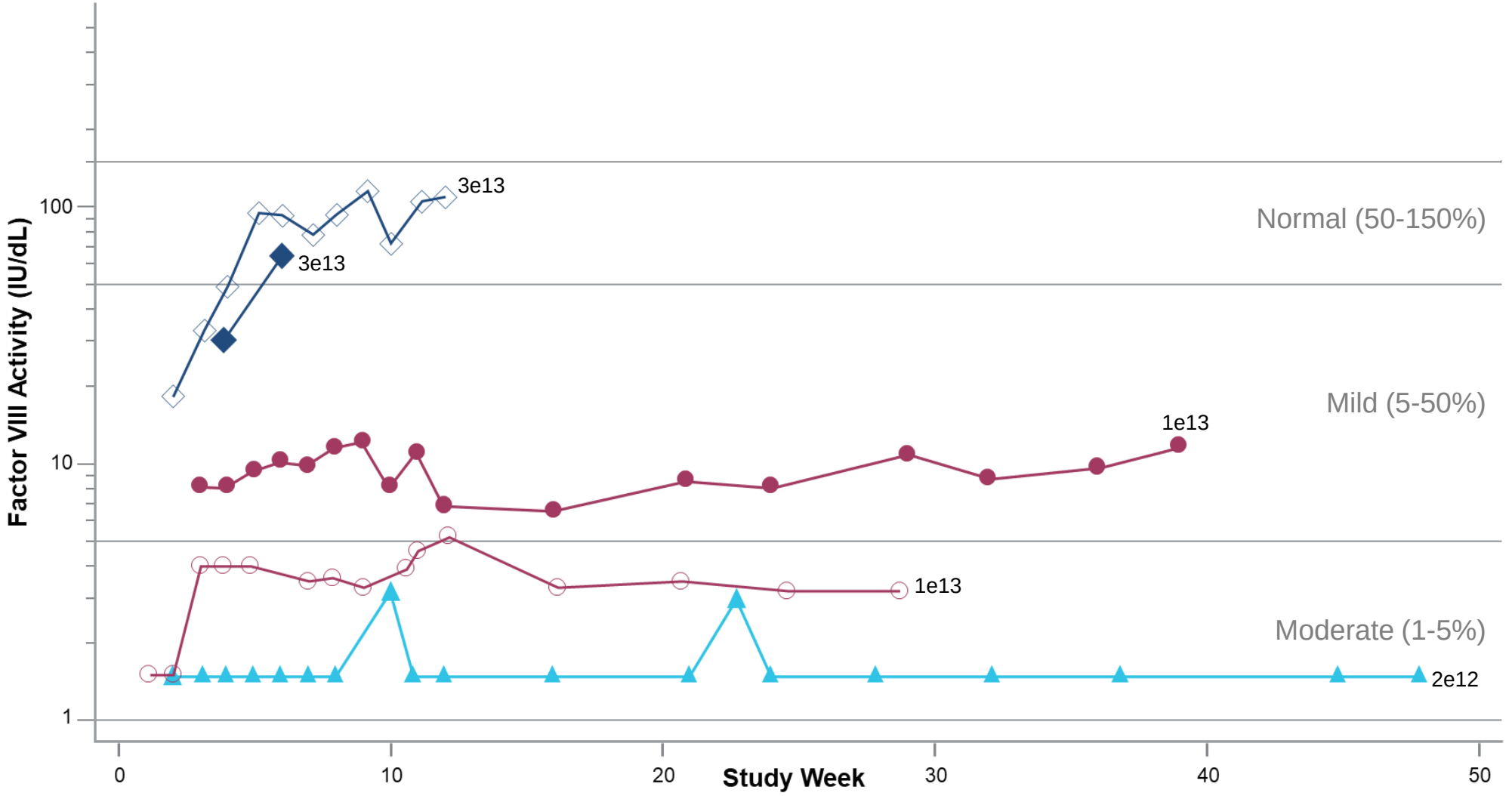
Same color indicates same cohort

Patient 4 Week 52 value excluded as values indicate an artifact, as both one-stage and chromogenic assay values are identical only after factor intake. New samples are being collected to confirm

Program: FVIII-Coagulation_ReadOut.sas Run Date: 27MAR19 by mtian

Data were announced April 2, 2019

SB-525: Factor VIII activity – chromogenic, log scale*



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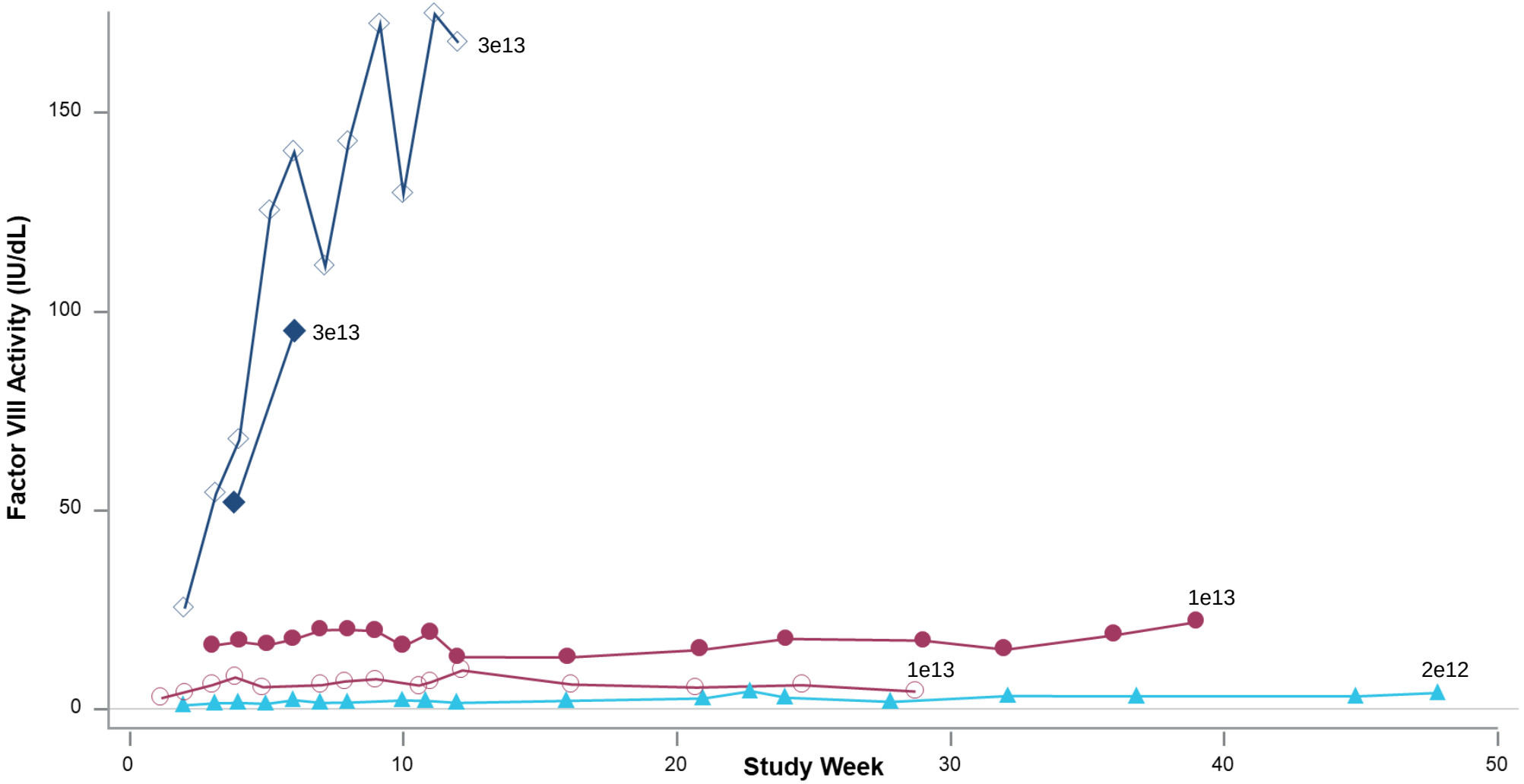
Program: FVIII-Coagulation_ReadOut.sas Run Date: 27MAR19 by mtian

*Data were announced April 2, 2019

SB-525: Factor VIII activity – one-stage clotting, linear scale*



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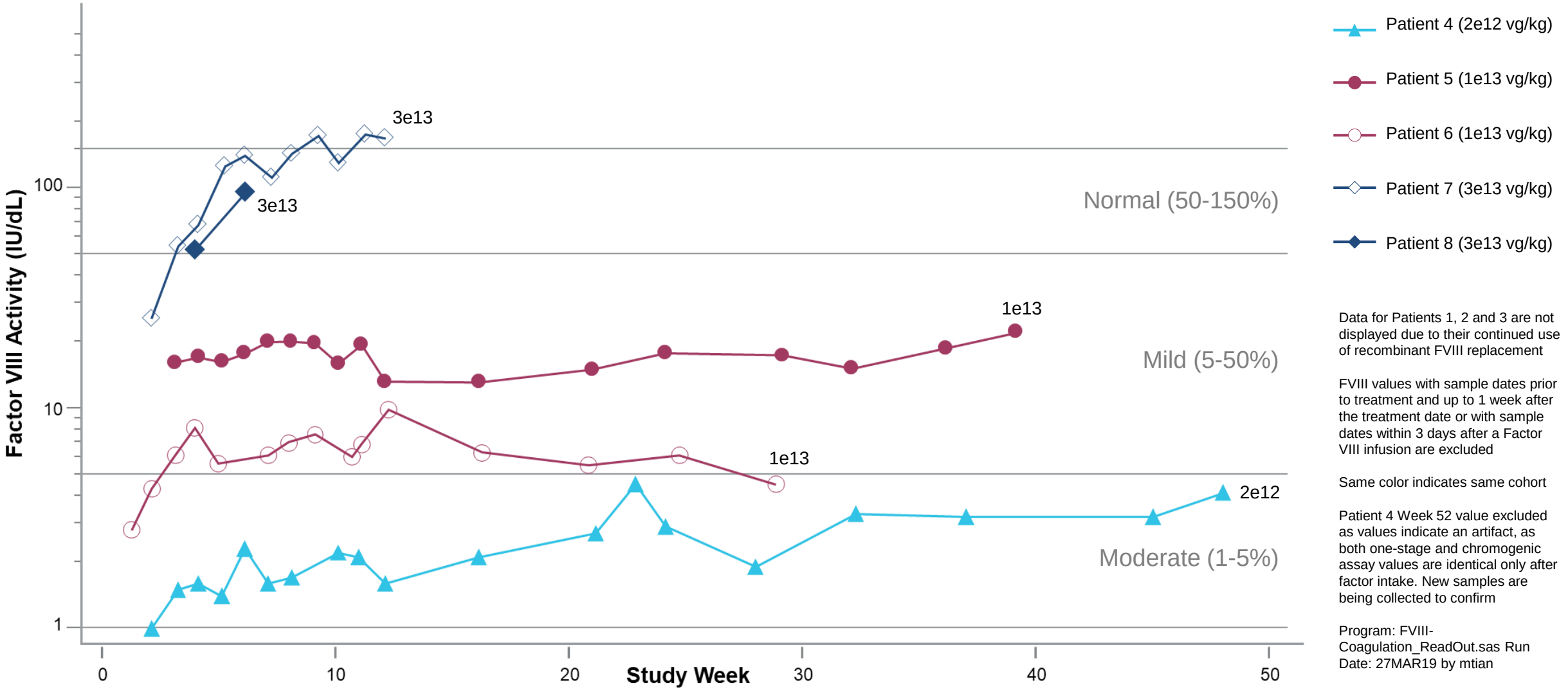

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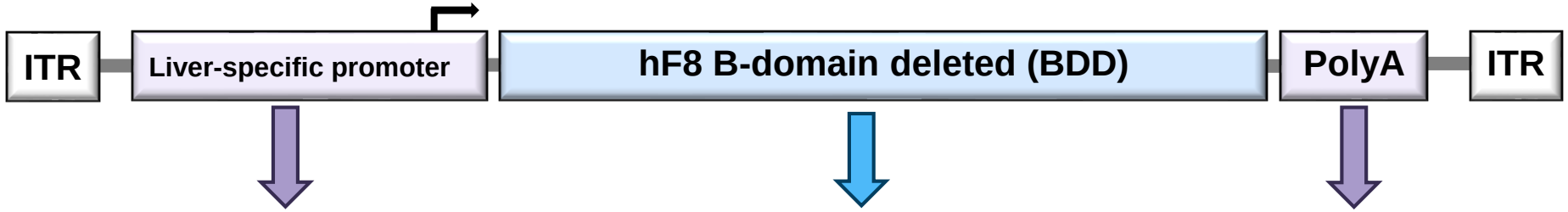
*Data were announced April 2, 2019

SB-525: Factor VIII replacement usage reduction*

Subject (dose vg/kg)	Follow-up	Spontaneous bleeds	Regimen before injection	Total infusions since injection post prophylactic period
8 (3e13)	Week 6	0	3-4/week	0
7 (3e13)	Week 12	0	2/week	0
6 (1e13)	Week 28	0	1/3 weeks	0
5 (1e13)	Week 40	2	3/week	8
4 (2e12)	Week 48	3	3/week	9

*Data were announced April 2, 2019

Experience with AAV manufacturing and gene construct design can be translated across our gene therapy platform



Promoter module modifications

- Assembled different permutations of liver-specific promoter elements
- A systematic mutational design approach was used to improve regions of the promoter module

