

# Corporate Presentation

November 2019



# Forward-Looking Statements

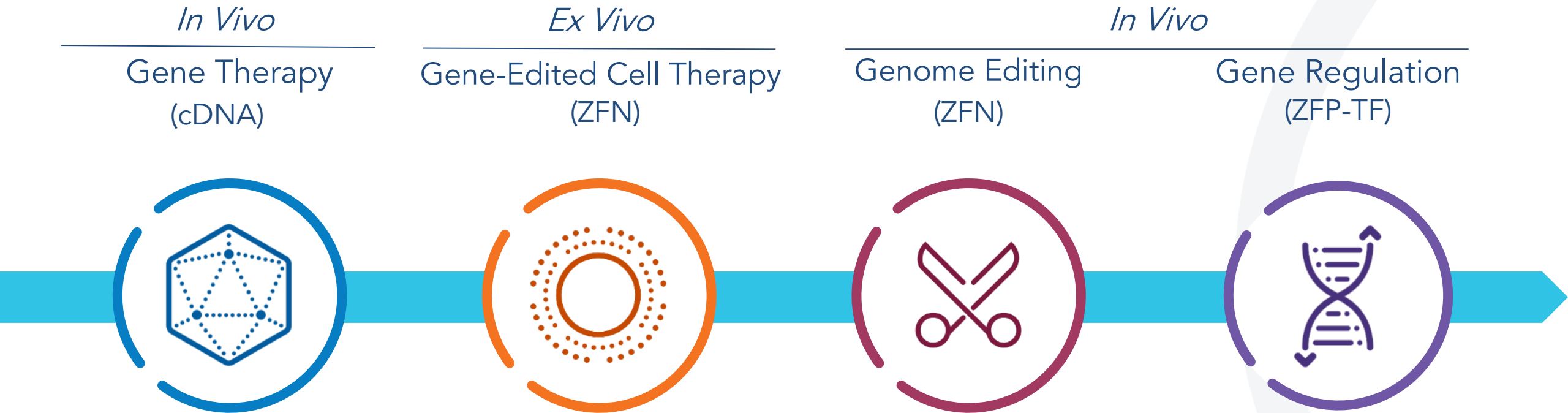
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*This presentation contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, as amended. These forward-looking statements include, but are not limited to, the therapeutic potential of Sangamo's product candidates; the design of clinical trials and expected timing for initiation, enrollment and presentation of data; anticipated clinical development and other milestones; the expected benefits of Sangamo's collaborations; the anticipated 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 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 CAR-T and CAR-Tregs 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 Sangamo's dependence on the success of clinical trials of its lead programs; 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 Sangamo's product candidates; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; Sangamo's limited experience in conducting later stage clinical trials and the potential inability of Sangamo and its partners to advance any of Sangamo's 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; and the potential for technological developments by Sangamo's competitors that will obviate Sangamo's gene therapy technology. 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 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. 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.*



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

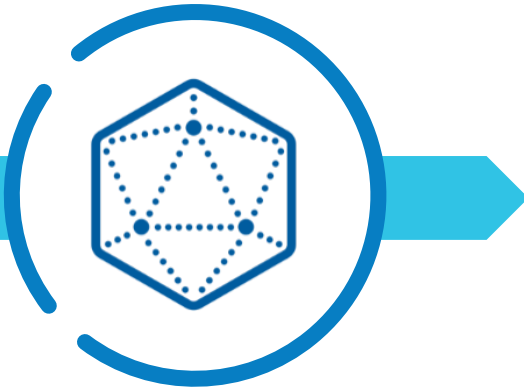


# Our capabilities allow us to design therapeutic approaches targeting the underlying genetic causes of disease

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*In Vivo*

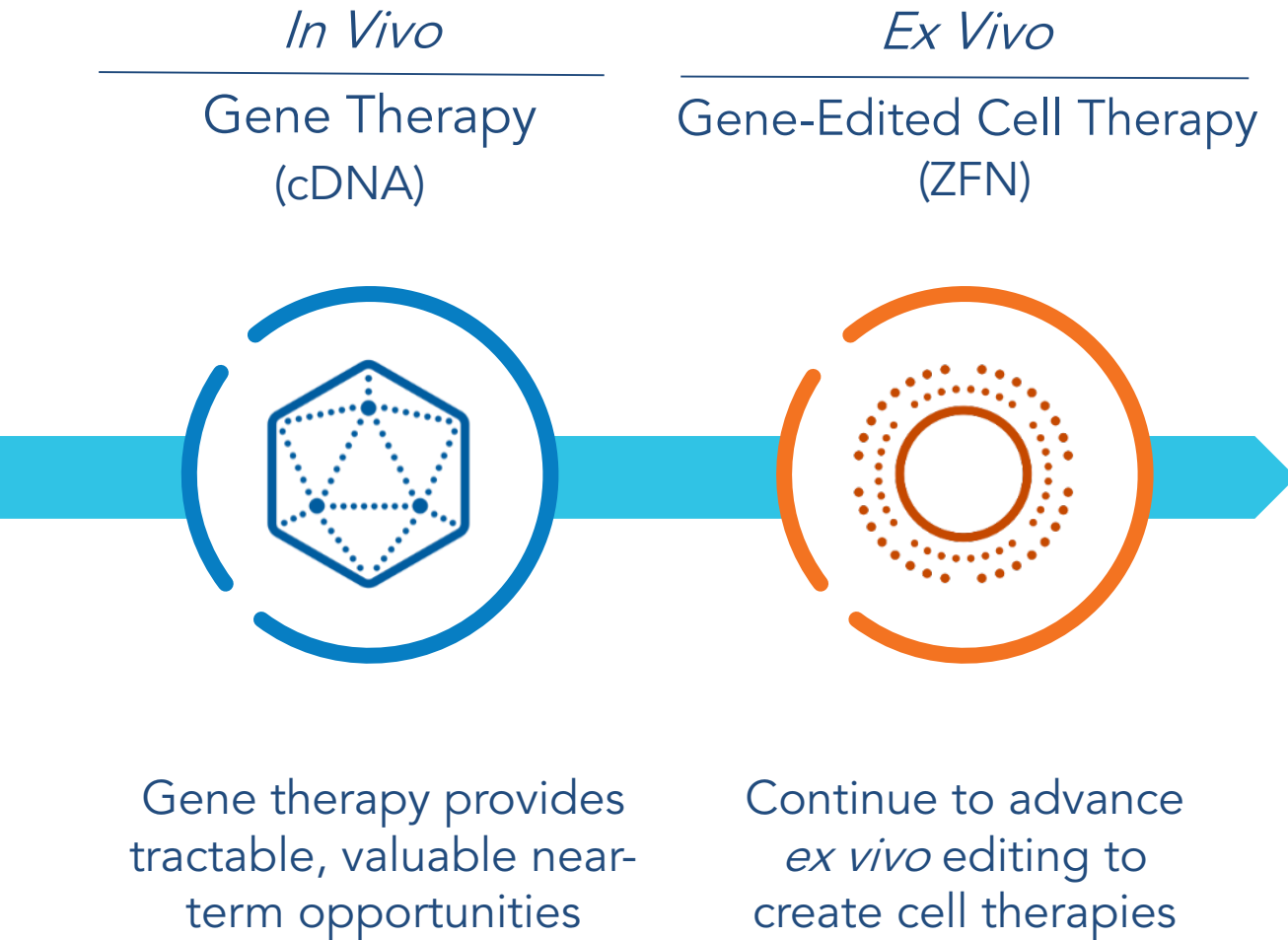
Gene Therapy  
(cDNA)