Transgene modifications

- Optimized the F8 cassette

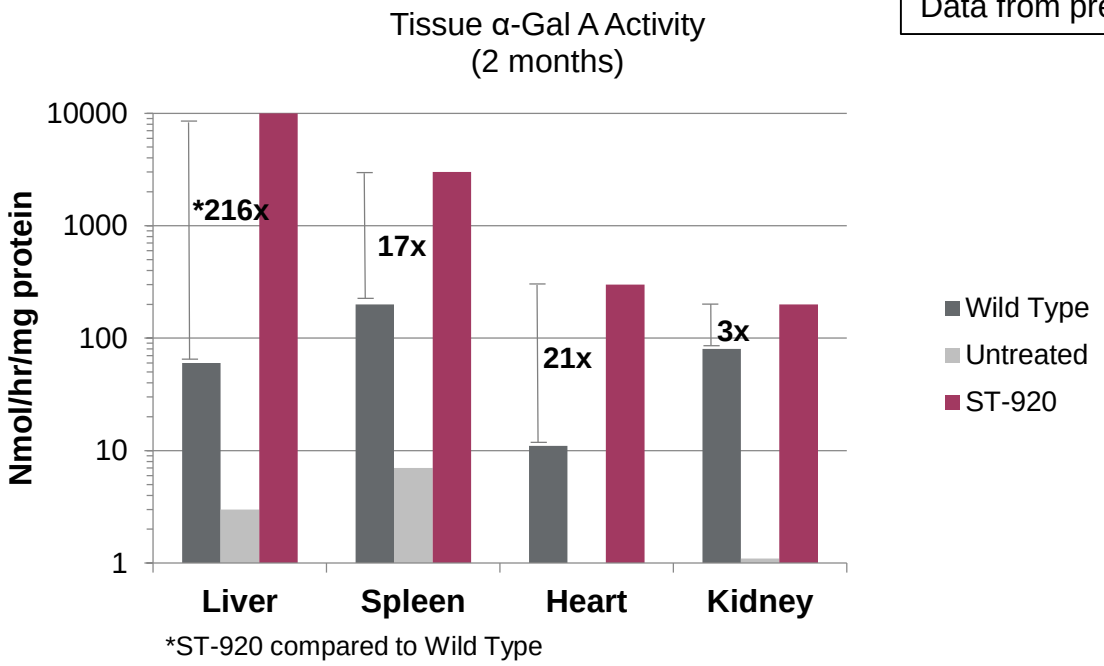
Other modifications

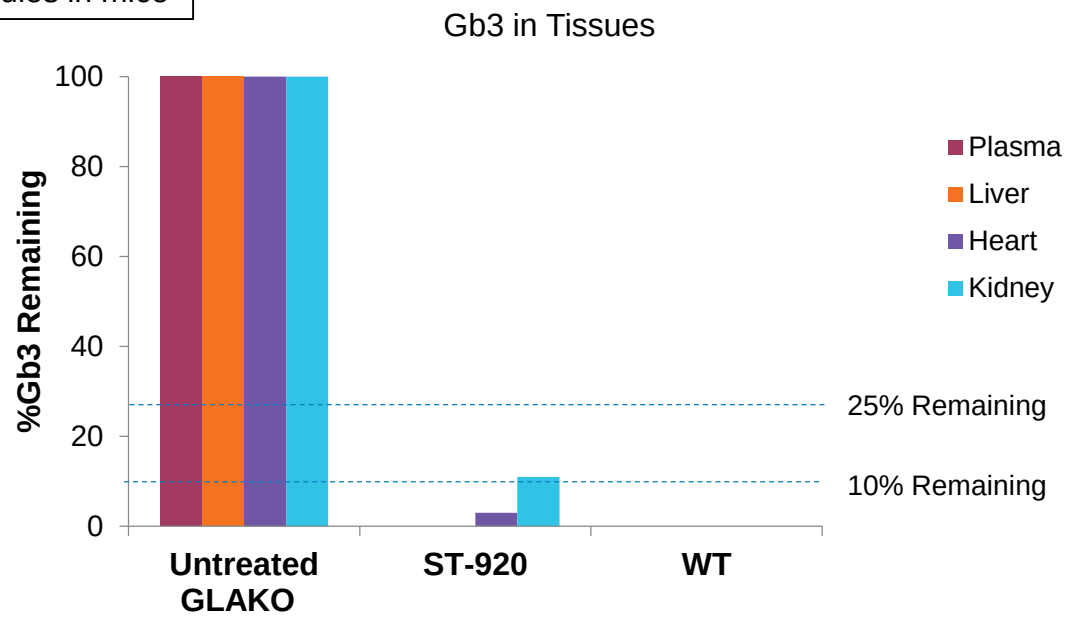
- Identified minimal synthetic polyA
- Removed unnecessary nucleic acids to reduce size
- Optimized sequences outside transgene

ST-920, gene therapy for Fabry disease
Designed to express α-Gal A enzyme

- 5,000 – 6,000 Fabry patients in US / EU; most diagnosed as adults
- Weekly and bi-weekly ERT infusions (standard of care) may not clear all substrate from secondary organs
- IND accepted by FDA. ST-920 clinical trial initiation expected in 2019

Data from preclinical studies in mice





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

Gene therapy: upcoming milestones

SB-525: hemophilia A

- enroll 3e13 vg/kg expansion cohort
- present data at an upcoming scientific meeting

ST-920: Fabry disease

- clinical trial initiation in 2019

Ex Vivo Gene-Edited Cell Therapy

ST-400: Beta thalassemia

BIVV003: Sickle cell disease

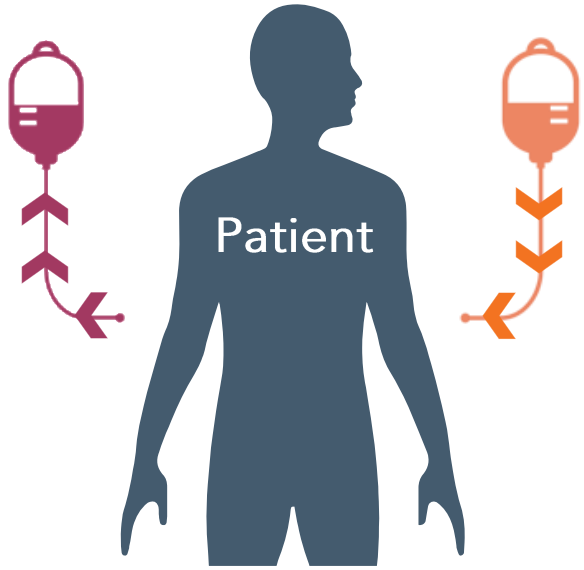
TX200: Solid Organ Transplant (CAR-Treg)

KITE-037: Allogeneic anti-CD19 CAR-T

Autologous, *ex vivo* gene-edited cell therapy product candidates for beta thalassemia and sickle cell disease

Apheresis
Isolate CD34+ Hematopoietic stem cells from patient's blood

1

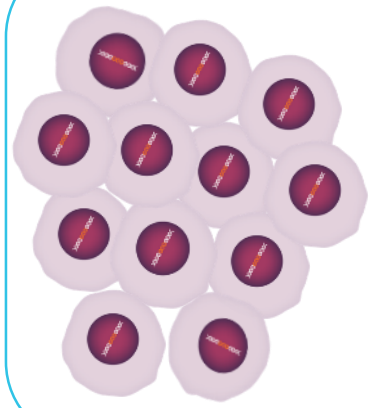


4

Infusion
ST-400 stem cells are infused back to the patient (with myeloablative pre-conditioning to promote engraftment)

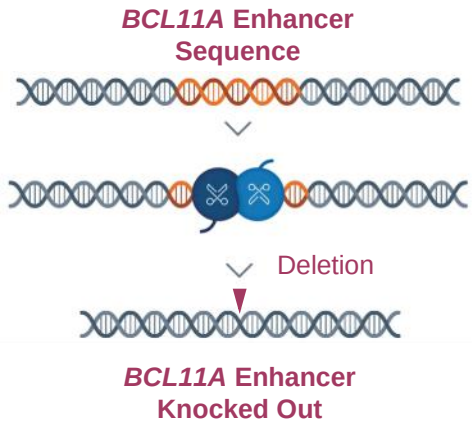
Functional RBCs with fetal hemoglobin produced from ST-400 stem cells

cGMP Manufacturing Facility



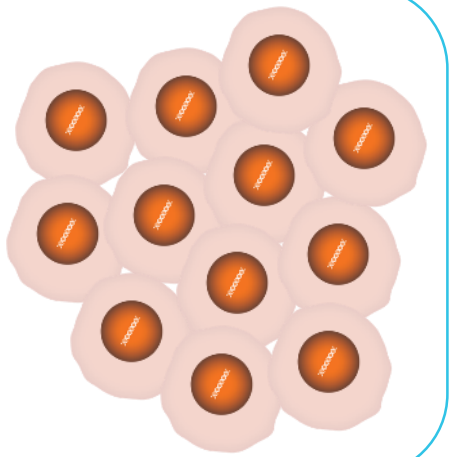
2

Gene editing
Manufacture ST-400 stem cells via transient, non-viral delivery of ZFN mRNA



3

Harvest
ST-400 stem cells are cryo-preserved and shipped to treatment center



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ST-400, gene-edited cell therapy for beta thalassemia

Phase I/II Open Label Study

Patient Enrollment Ongoing

Potential Advantages

- Leverages naturally-occurring, protective mechanism to increase fetal-hemoglobin to reduce or potentially eliminate blood transfusions
- Highly efficient, precise gene editing
- Non-viral delivery of ZFNs

Next steps

- Continue patient enrollment

IND open

Goals

- Patient safety
- Successful engraftment
- Fetal hemoglobin (HbF) production
- Reduction / elimination of transfusions

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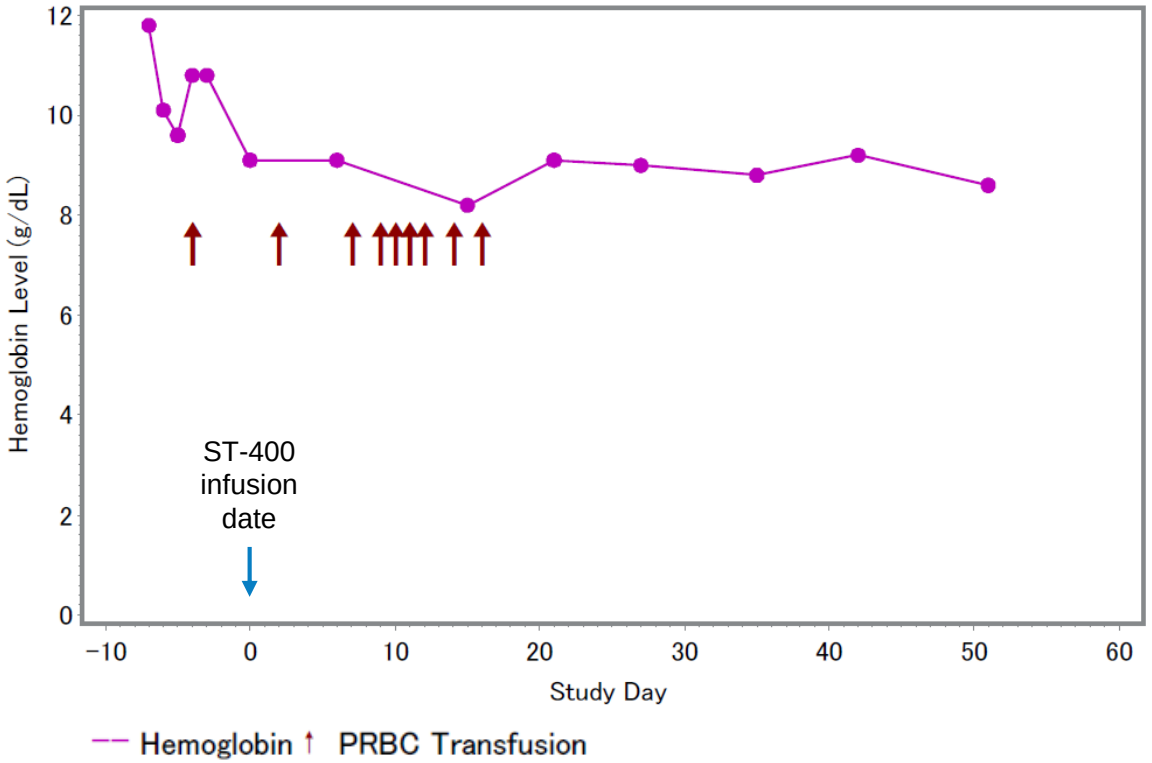
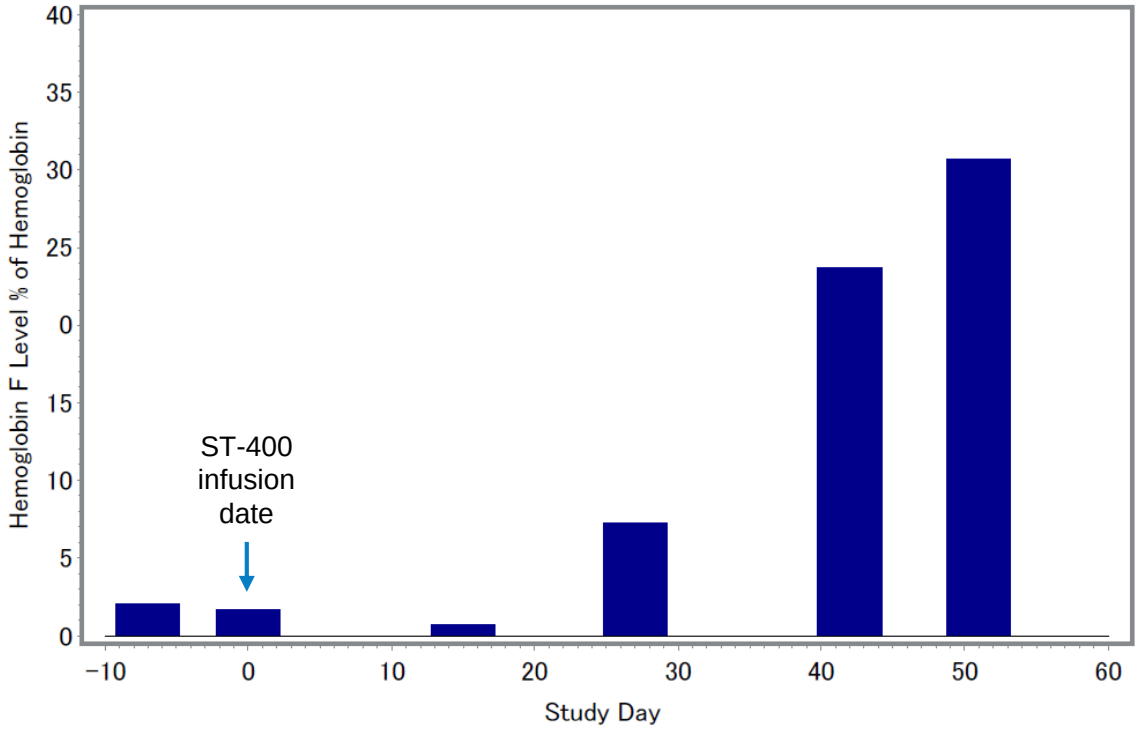
ST-400: Phase 1/2 Thales study summary

- ST-400 product candidate characteristics:
  - Non-viral delivery of ZFNs
  - *Ex Vivo* cellular editing of CD34+ HSCs
  - Disruption of *BCL11A* enhancer intended to upregulate endogenous fetal Hb production in RBCs
- First patient has most severe form of transfusion-dependent beta thalassemia (β^0/β^0)
- During ST-400 infusion, patient experienced a serious adverse event (allergic reaction) that rapidly resolved with medical management
- Patient 1 demonstrated neutrophil and platelet recovery within two and four weeks of infusion, respectively, indicating successful reconstitution of ST-400 hematopoiesis following conditioning
- Indels were detected in circulating white blood cells, indicating successful editing of *BCL11A* erythroid specific enhancer

ST-400: Total hemoglobin and fetal hemoglobin in a β^0/β^0 beta thalassemia patient at 7 weeks post-transfusion*



Total Hb levels of ~9 g/dL



Fetal Hb levels of ~31%

The patient received several PRBC transfusions for approximately two weeks after the ST-400 infusion

Enrollment in the THALES study is ongoing. Sangamo expects to present longer-term ST-400 data in Q4 2019, including results from additional patients. Until that time, Sangamo is not planning to report additional clinical data from the program.