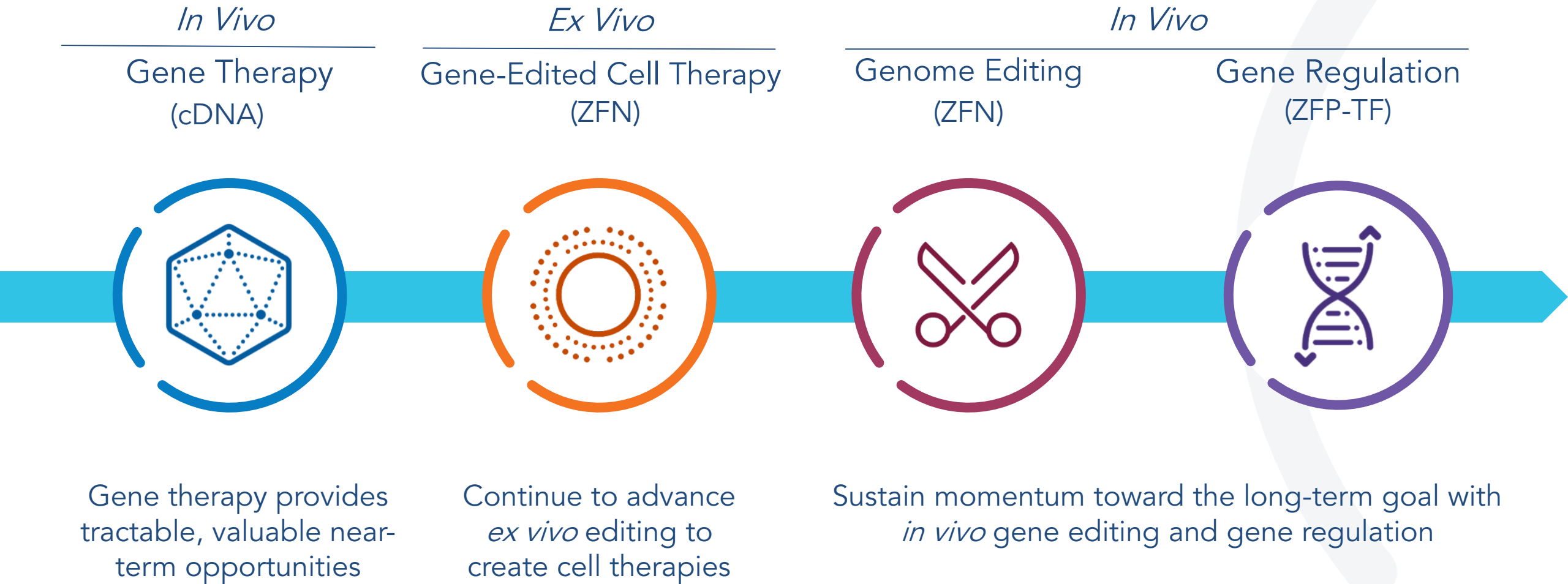
Gene therapy provides  
tractable, valuable near-  
term opportunities



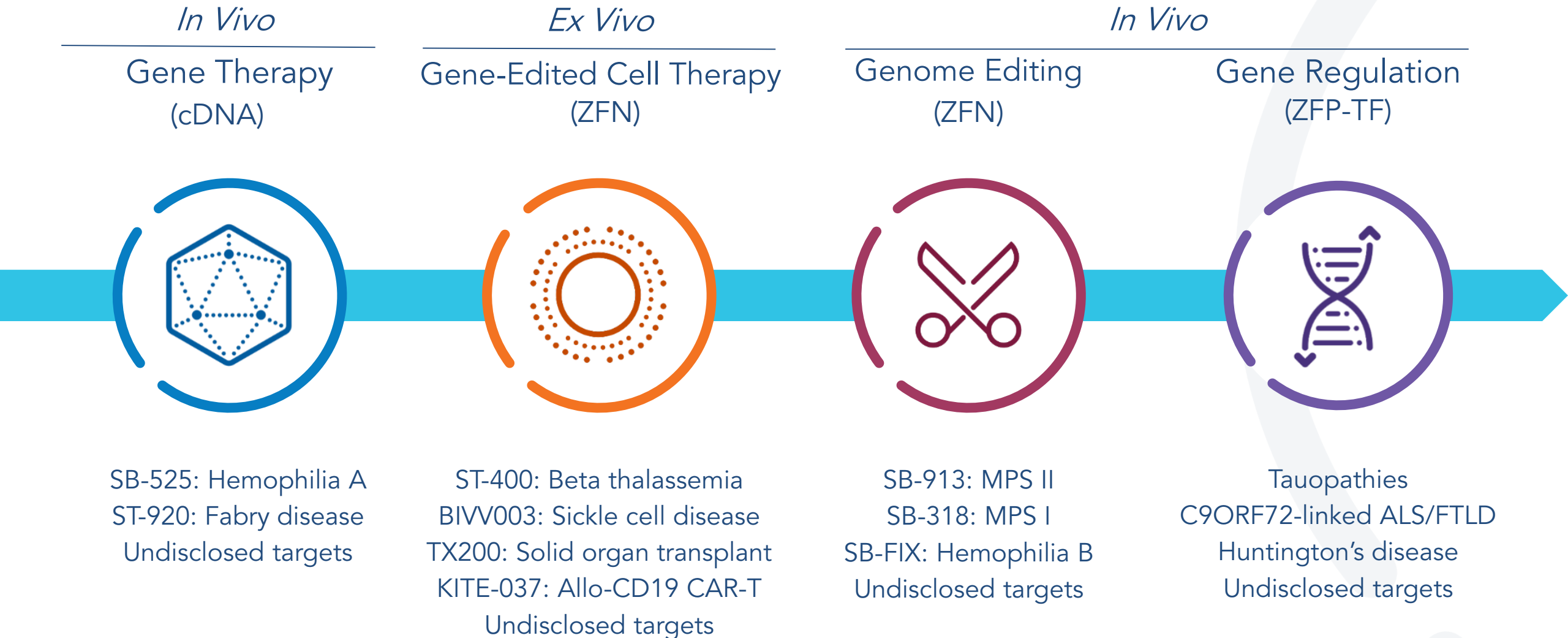
# Our capabilities allow us to design therapeutic approaches targeting the underlying genetic causes of disease



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















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





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

Therapeutic Area	Research	Preclinical	Phase 1/2	Phase 3	Partner
Gene Therapy					
Hemophilia A (SB-525)					
Fabry Disease (ST-920)					
Ex Vivo Gene-Edited Cell Therapy					
Beta-thalassemia (ST-400)					SANOFI 
Sickle Cell Disease (BIVV-003)					SANOFI 
Solid Organ Transplant (TX-200)					
Oncology (KITE-037)					
In Vivo Genome Editing					
MPS I (SB-318)					
MPS II (SB-913)					
Hemophilia B (SB-FIX)					
In Vivo Gene Regulation					
Tauopathies					
ALS/FTLD					
Huntington's Disease					

# Gene Therapy

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

# SB-525, gene therapy for hemophilia A



## Phase I/II Open Label Study (ALTA)



- Orphan Drug
- Fast Track
- RMAT



- Orphan Medicinal Product

## Goals

Patient safety

FVIII activity

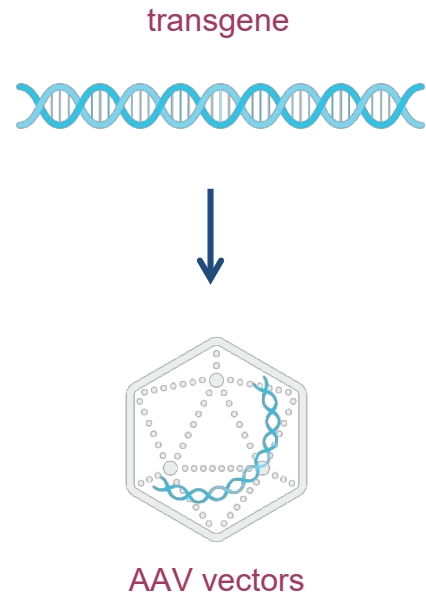
Reduction of bleeding events

Reduction of factor replacement use

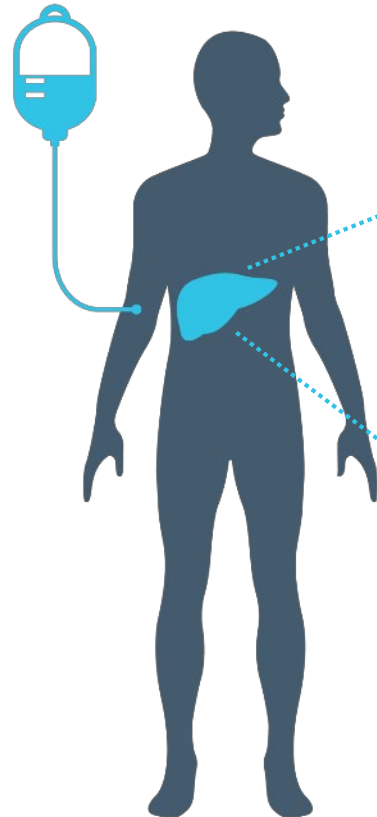
# Sangamo's gene therapy platform: potential for potent therapeutic solutions for monogenic diseases



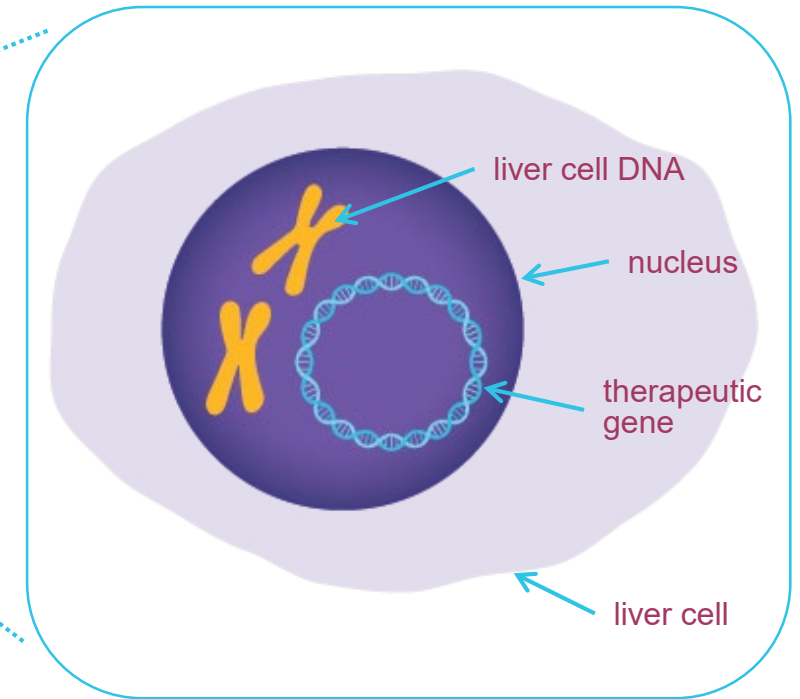
## Packaging into AAV vectors



## Delivery



## To the liver



**2019 International  
Society on  
Thrombosis and  
Haemostasis**

**Melbourne,  
Australia  
July 6<sup>th</sup>, 2019**

***Initial results 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, Kimo Stine, Nathan Visweshwar, Thomas Harrington, Andrew D. Leavitt, Steven Arkin, Gregory Di Russo, Edward Conner and Didier Rouy**

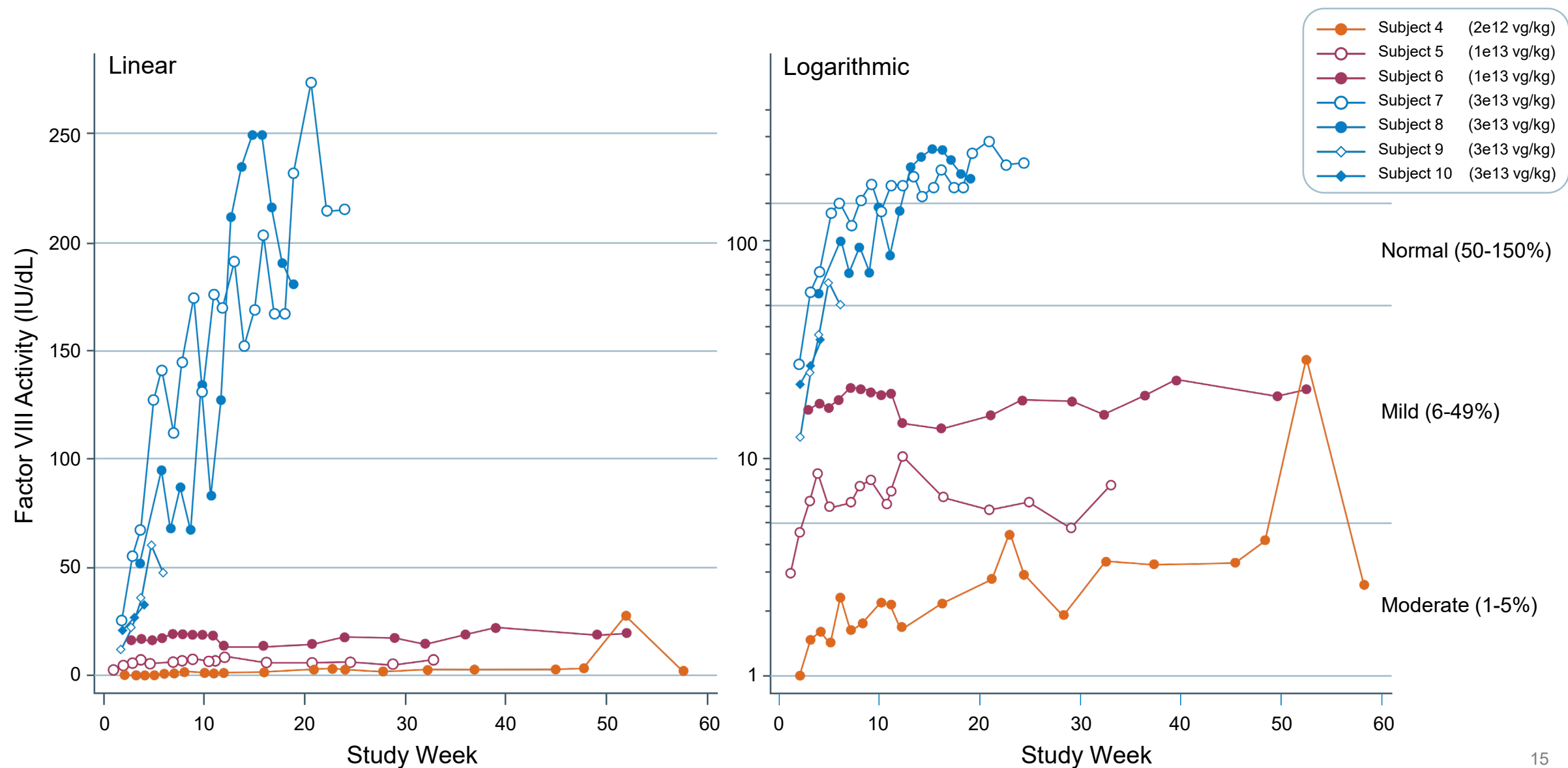
# Treatment-Related Adverse Event (TRAE) Summary