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*Seven-week data were announced April 2, 2019

Cell therapy platform

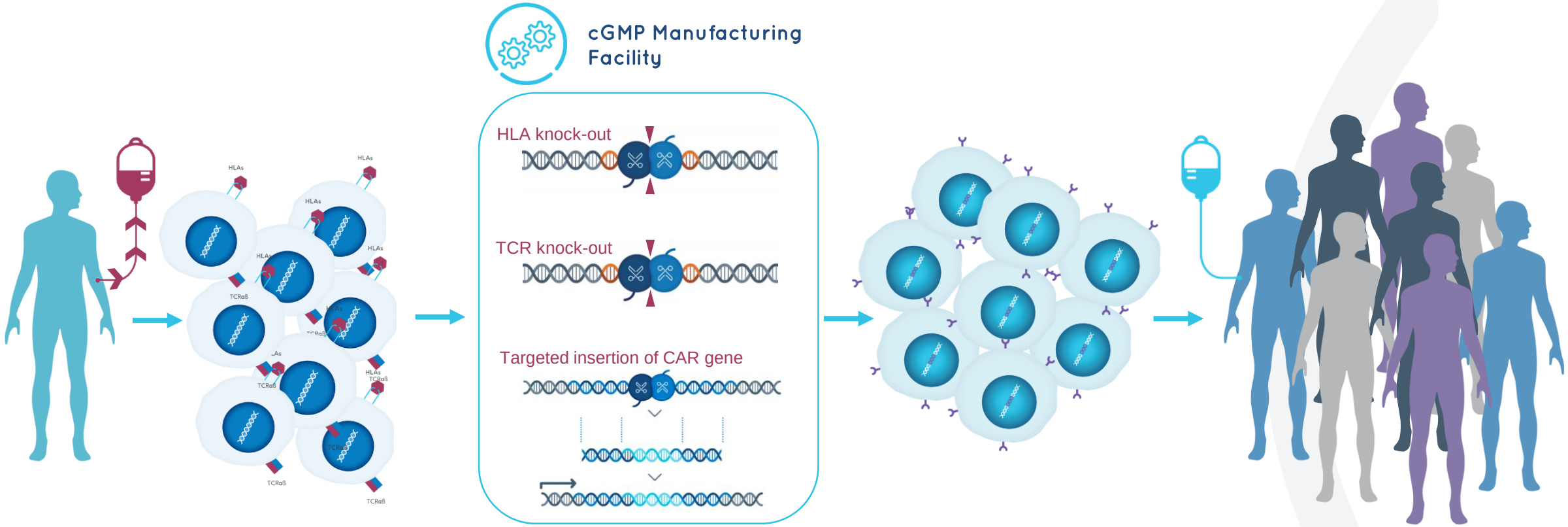
ST-400: beta thalassemia

BIVV003: sickle cell disease

CAR-T therapy for oncology

CAR-Tregs for immunology

Manufacturing allogeneic T-cell therapies with ZFNs



1 Apheresis (Healthy Donor)

Isolate T-cells from a healthy donor's blood

2 T-cell Manufacturing

Transient, non-viral delivery of ZFN mRNA to manufacture universal CAR-T cells via single-step, multiplexed gene editing

3 Harvest & Storage

Universal CAR-T cells are harvested, cryo-preserved and stored in a secure cell bank

4 Infusion (Patients)

Universal, off-the-shelf CAR-T cells are infused into new patients, on-demand

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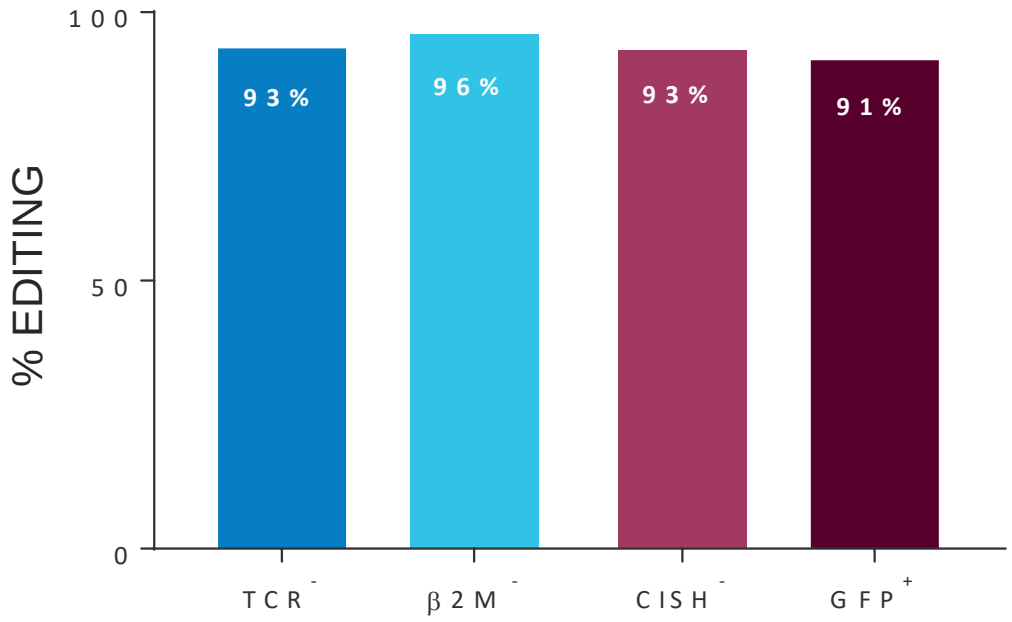
Simultaneous multiplex editing efficiencies with 3x ZFN KO and 1x targeted integration

POTENTIAL APPLICATION:
Universal T cells with checkpoint gene knock-out

SINGLE STEP EDITING

ZFN Knock-out
- TCR (TRAC)
- HLA-class I (β2M)
- CISH (checkpoint gene)

Targeted Insertion
- GFP (into TRAC)

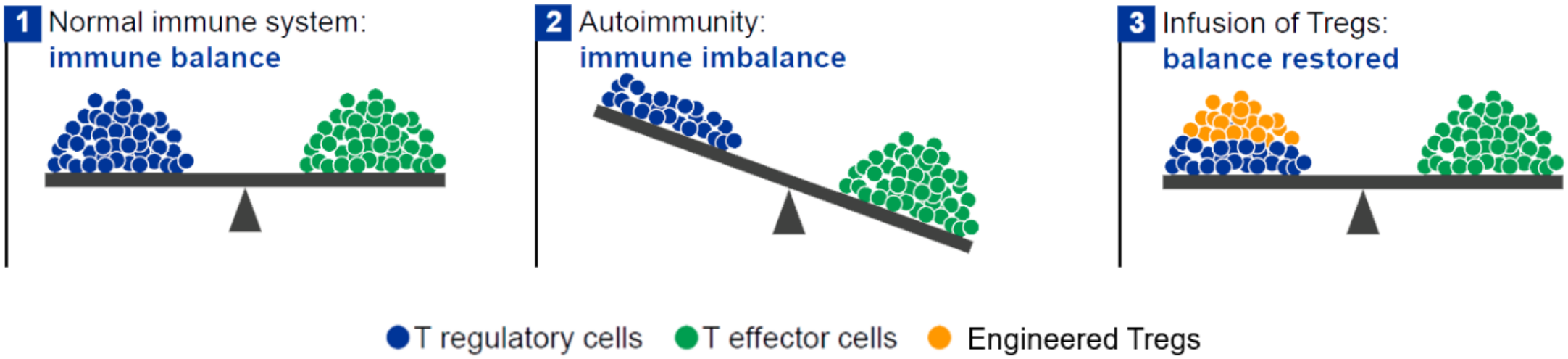


76% of cells have all 4 edits

*This work was conducted with a generic CAR-T sequence and is distinct from Sangamo's current collaboration with Kite, a Gilead company

Regulatory T cells (Tregs): a new class of cell-based therapeutics

- Tregs maintain immune homeostasis at various tissues
- The suppressive function of Tregs inhibits mounting inflammatory responses. i.e. Tregs confer tolerance
- Tregs can be used as a cell-based therapy across various applications where induction of immune tolerance can restore homeostasis and counter disease-state
  - e.g. prevention of transplant rejection, treatment of a multitude of autoimmune diseases



CAR-Tregs have the potential to generate antigen and tissue specific cell therapy products for immunology

Cell Product Characteristics

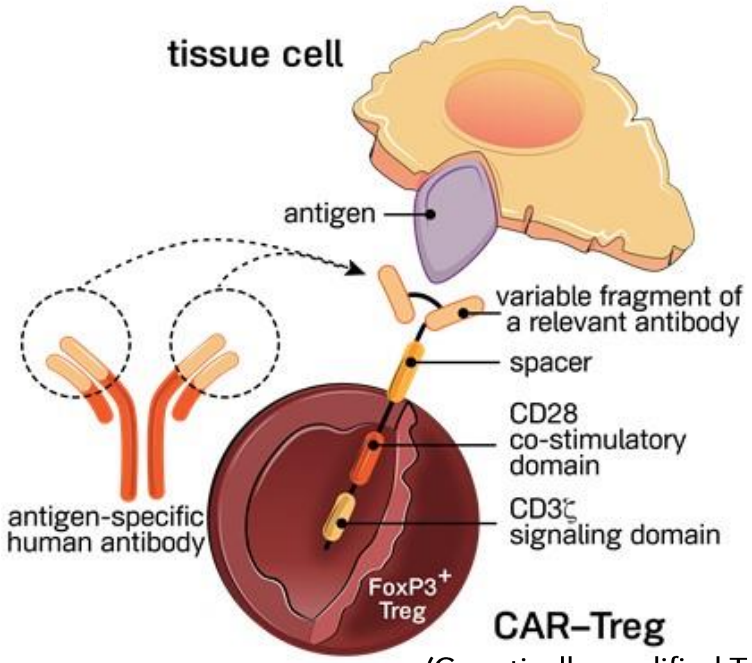
Engineered CAR-Tregs

Antigen localized: tissue-specific activity

Antigen activated: better controlled cell product and dosing

Robust and scalable processes

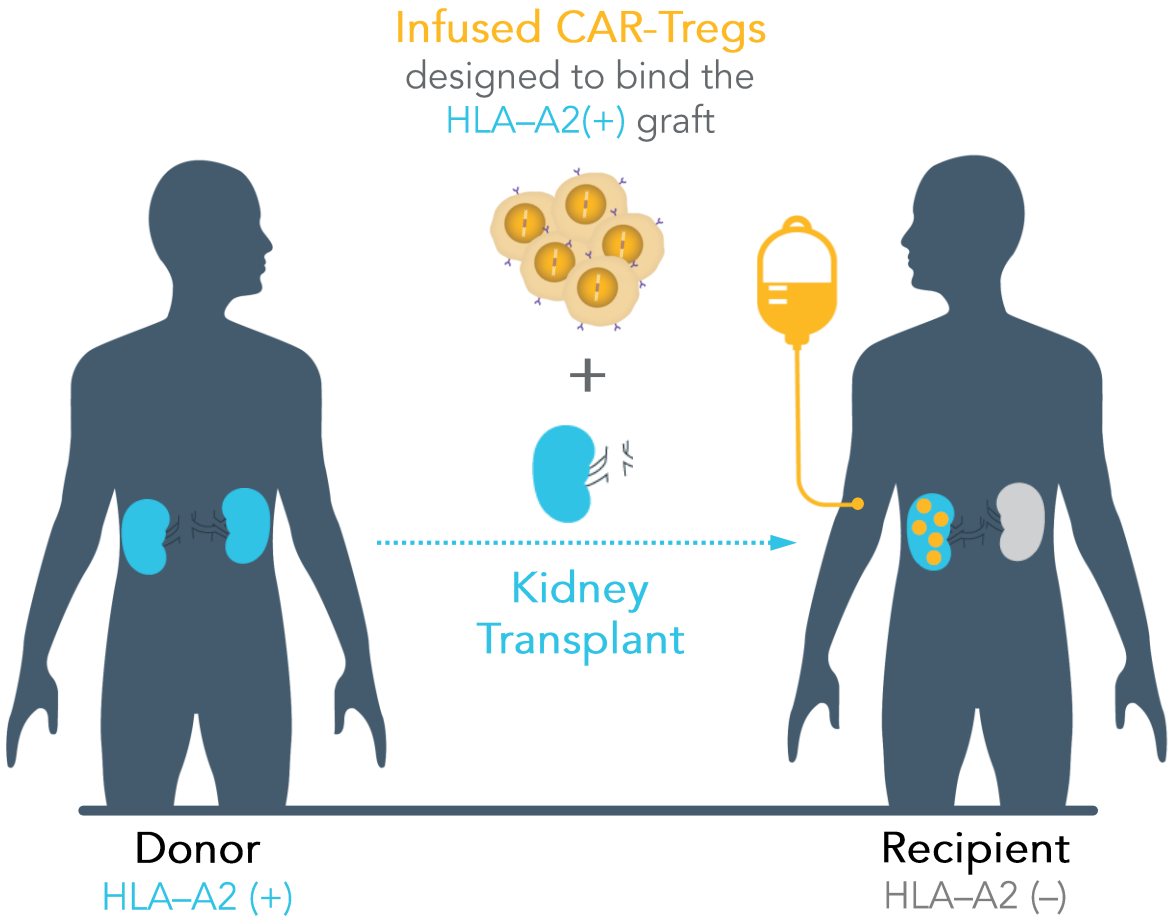
Antigen-specific CAR-Treg



(Genetically modified Treg)

TX200: HLA-A2 CAR-Treg for solid organ transplant

Induction of site-specific immune tolerance



- HLA-A2 antigen on graft is recognized by CAR-Treg cells
- Activated CAR-Treg cells exert **site specific** suppressive function
- Goal: Achieve tolerance and long-term protection of graft

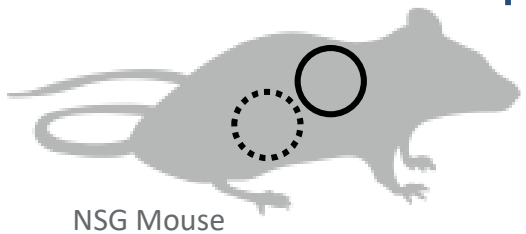
Phase 1/2 clinical trial initiation expected in 2019

HLA-A2 CAR-Tregs achieve precise and durable targeting of skin graft in a mouse model

THE UNIVERSITY OF BRITISH COLUMBIA

CDRD

Skin Transplants

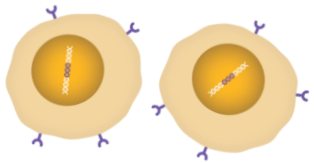


NSG Mouse

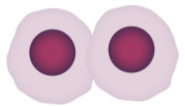
— HLA–A2(–)

····· HLA–A2(+)

I.V. Injection



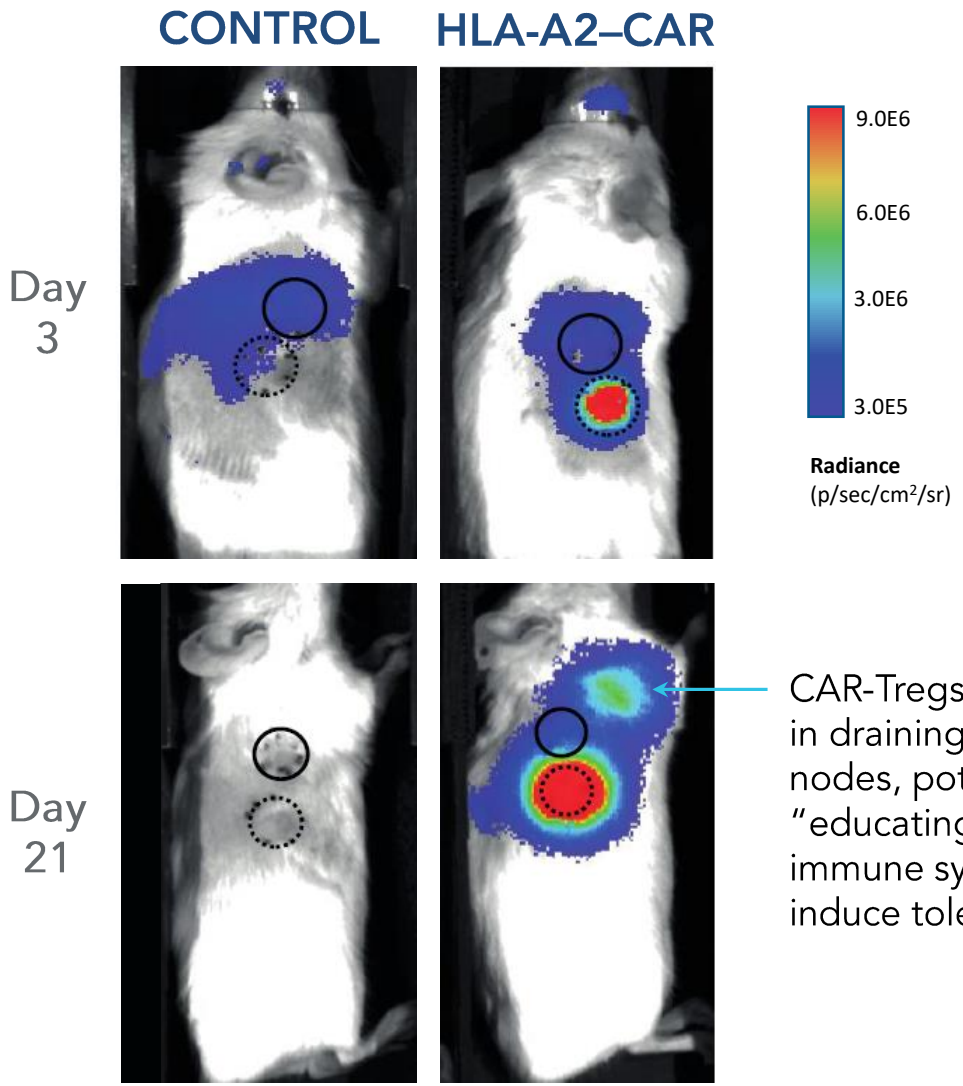
CAR(+) Luciferase(+) Treg Cells



Peripheral Blood Mononuclear Cells

Imaging

CAR-Tregs home to intended HLA-A2+ site only



CAR-Tregs present in draining lymph nodes, potentially "educating" the immune system to induce tolerization

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Data from Megan Levings, PhD, University of British Columbia

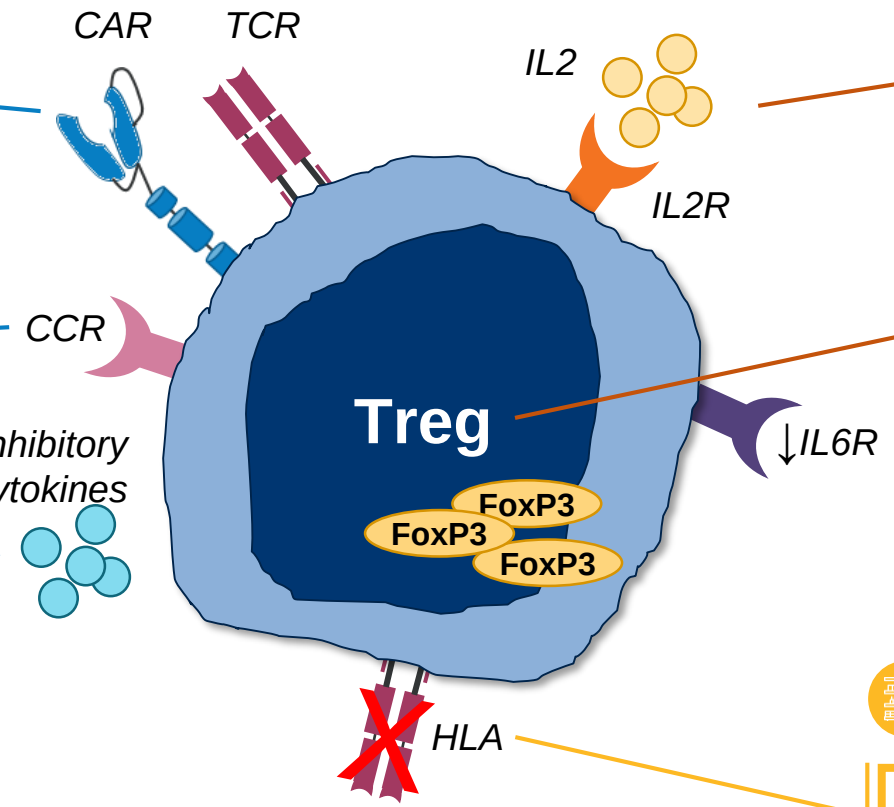
Sangamo plans to develop next generation CAR-Treg products with ZFN multiplex editing

Increase Efficacy + Potency

Target tissue-specific antigen(s) w/CAR

Promote localization to disease site(s) with chemokine receptors

Bolster immunosuppressive function



Increase Persistence + Stability

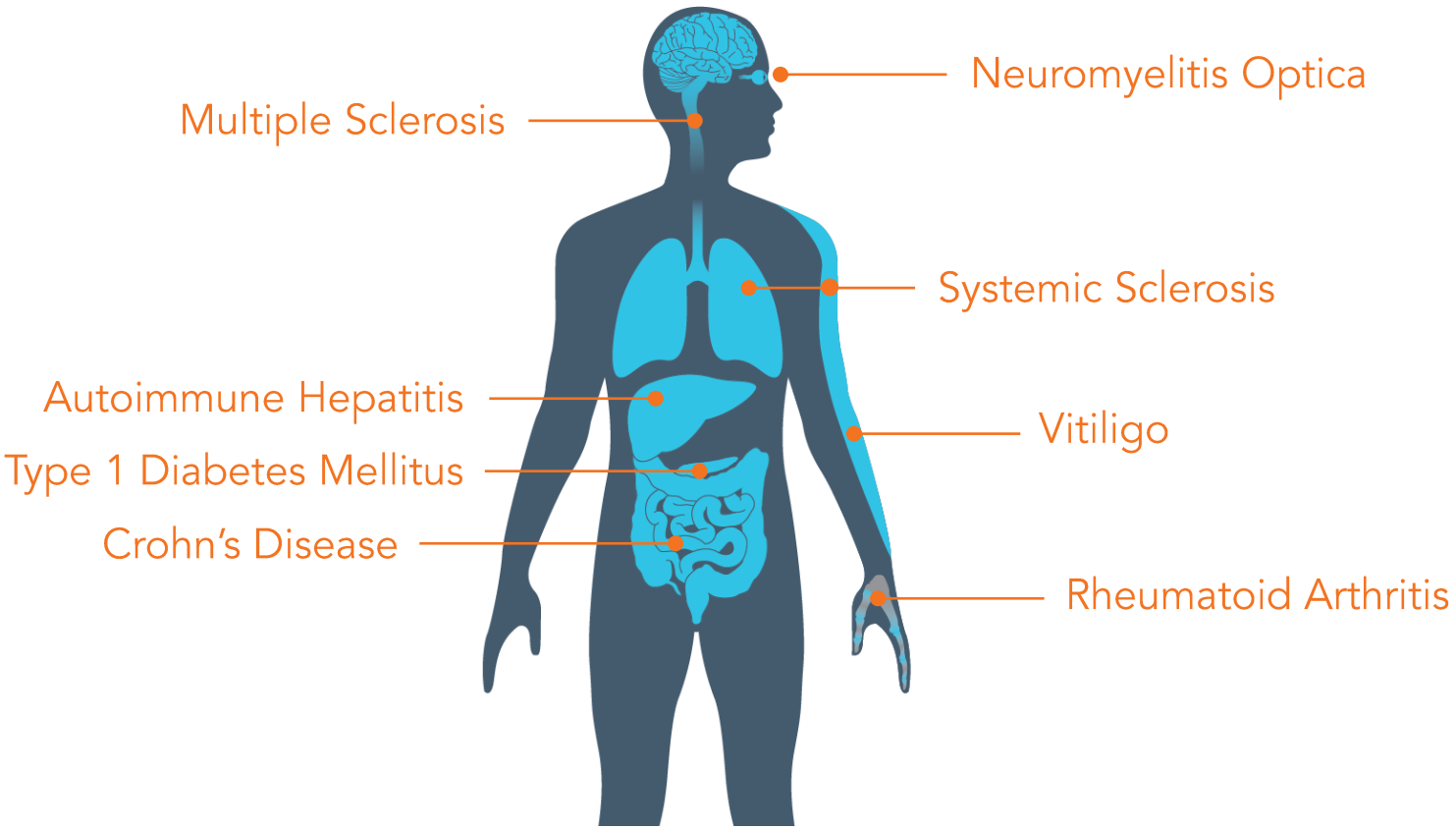
Increase Treg proliferation and durability

Improve CAR-Treg stability and safety

Off-The-Shelf Approach

Genetic engineering to allow allogeneic application of CAR-Tregs

Significant unmet medical need in autoimmune diseases



CAR-Treg cell therapies could address several autoimmune diseases with large patient populations and high unmet need

Ex Vivo gene-edited cell therapy: upcoming milestones

ST-400: beta thalassemia

- complete patient enrollment
- present longer-term data (4Q 2019)

BIVV003: sickle cell disease

- complete patient enrollment (Sanofi)

TX200: solid organ transplant

- file CTA

KITE-037: Allogeneic anti-CD19 CAR-T

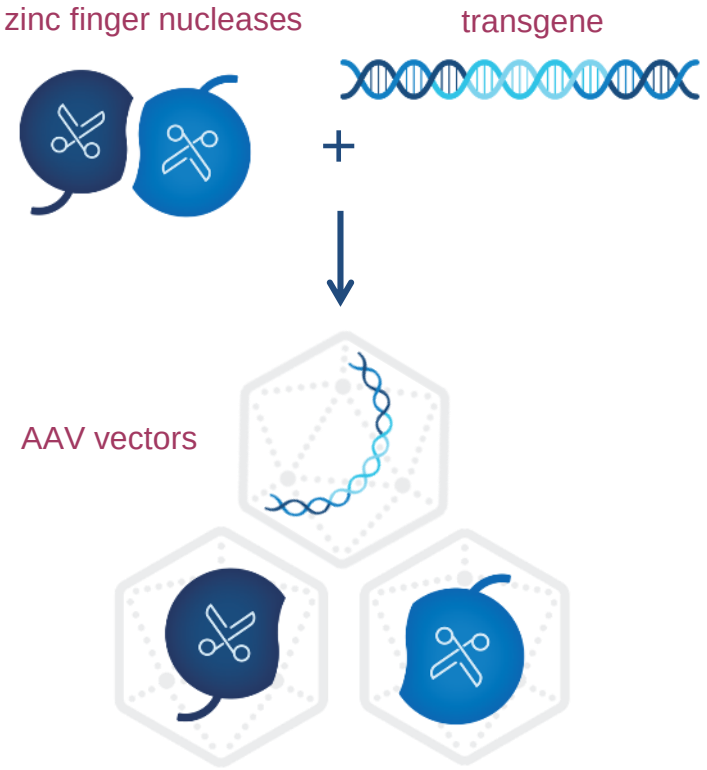
- initiate clinical trial in 2020 (Kite-Gilead)

In Vivo Genome Editing

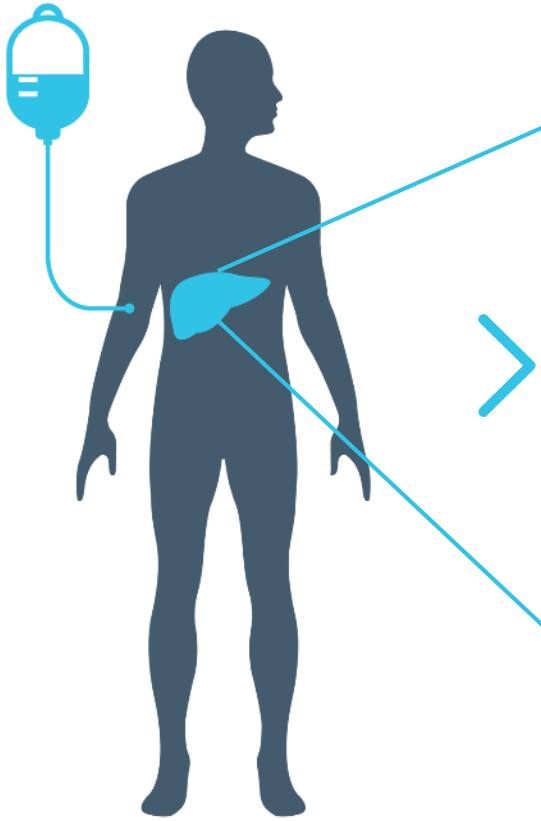
- SB-913: MPS II
- SB-318: MPS I
- SB-FIX: hemophilia B

In Vivo genome editing: harnessing the albumin locus in the liver

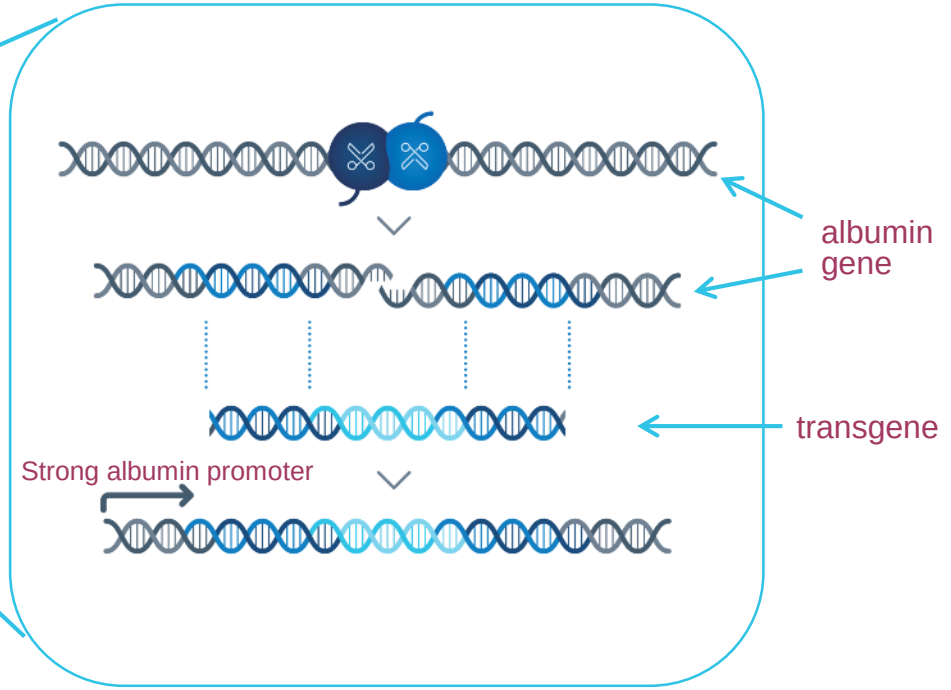
Packaging into AAV vectors



Delivery



In the liver



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In Vivo genome editing: SB-913 (MPS II), SB-318 (MPS I) and SB-FIX (hemophilia B)