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=4) n(%) [T]	Overall (N=10) n(%) [T]
Any treatment-related event	0	2 (100) [4]	0	3 (75) [8]	5 (50) [12]
Alanine aminotransferase increased	0	2 (100) [3]	0	1 (25) [1]	3 (30) [4]
Pyrexia	0	0	0	3 (75) [3]*	3 (30) [3]
Aspartate aminotransferase increased	0	1 (50) [1]	0	0	1 (10) [1]
Fatigue	0	0	0	1 (25) [1]	1 (10) [1]
Hypotension	0	0	0	1 (25) [1]**	1 (10) [1]
Myalgia	0	0	0	1 (25) [1]	1 (10) [1]
Tachycardia	0	0	0	1 (25) [1]	1 (10) [1]

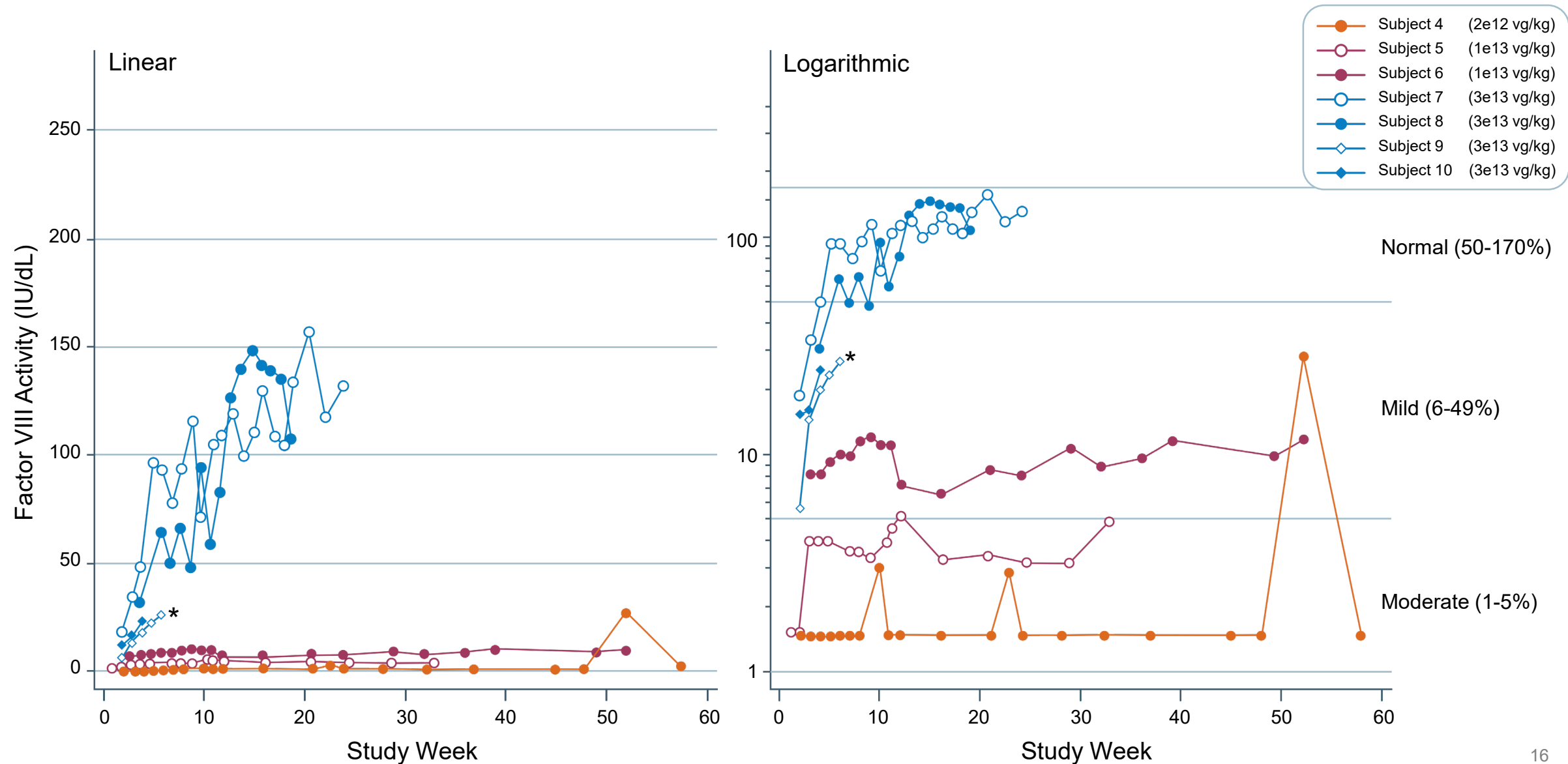
N= Total number of subjects in each treatment group, n= number of subjects in each system organ class (SOC), [T]= total number of treatment-related adverse events. \*All 3 events were reported as Grade 2 \*\* Grade 3 event reported