- Phase 1/2 clinical trials evaluating these programs are ongoing and data will continue to accumulate throughout 2019. No additional patients will receive the first-generation ZFNs
- As previously announced, Sangamo plans to initiate a new SB-913 clinical trial in 2H 2019 evaluating second-generation ZFNs for MPS II
- Based on data from second-generation ZFN study, Sangamo will make Phase III decision for the SB-913 (MPS II) program in 2020 and determine next steps for the SB-318 (MPS I) and SB-FIX (hemophilia B) programs

Second-generation ZFN enhancements improve precision, efficiency and specificity of *in vivo* genome editing

ZFN mRNA Transcription

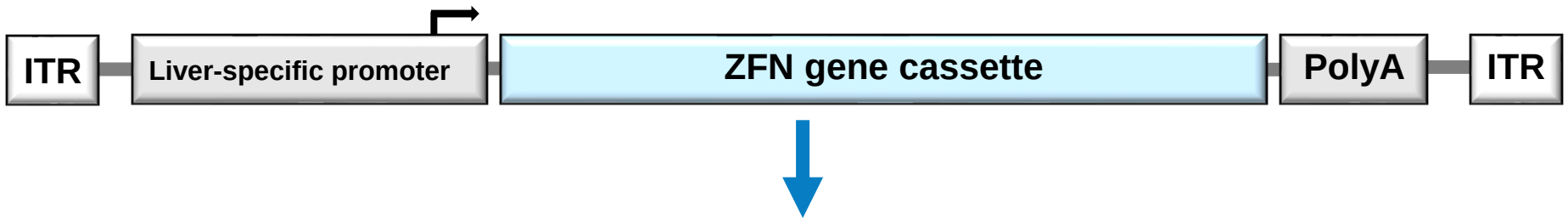
ZFN Protein Translation

ZFN Protein Nuclear Import

ZFN Binding and Cleavage

Transgene Integration

Modifications to the AAV-ZFN expression construct resulting in increased ZFN activity



Transgene Modifications

- Addition of a 5'UTR enhances translation
- Addition of an N-terminal peptide increases expression levels
- Addition of an expression enhancer increases ZFN mRNA stability and translation

Inclusion of transcriptional elements each independently lead to an increase in ZFN activity, resulting in overall greater ZFN protein expression

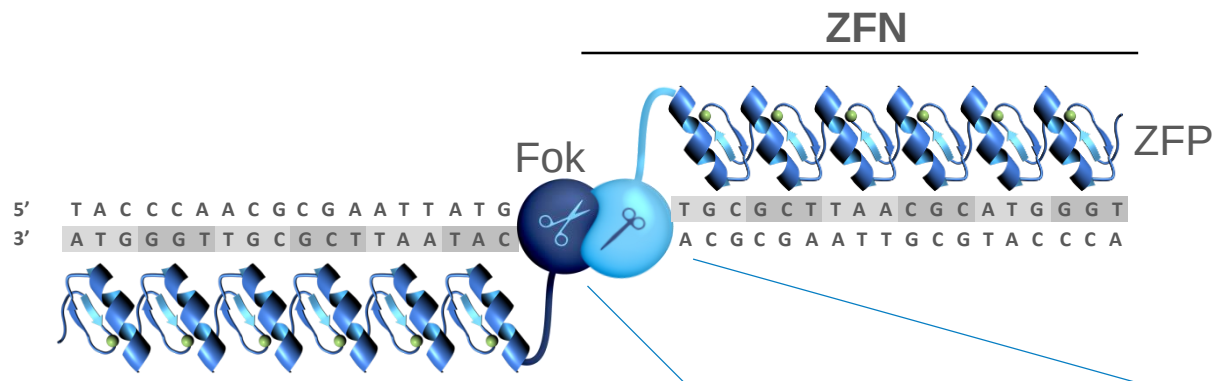
Research & Development

Enhancements to ZFN specificity

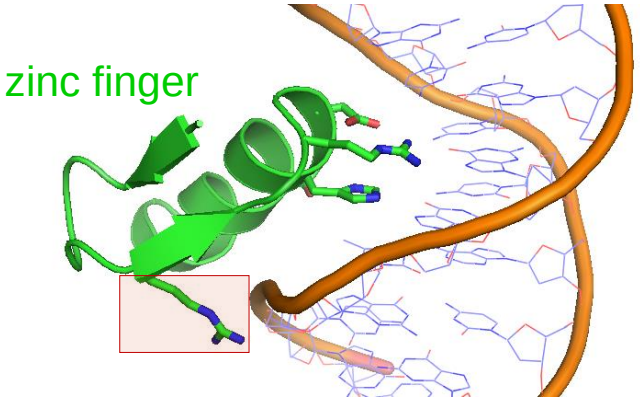
C9ORF72-linked ALS/FTLD

Tauopathies and Huntington's disease

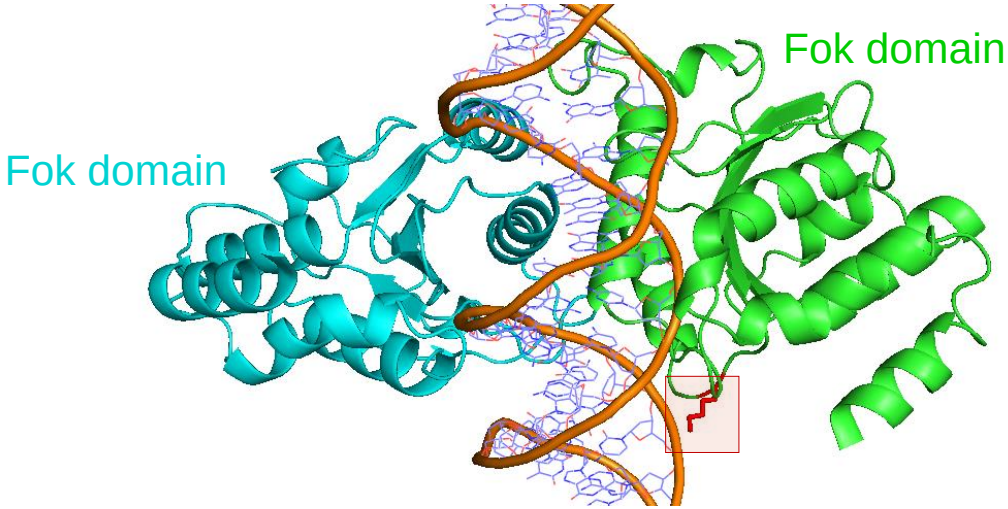
ZFN specificity optimized via two orthogonal approaches



1) Removing Arg-phosphate contacts



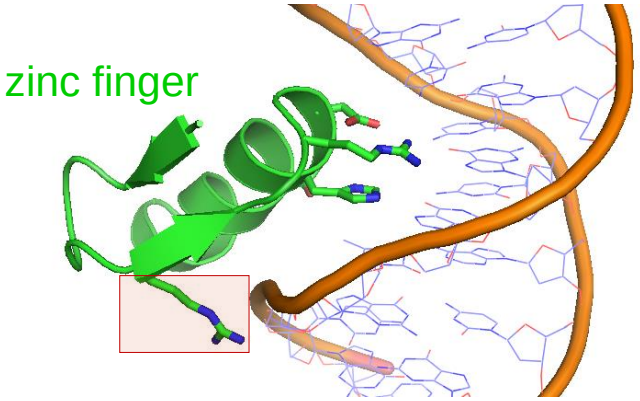
2) Substituting key FokI residues



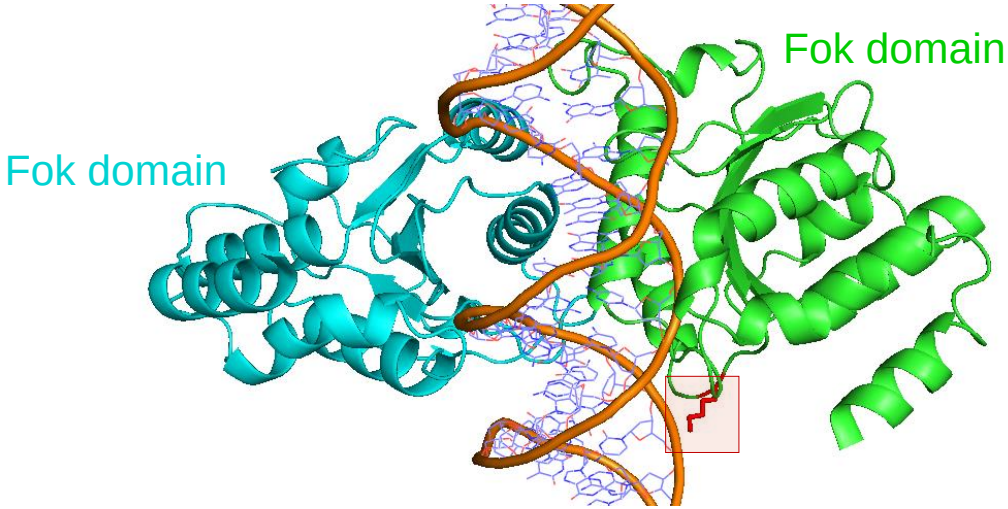
Independent tuning of dissociation and catalysis

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} E + P$$

1) Removing Arg-phosphate contacts
→ to tune dissociation rate (k_{-1})



2) Substituting key FokI residues
→ to modulate rate of catalysis (k_2)



Gene regulation platform

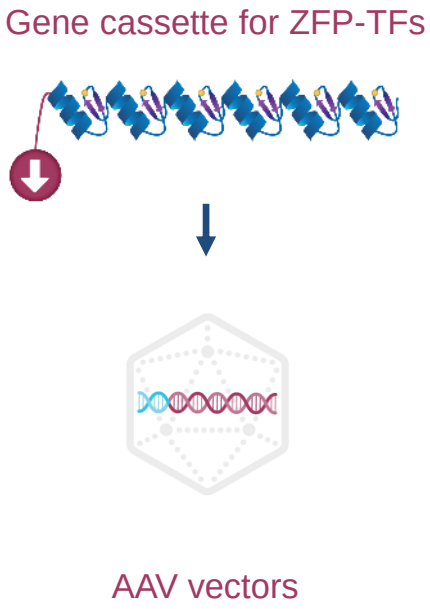
Huntington’s disease

C9ORF72-linked ALS/FTLD

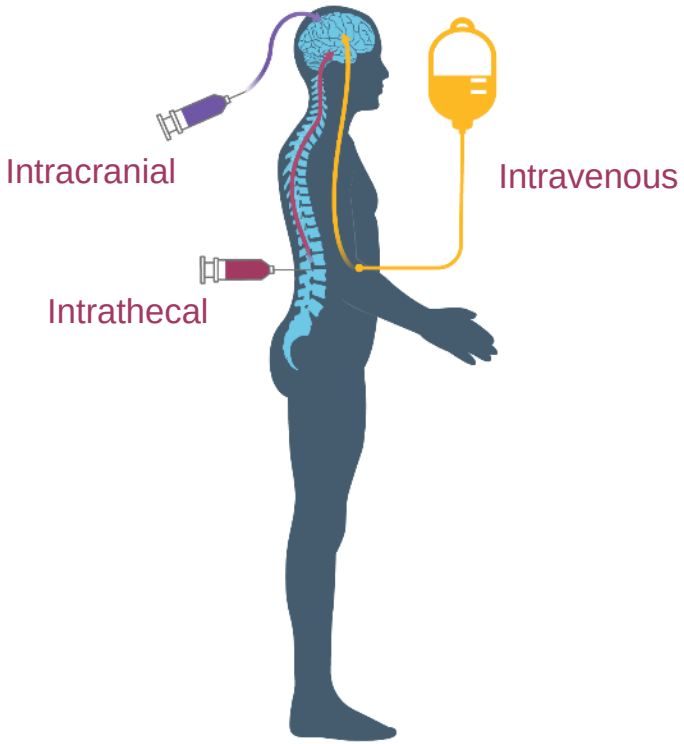
Tauopathies

Sangamo's gene regulation platform: precise and specific regulation of a mutated gene allele to treat CNS diseases

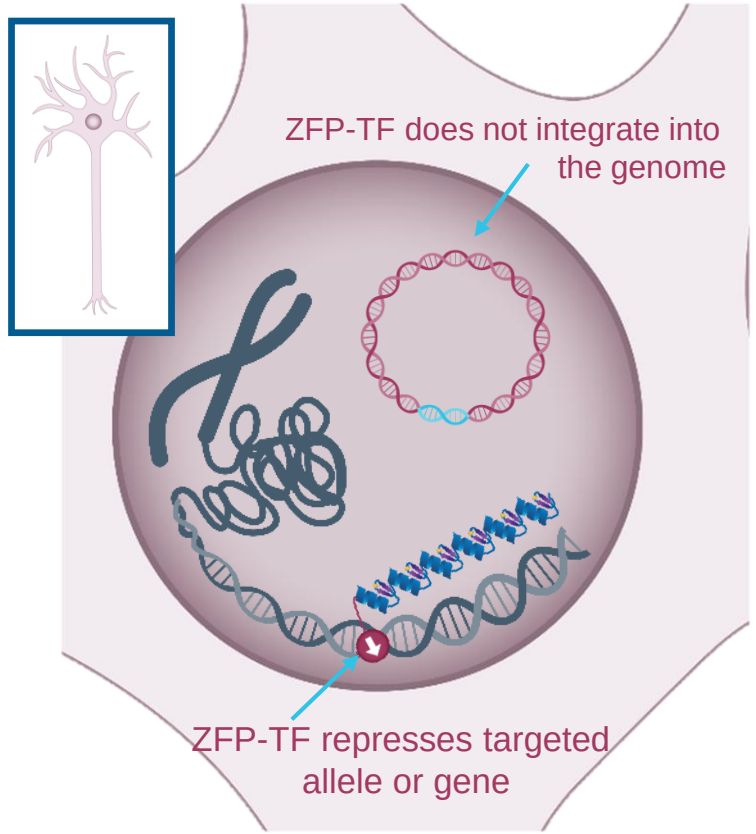
Packaging into AAV vectors



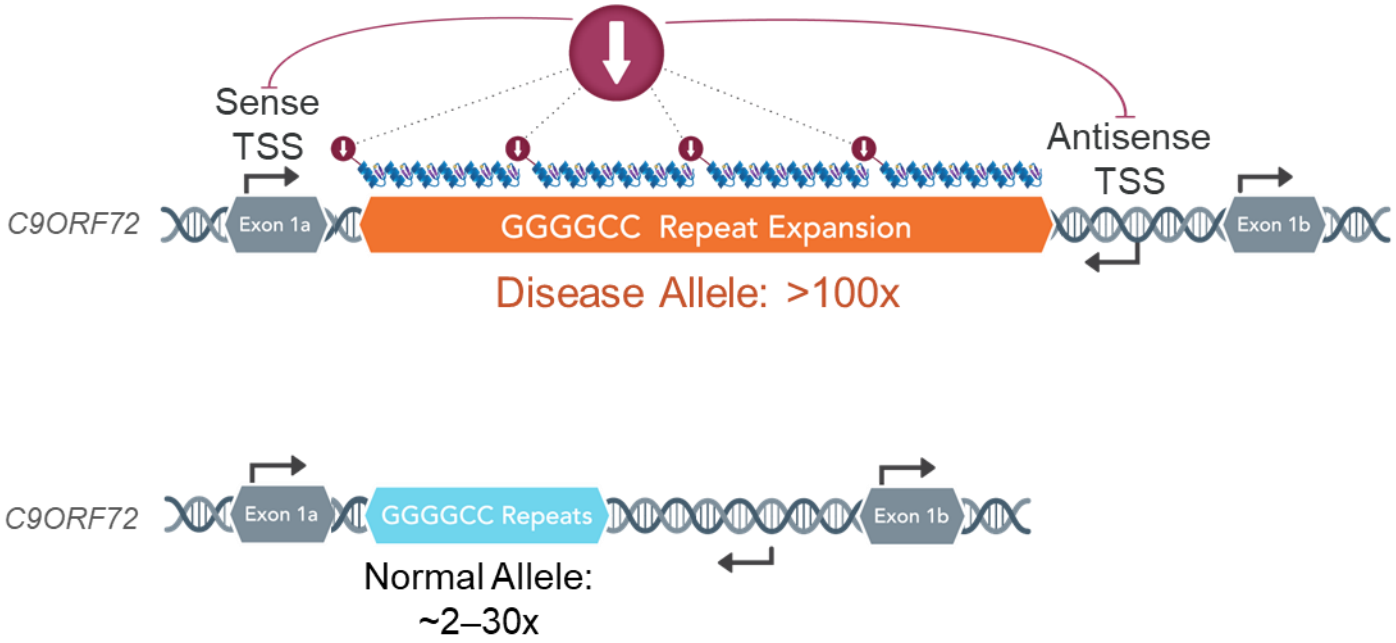
Potential Routes of Administration



In Neurons



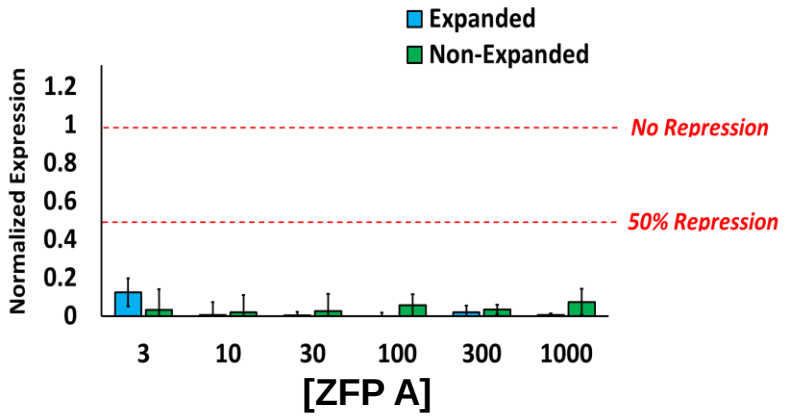
Allele specific repression of C9ORF72 with ZFP-TFs exemplifies Sangamo's differentiated therapeutic approach to CNS diseases



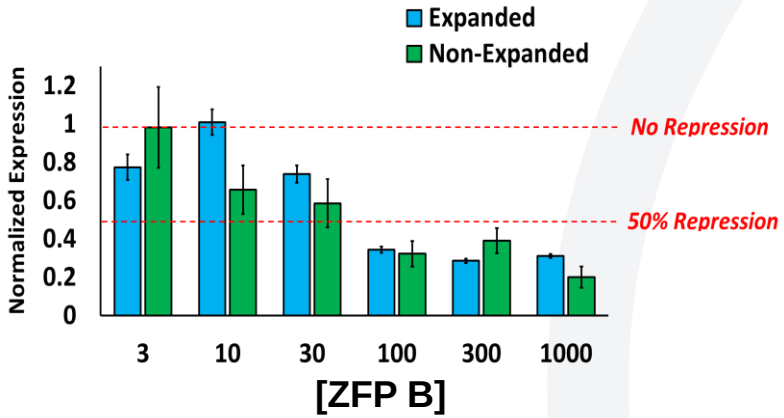
- Expansion of the GGGCC six base pair repeat causes neuronal degeneration.
- Cooperative inhibition by ZFP-TFs represses mutant C9 transcripts in an allele-specific fashion.

ZFPs are capable of maintaining allele-selectivity over a wide dose range

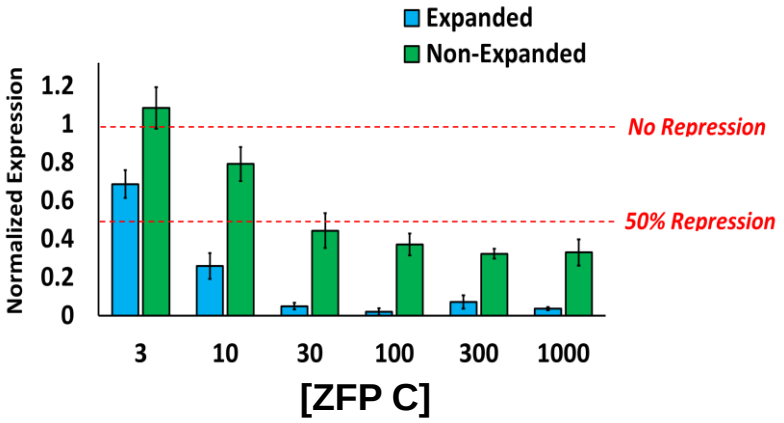
Full repression

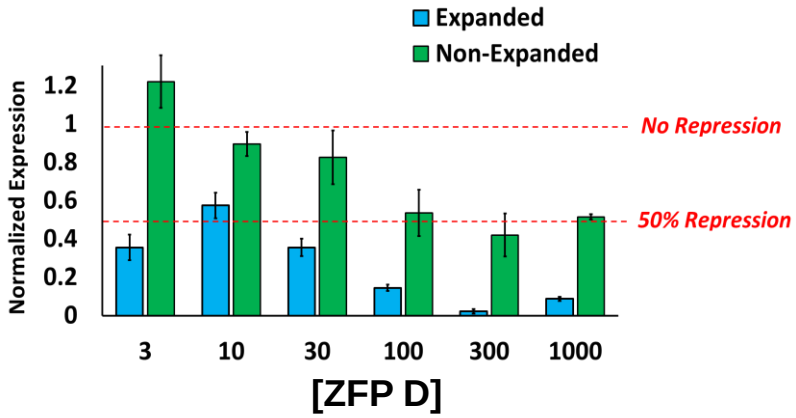


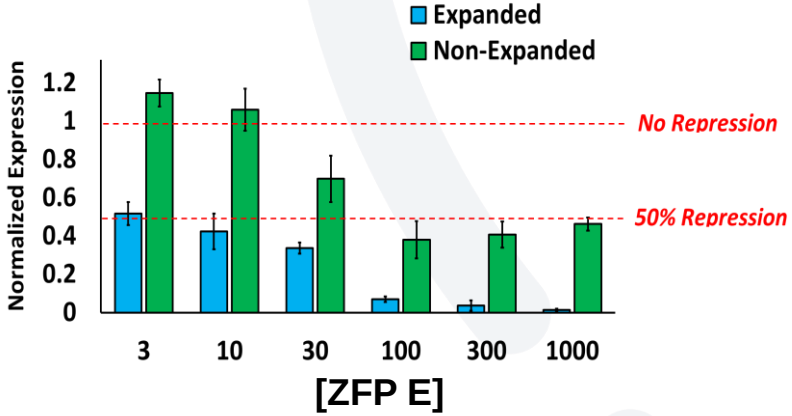
Non-selective repression



Selective repression







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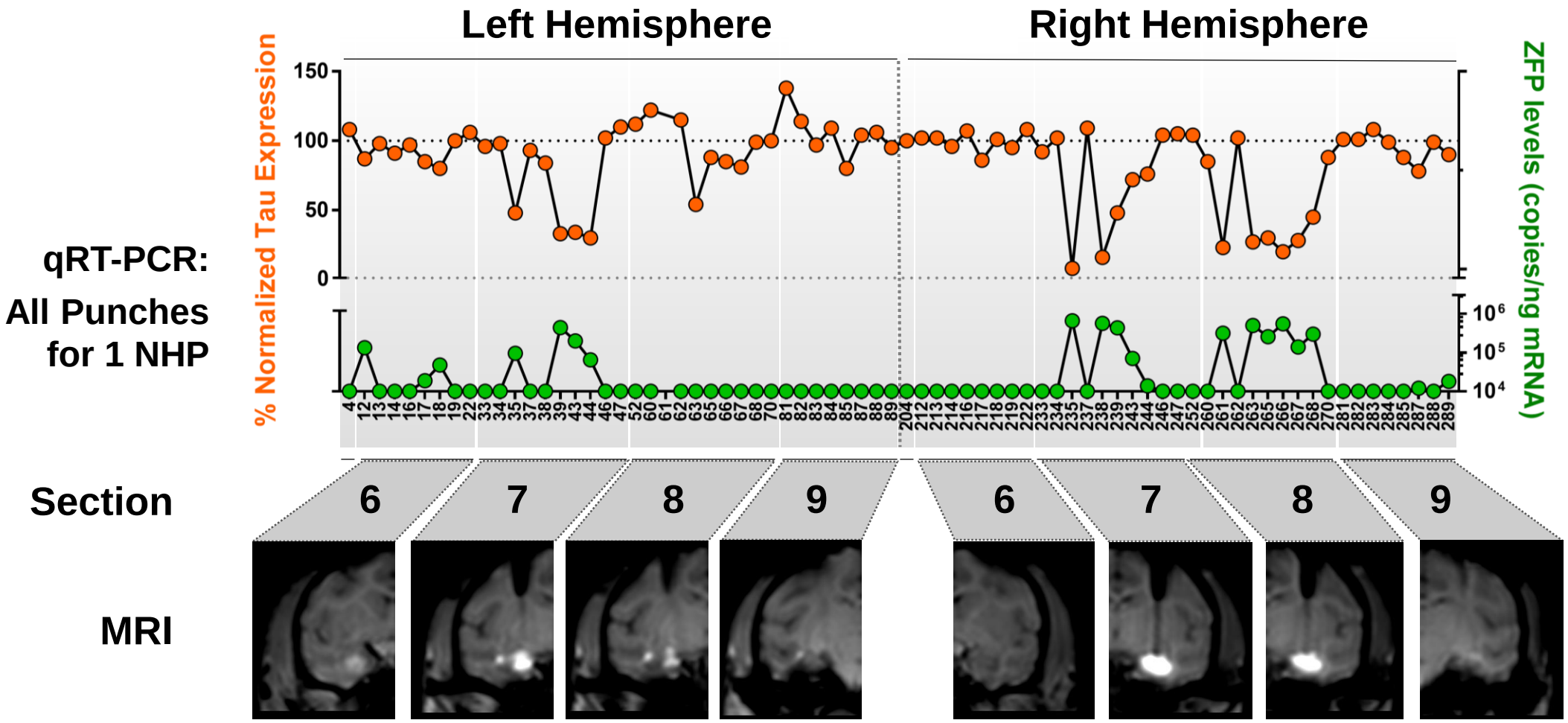
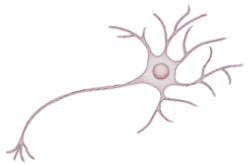
>80% tau reduction achieved in regions of non-human primate brain with AAV coverage



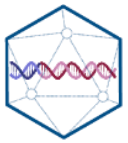
ZFP expression and tau reduction are closely correlated

Highly-specific, >98% human tau reduction in iPS neurons



iPS Neurons

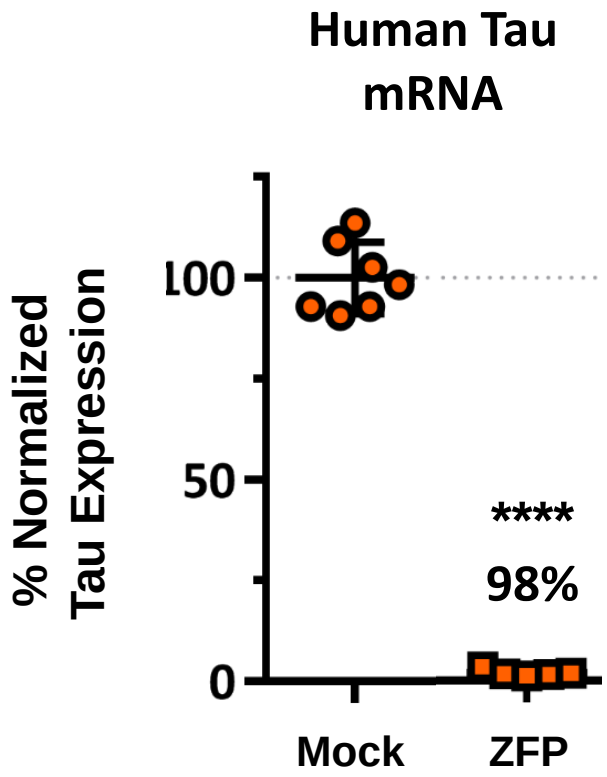
+

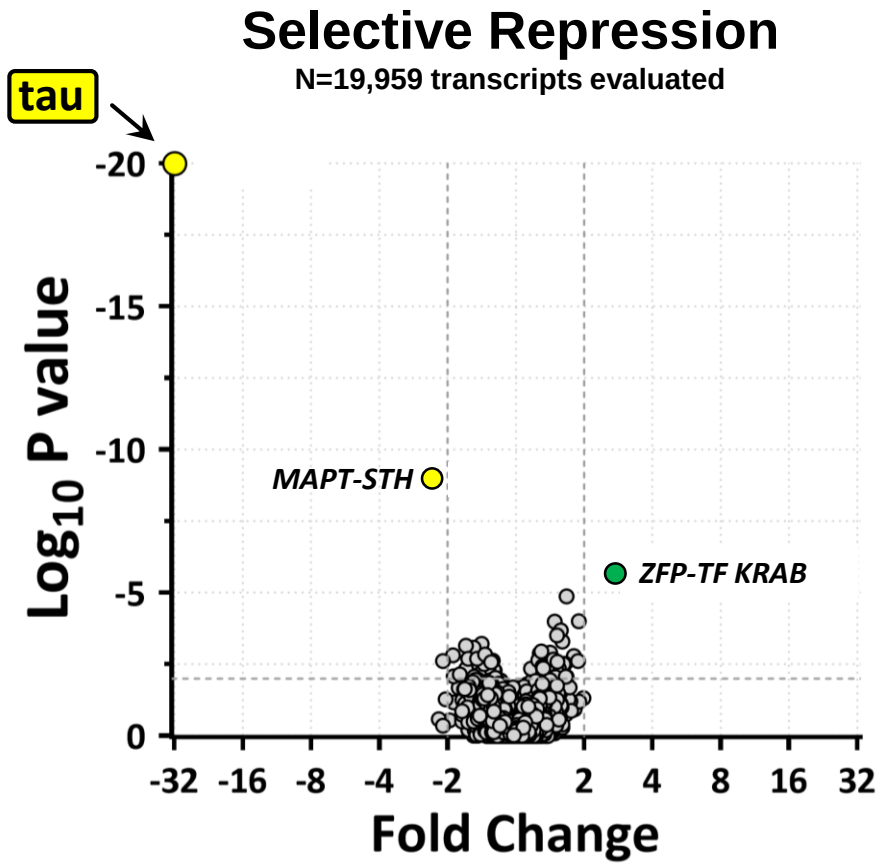


AAV6 + ZFP

19d

qRT-PCR
microarray





**** P < 0.0001, n = 5-7 biological replicates. Dose: 1E5 VG per cell. Human Clariom S Genechip.

Finance and Operations

Manufacturing

Upcoming milestones

Q1 2019 financial results and 2019 guidance

	Q1 2019	Q1 2018
Revenues	$in MM, except per share data	
	8.1	12.6
Operating Expenses		
R&D	34.9	23.5
G&A	17.1	10.1
Total Operating Expenses	52.0	33.6
Operating Loss	(43.9)	(21.0)
Net Loss	(42.2)	(20.2)
Net Loss per Share	($0.41)	($0.23)
Cash Position		
Ending Cash Balance	$351.6M	$234.9M