# Factor VIII activity: One-stage

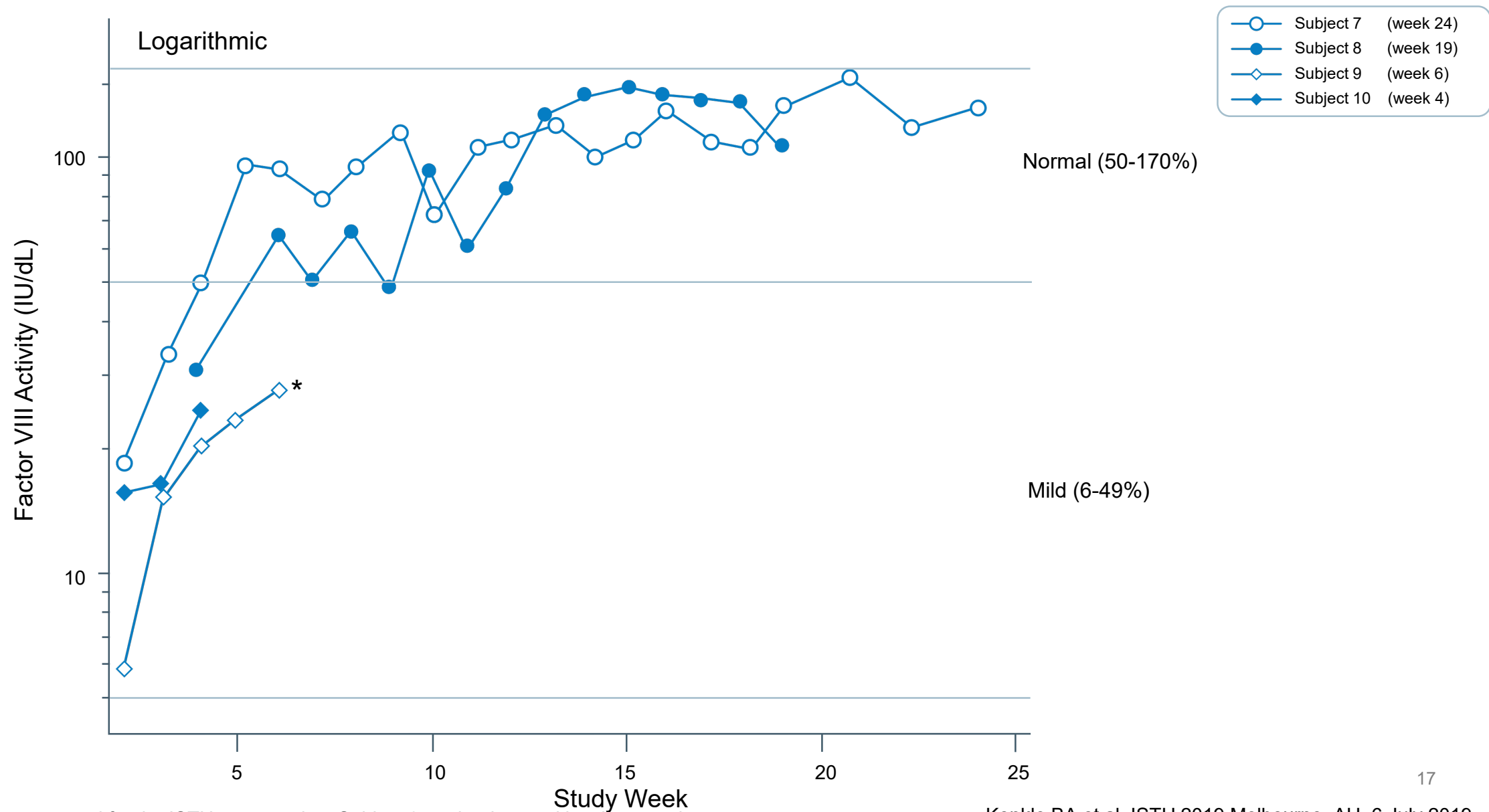


# Factor VIII activity: Chromogenic



\* Subsequent to the data cut used for the ISTH presentation, Subject 9 attained normal levels at week 7

# Factor VIII activity: Chromogenic, Cohort 4 (3e13 vg/kg)



# Spontaneous Bleeding Episodes

Dose Cohort (dose vg/kg)	Subject	Follow-Up (weeks)	Bleeding Episodes ≥3 weeks Post Treatment
1 (9e11)	1	93	7
1 (9e11)	2	83	5
2 (2e12)	3	73	8
2 (2e12)	4	66	5
3 (1e13)	5	50	5
3 (1e13)	6	41	0
4 (3e13)	7	24	0
4 (3e13)	8	18	0
4 (3e13)	9	5	0
4 (3e13)	10	2	n/a*

\*n/a: < 3 weeks of follow-up at time of data cut

# 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
1 (9e11)	1	93	2/Week	115
1 (9e11)	2	83	2/Week	26
2 (2e12)	3	73	2/Week	13
2 (2e12)	4	66	3/Week	9
3 (1e13)	5	50	Every Other Day	11
3 (1e13)	6	41	Every Other Day	0
4 (3e13)	7	24	Every 4 Days	0
4 (3e13)	8	18	Every Other Day	1*
4 (3e13)	9	5	Every 3 Days	0
4 (3e13)	10	2	Every 3 Days	n/a <sup>§</sup>

\*Prophylactic coverage stopped 3 weeks and 2 days after SB-525 administration, <sup>§</sup>n/a: < 3 weeks of follow-up at time of data cut

**2019 American  
Society of  
Hematology**

**Orlando, Florida  
December 7<sup>th</sup>, 2019  
5:30pm ET**

***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 Patients with Severe  
Hemophilia A***

**Barbara A. Konkle, Kimo Stine, Nathan Visweshwar, Thomas  
Harrington, Andrew D. Leavitt, Adam Giermasz, Steven Arkin,  
Gregory Di Russo, Ashley Snyder, Adrian Woolfson and Didier Rouy**



# 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

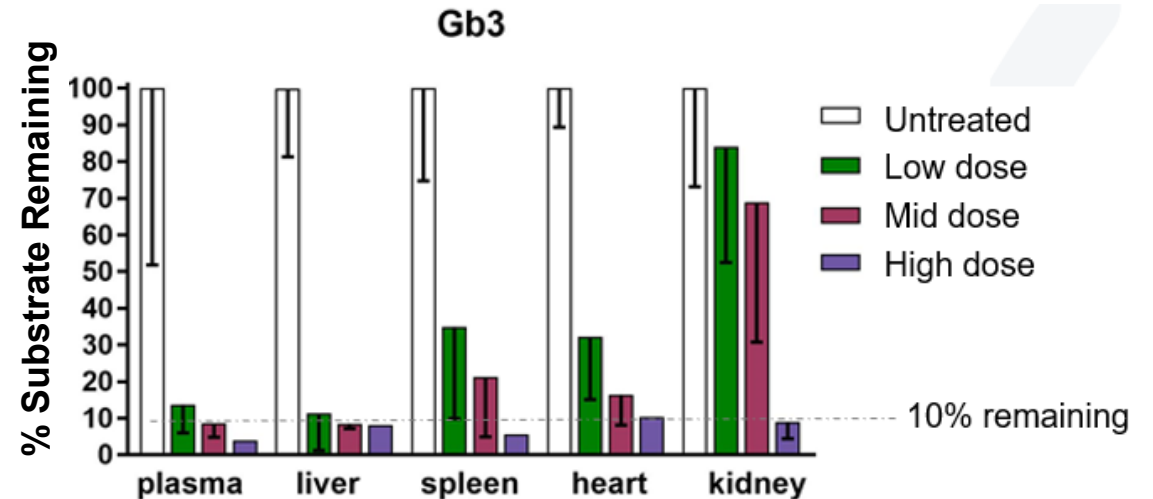
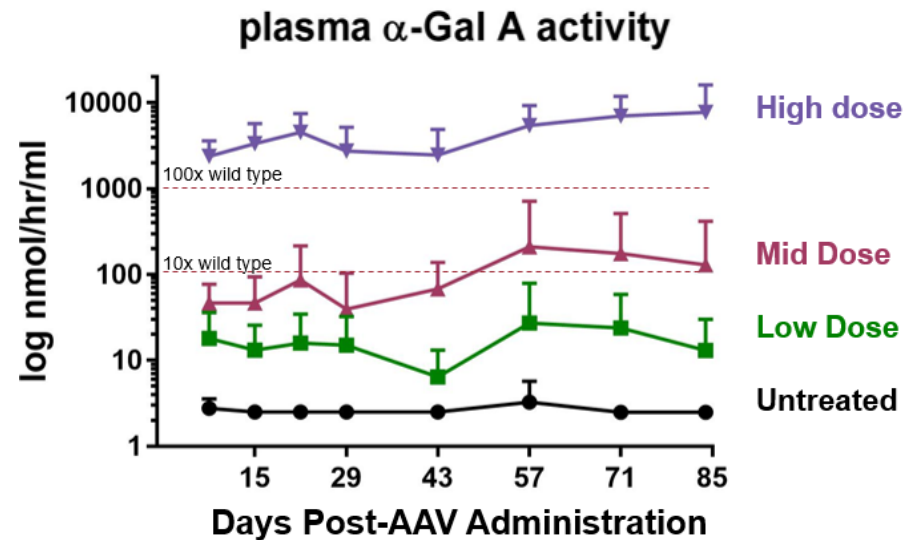
# ST-920, gene therapy for Fabry disease