2019 Guidance

Operating expenses:
$210-220M

Cash runway:
Through year-end 2021*

**Including $136.2 million (net proceeds) from the April 2019 common stock offering*

Sangamo THERAPEUTICS

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

*Digital rendering of Sangamo cGMP facility

Ensuring control of quality, cost and timelines

- Construction of in-house phase 1/2 cGMP manufacturing facility at Sangamo is underway
  - Expected to be operational in 2020
- Expanded Brammer agreement provides access to dedicated AAV manufacturing capacity up to 2000-L bioreactor scale for late-stage clinical and large-scale commercial grade supply
  - Allows Sangamo to leverage Brammer AAV manufacturing know-how in Brisbane facility
  - Enables seamless transition from early to late stage development and manufacturing
  - Sangamo and Brammer have worked together for more than a decade

Milestones and catalysts

Gene therapy	SB-525: hemophilia A	– enroll expansion cohort – present longer-term data
	ST-920: Fabry disease	– clinical trial initiation in 2019
Ex Vivo gene-edited cell therapy	ST-400: beta thalassemia	– complete patient enrollment – present longer-term data (4Q 2019)
	BIVV003: sickle cell disease	– complete patient enrollment (Sanofi)
	TX200: solid organ transplant	– file CTA in 2019
	KITE-037: Allo-CD19 CAR-T	– initiate clinical study in 2020 (Kite-Gilead)
In Vivo genome editing	SB-913: MPS II SB-318: MPS I SB-FIX: hemophilia B	– initiate second generation SB-913 MPS II clinical trial in 2H 2019

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Key takeaways

- Genomic medicine company building value with gene therapy, *ex vivo* gene-edited cell therapy, *in vivo* genome editing and gene 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
- Flow of clinical data readouts in 2019 and 2020 following enrollment progress of last twelve months
- Strong balance sheet, four validating biopharma partnerships (Kite, Pfizer, Sanofi, Takeda), and manufacturing capabilities

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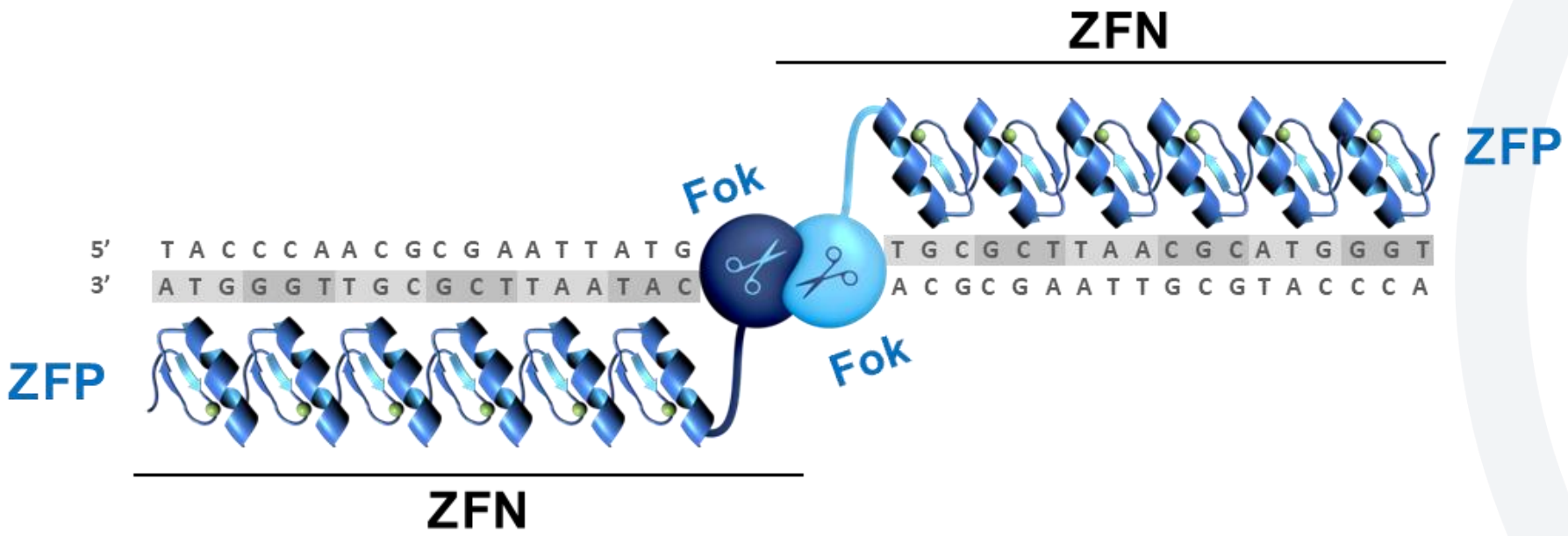
THERAPEUTICS

ZFP Technology

Zinc finger proteins

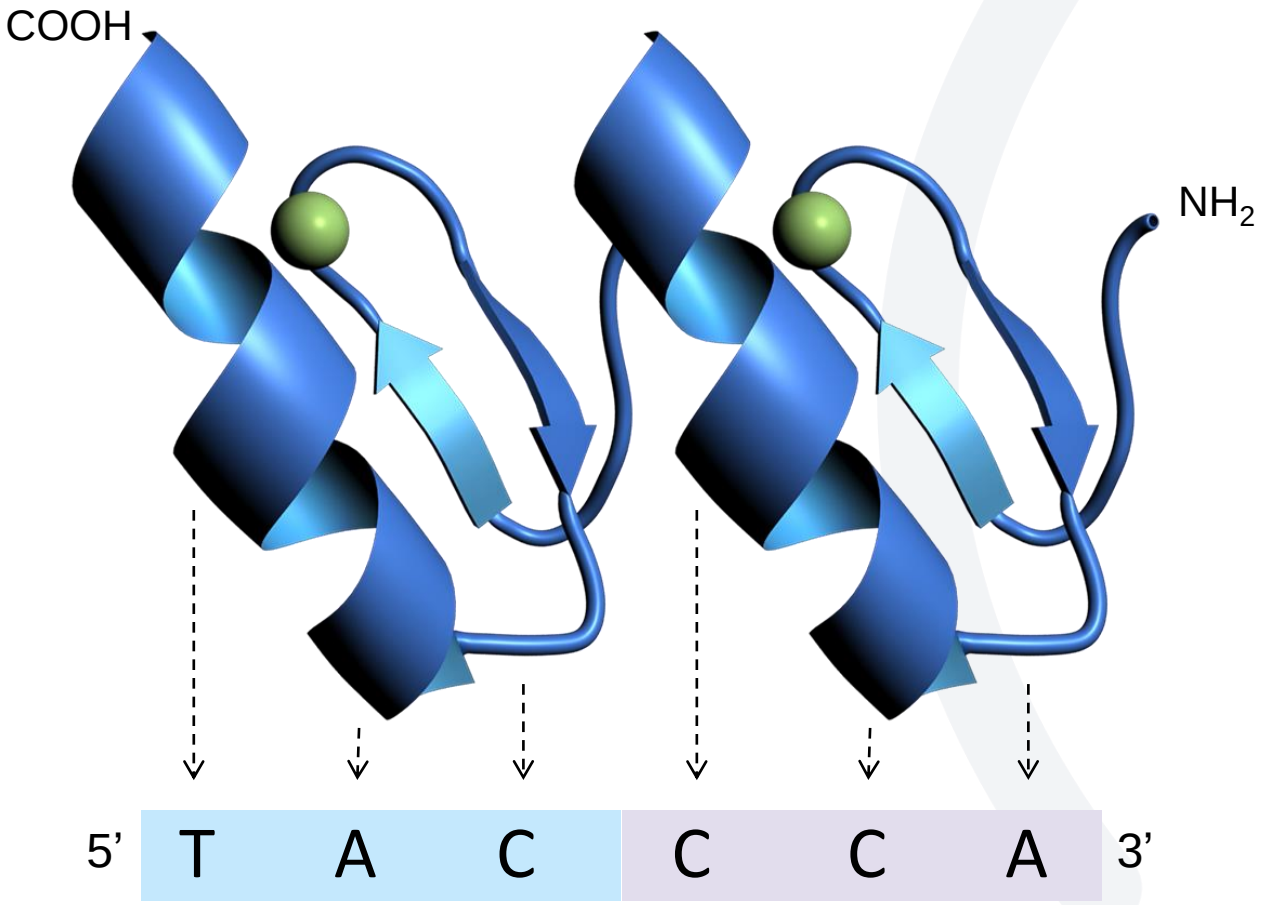
New ZFP architectures

ZFNs: The platform of choice for therapeutic gene editing

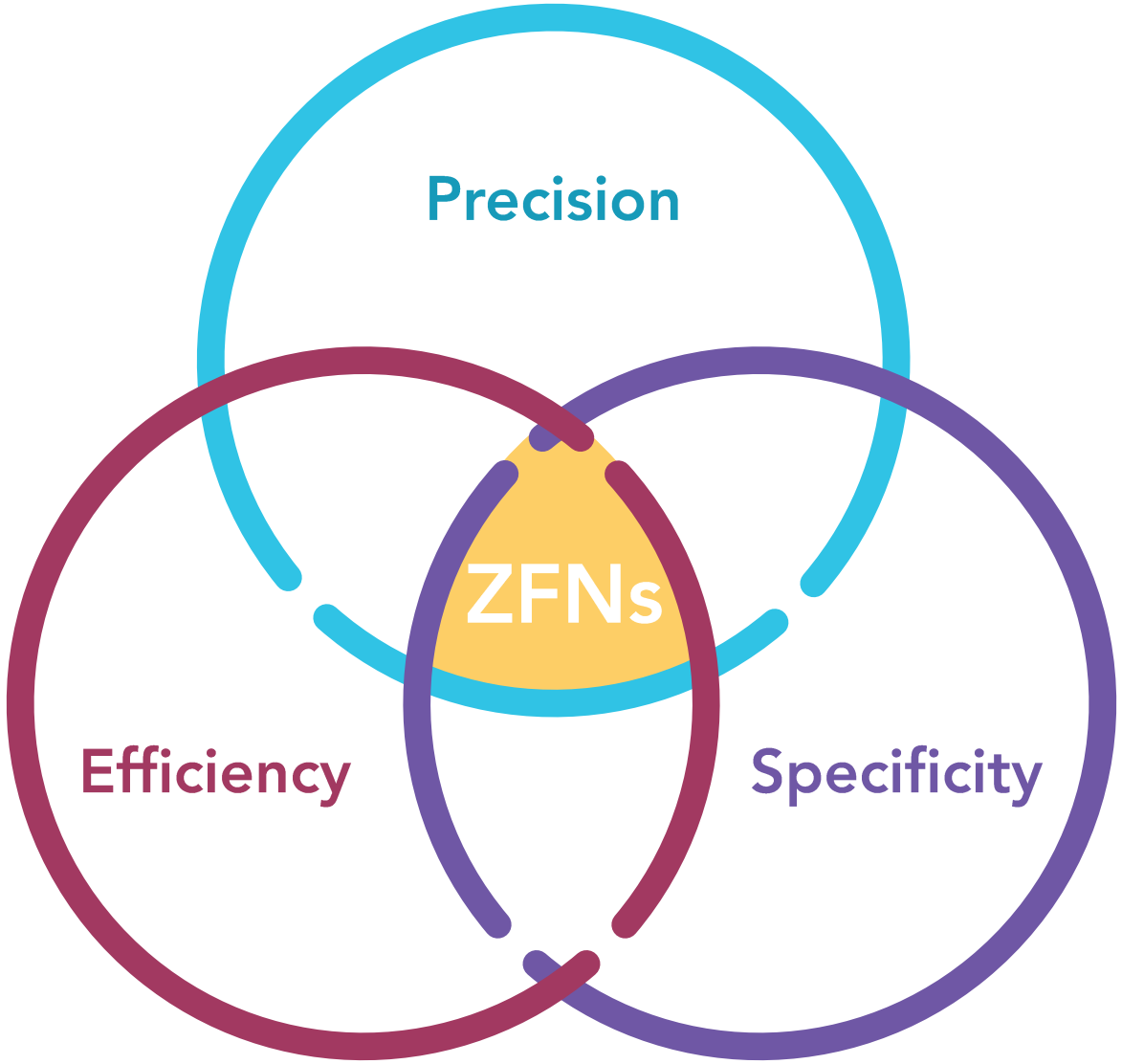


Sangamo's engineered zinc finger proteins

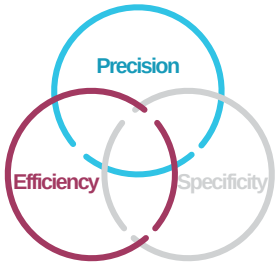
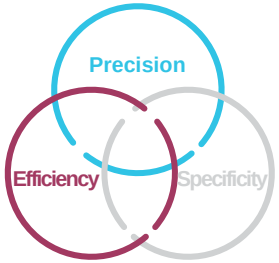
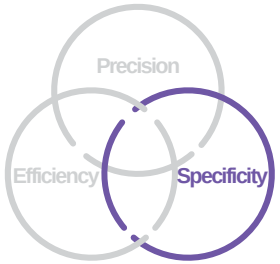
- A naturally occurring class of proteins which upregulate or downregulate gene expression
- Sangamo's ZFP library is derived from selected, designed and natural fingers



ZFNs: The platform of choice for therapeutic gene editing



Recent innovations drive performance

	Innovation	Result
	**New linkers** for configuring DNA-binding modules	**300-fold** increase in design options for targeting any given sequence
	**New dimer architectures** yield higher modification activity	Increase DNA editing efficiency to as high as **99.5%**
	**Phosphate contact** tuning via replacement of key residues	Improved specificity (**>1000** fold reduction of off-target cleavage)