## Designed to express $\alpha$ -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
- ST-920 clinical trial initiated. First patient enrollment expected by year-end 2019
- US FDA orphan drug designation granted; UK approval granted for CTA

Data from preclinical studies in mice using a precursor to ST-920. AAV produced using clinical scale manufacturing methods



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

# *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



Patient



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



2

**Gene editing**

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

**BCL11A Enhancer Sequence**



**Deletion**

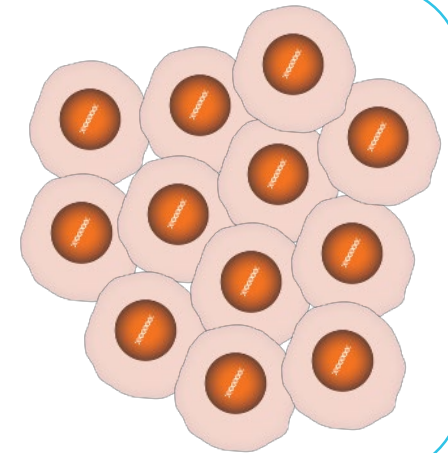


**BCL11A Enhancer Knocked Out**

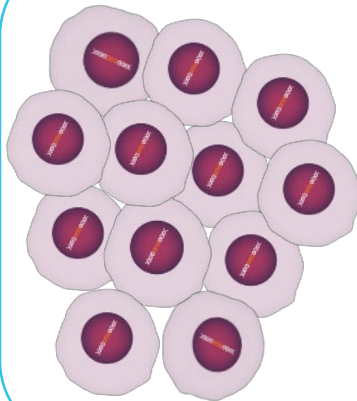
3

**Harvest**

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



cGMP  
Manufacturing  
Facility



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



## Phase I/II Open Label Study (THALES)

### April 2019

- First patient data presented (genotype  $\beta^0/\beta^0$ )

### November 2019

- 5 patients enrolled



### Next steps

- Complete enrollment of all 6 patients in 2019
- Additional preliminary data at ASH 2019
- Study results in 2020

## 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

## Goals

Patient safety

Successful engraftment

Fetal hemoglobin (HbF)  
production

Reduction / elimination  
of transfusions

# Wide genotypic diversity results in phenotypic variability in beta thalassemia

Increasing Severity: Anemia and Ineffective Erythropoiesis

Representative  
Genotypes

$\beta^0/\beta^{WT}$   $\beta^+/ \beta^{WT}$   $\beta^+/\beta^+$

- Normal hemoglobin or mild anemia
- Transfusions not required

$\beta^+/\beta^+$   $\beta^+/\beta^0$   $HbE/\beta^{+/0}$

- Moderate anemia; intermittent
- Infrequent transfusions required

$\beta^+/\beta^+$   $HbE/\beta^{+/0}$   $\beta^+/\beta^0$   $\beta^0/\beta^0$

- Severe anemia
- Regular transfusions required

- Hundreds of  $\beta^+$  mutations have variable ability to produce beta globin
- Any given beta globin genotype may be phenotypically modified by variants in alpha globin expression and/or gamma globin expression
- In beta thalassemia, this modification may either ameliorate or worsen the phenotype by reducing or increasing the alpha chain excess/imbalance, respectively



**2019 American  
Society of  
Hematology**

**Orlando, Florida  
December 9<sup>th</sup>, 2019  
6:00pm ET**

***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 Beta  
Thalassemia***

**Angela R. Smith, Gary J. Schiller, Gregory M. Vercellotti, Janet L.  
Kwiatkowski, Lakshmanan Krishnamurti, Erica B. Esrick, David A.  
Williams, Weston Miller, Adrian Woolfson, Mark C. Walters**