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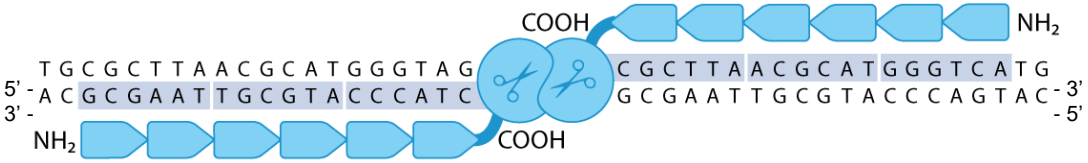
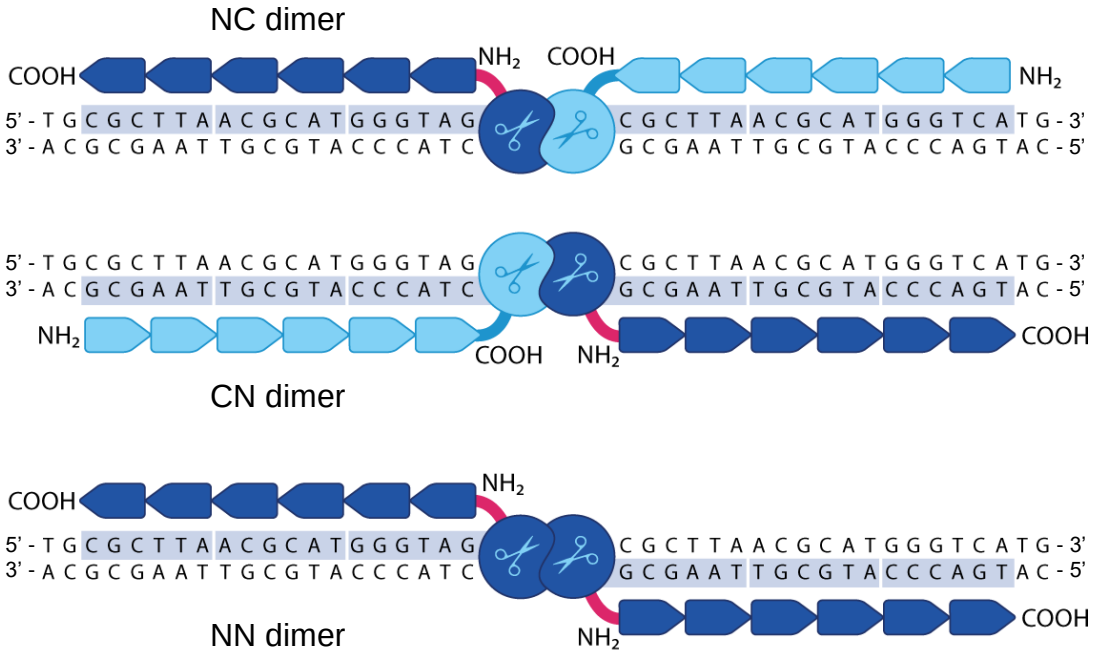
New linkers enable expanded set of ZFN architectures that increase targeting capabilities by 64-fold

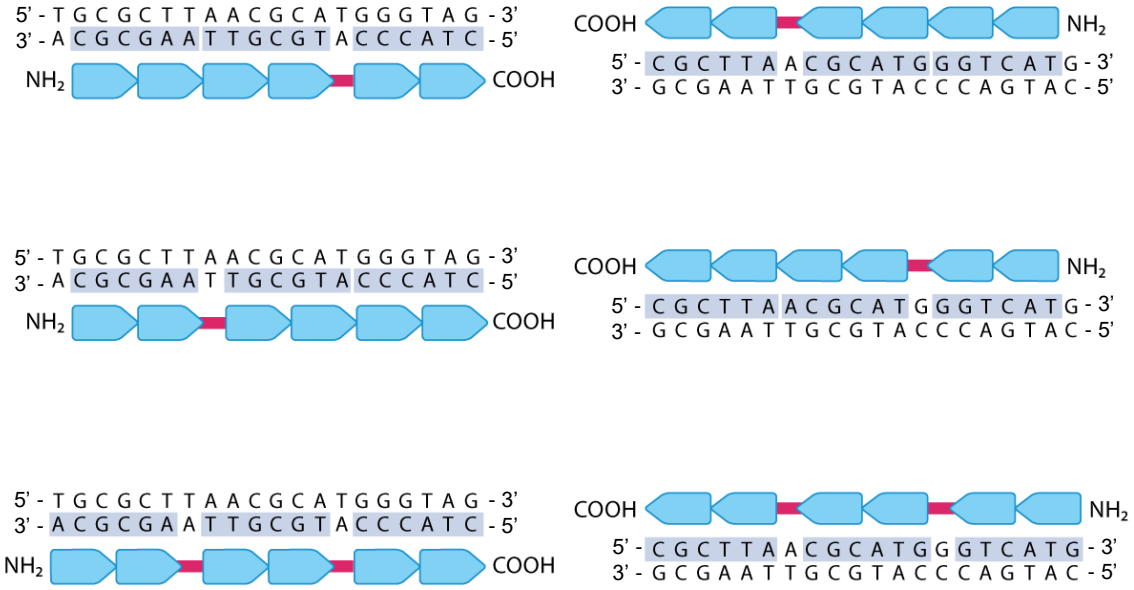
Canonical Dimer



New ZFP-FokI Linkages

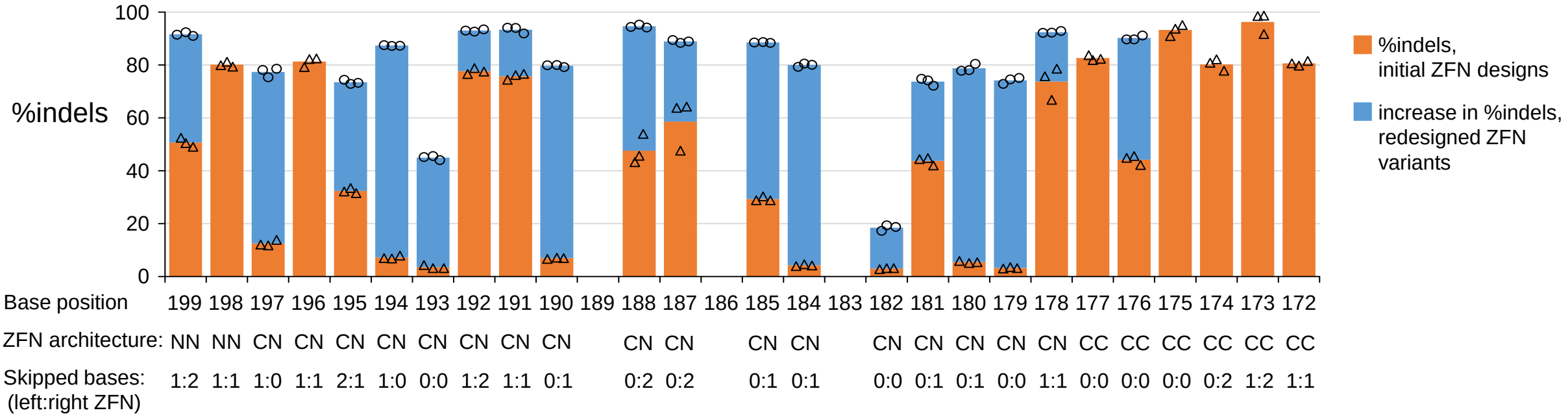


New Base-Skipping Linkers



Sangamo THERAPEUTICS

Engineerable ZFN platform enables precise targeting of a chosen DNA sequence with high levels of editing efficiency



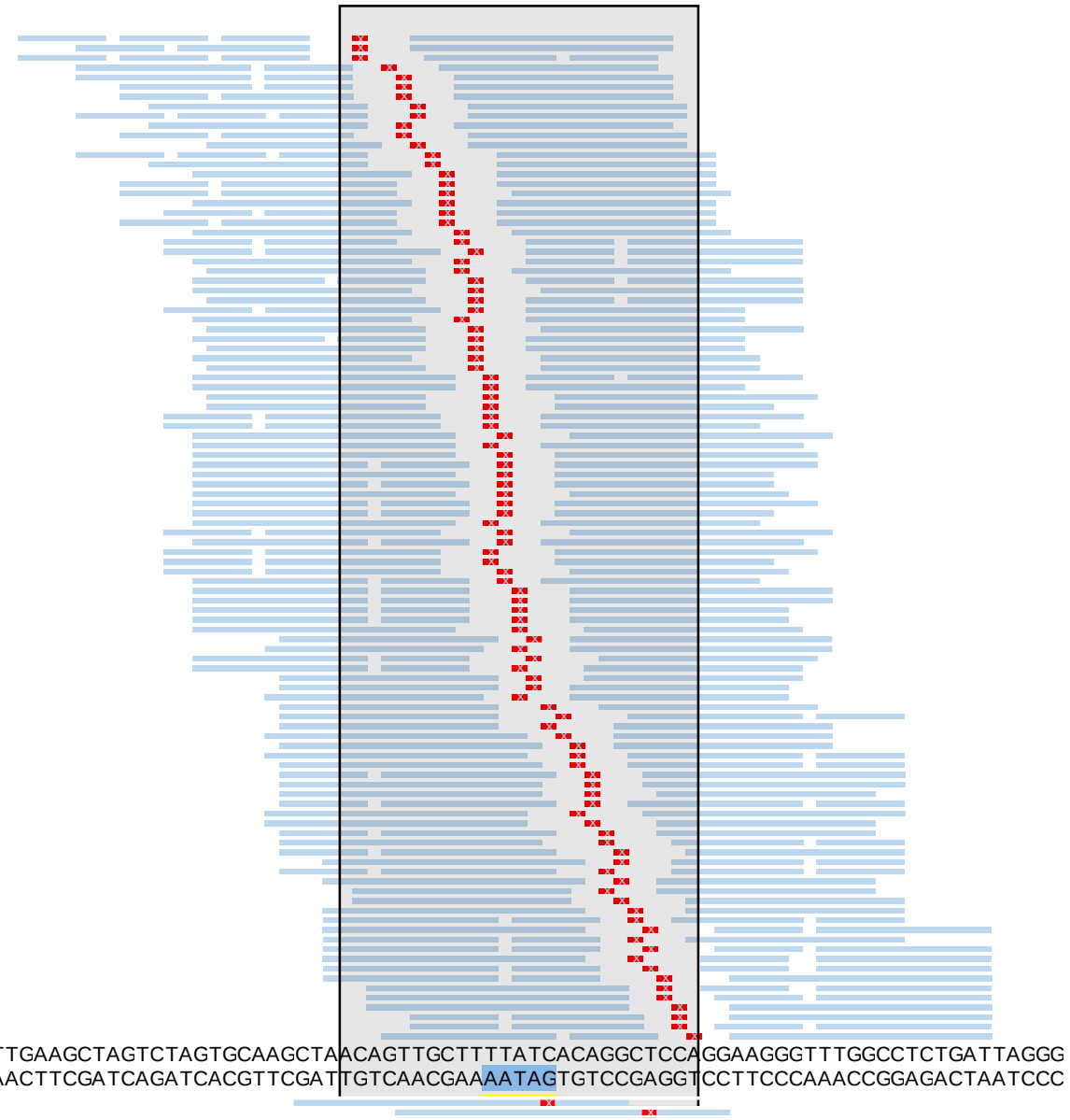
- Platform improvements yielded ZFN designs targeting 25 of 28 possible base steps of *HGB1* promoter region (shown in orange)
- Additional cycle of redesign yielded improved ZFN variants with significantly higher cleavage activity (shown in blue)

Sangamo THERAPEUTICS

New architectures yield a dense array of ZFN designs for optimal on-target efficiency and maximum therapeutic effect

Example: Critical GATAA element in BCL11A

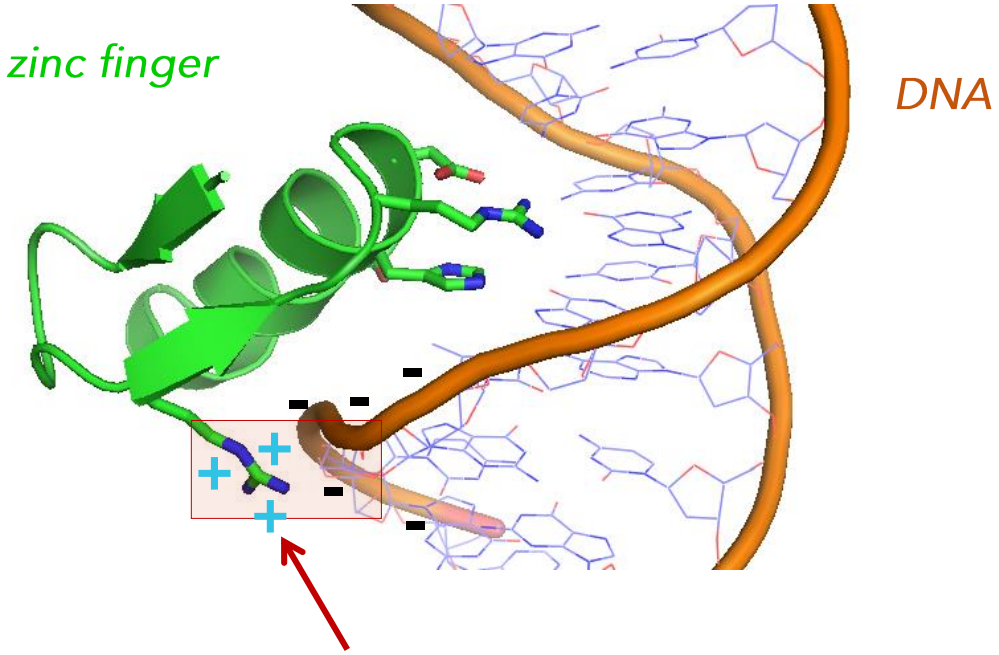
104 ZFN architectures available for targeting GATAA ± 10bp →



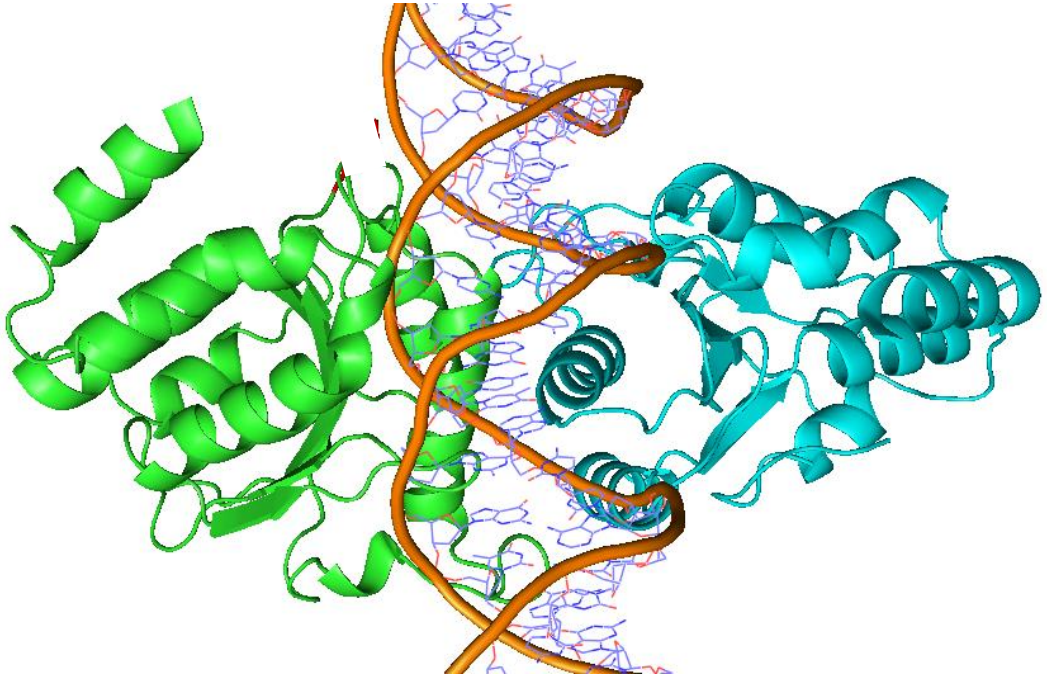
Two Cas9 designs →

Further protein engineering increases specificity while maintaining high levels of gene modification

Removal of conserved, non-specific phosphate contacts from zinc finger proteins increases targeting specificity



Modified Fok nuclease-DNA contacts significantly reduces off-target cleavage events



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