## Cell therapy platform

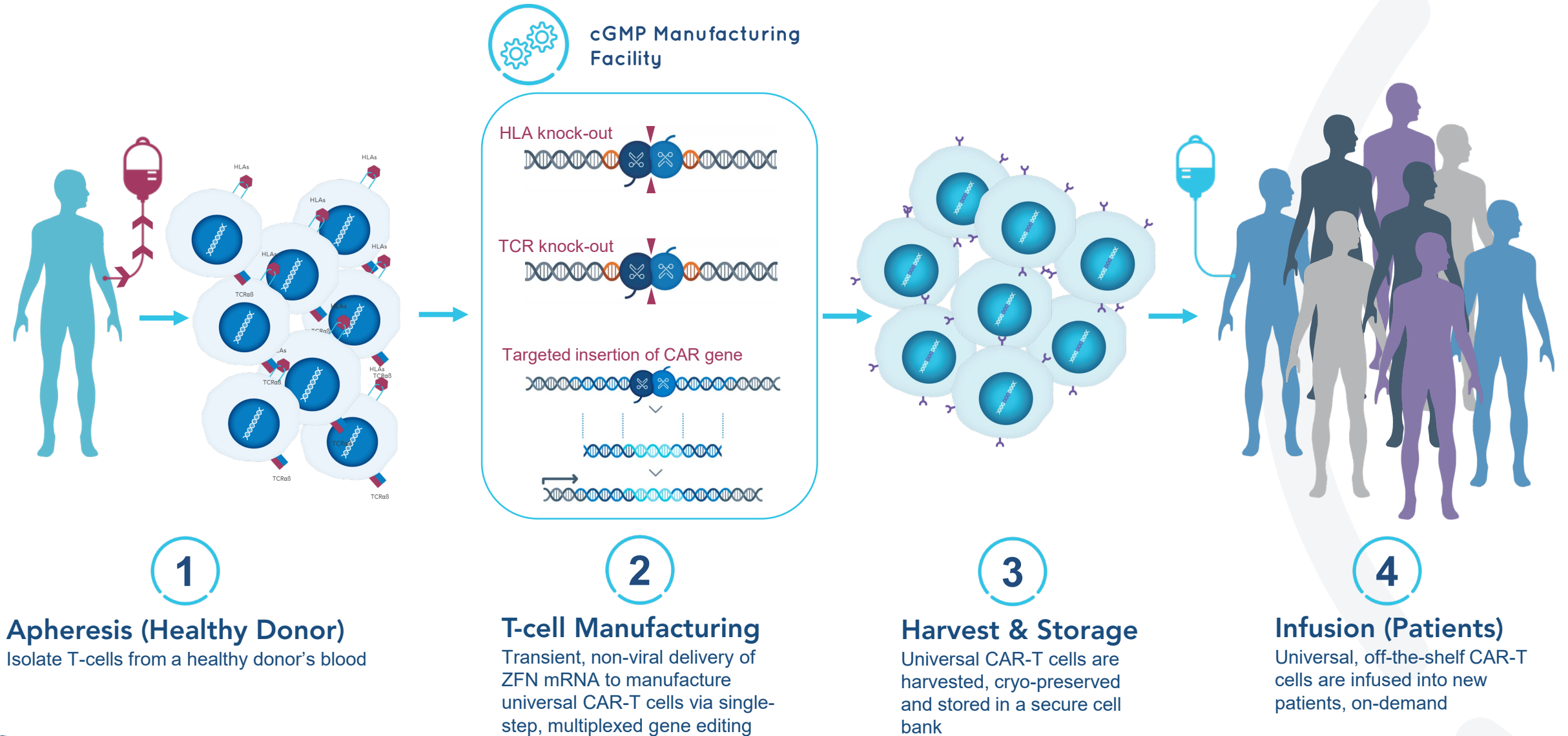
ST-400: beta thalassemia

BIVV003: sickle cell disease

CAR-T therapy for oncology

CAR-Tregs for immunology

# Manufacturing allogeneic T-cell therapies with ZFNs



# 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

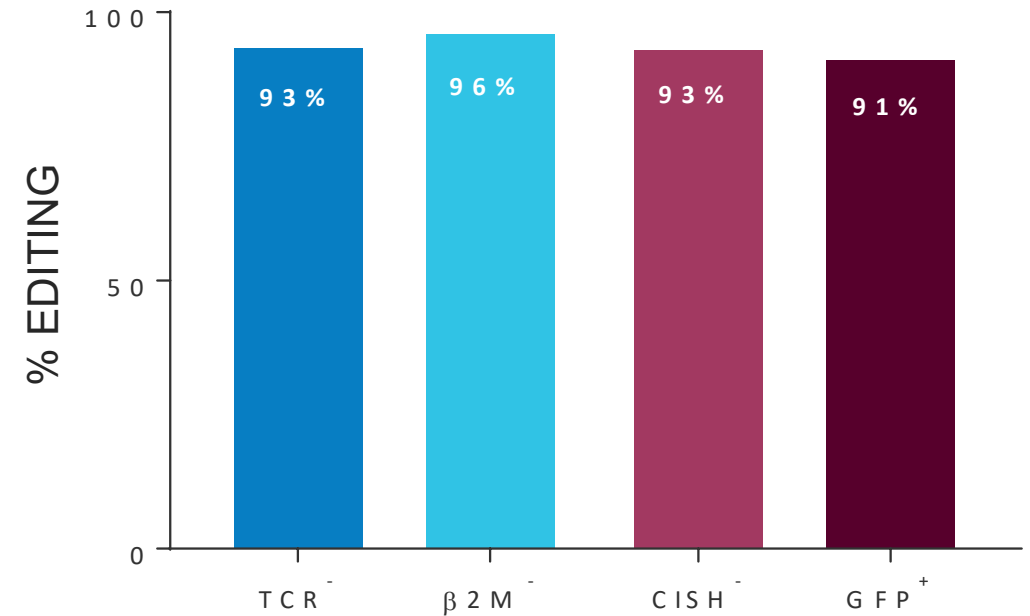


#### ZFN Knock-out

- TCR (TRAC)
- HLA-class I ( $\beta$ 2M)
- CISH (checkpoint gene)

#### Targeted Insertion

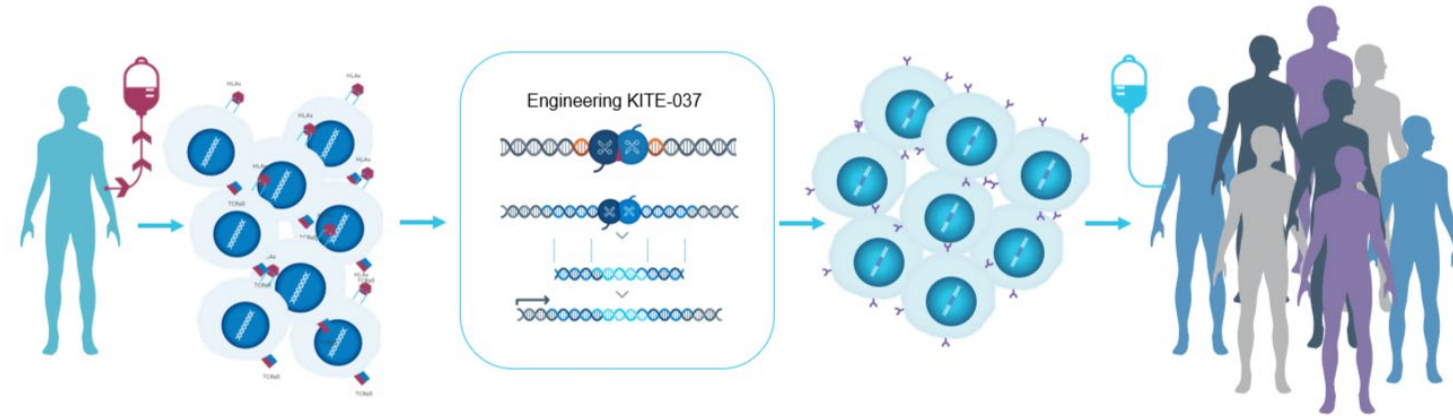
- GFP (into TRAC)



76% of cells have all 4 edits

# Kite collaboration next steps

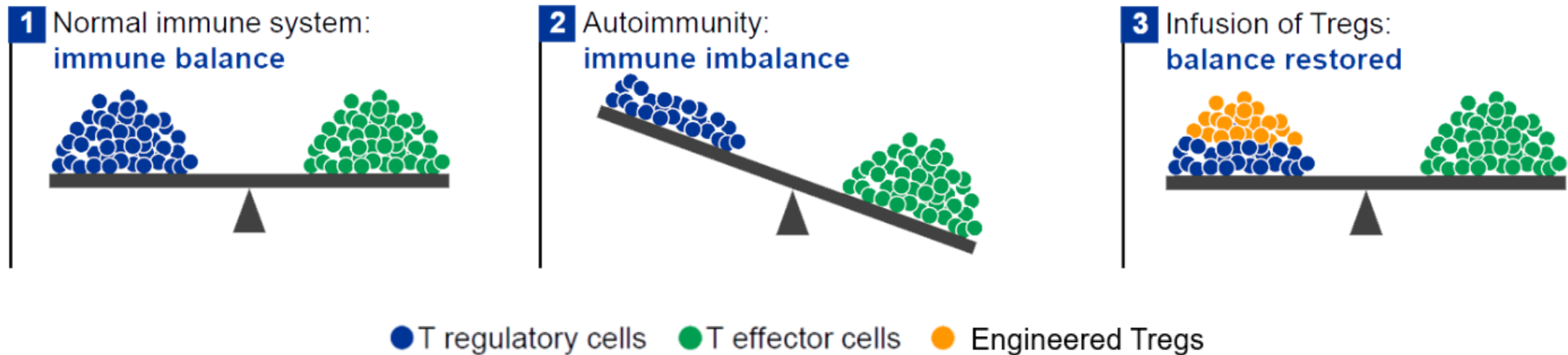
- **First product candidate is Kite-037, an allogeneic anti-CD19 CAR-T**
- Kite is planning to initiate a clinical study evaluating Kite-037 in 2020



# 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

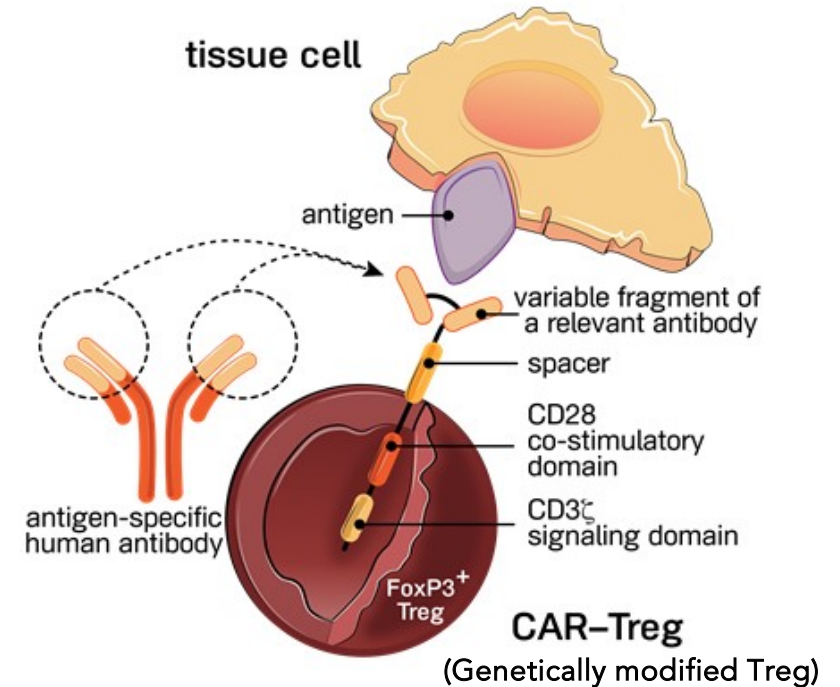
## Engineered CAR-Tregs

**Antigen localized:** tissue-specific activity

**Antigen activated:** better controlled cell product and dosing

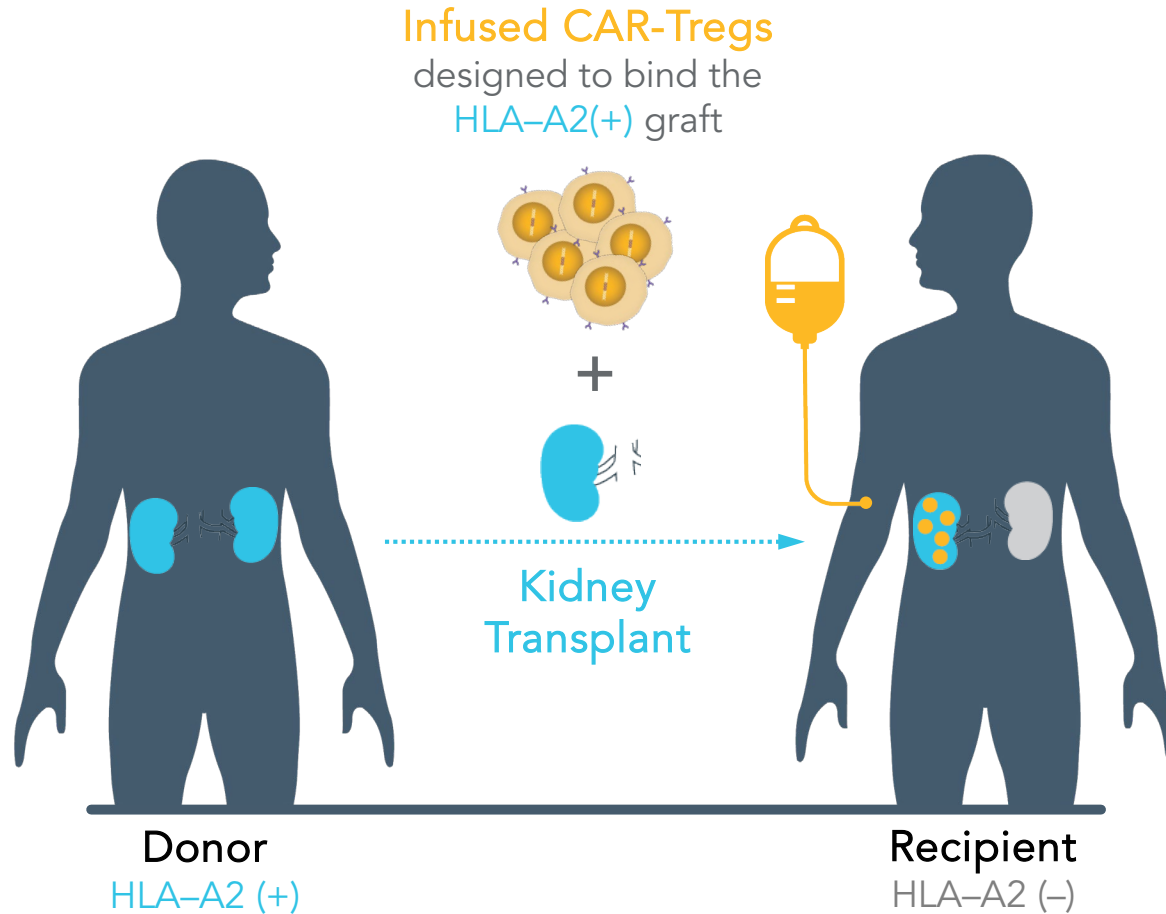
**Robust and scalable** processes

## Antigen-specific CAR-Treg



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

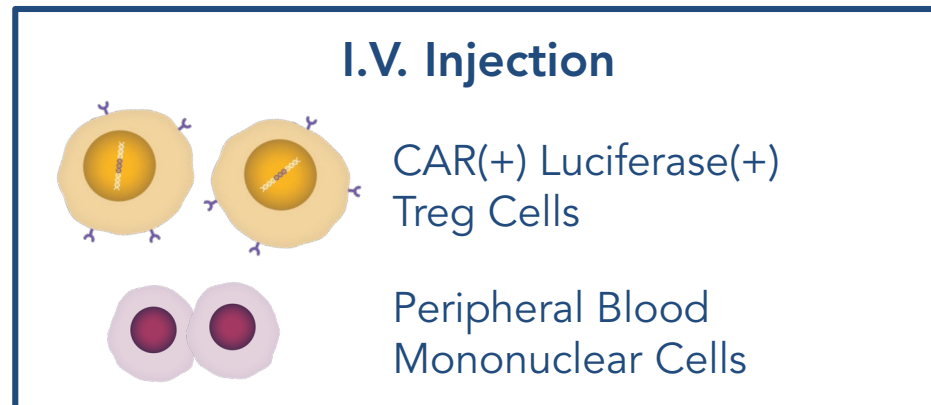
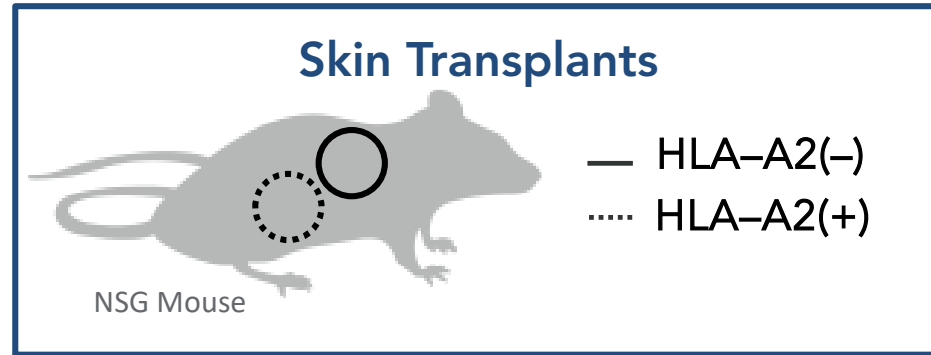
## Induction of site-specific immune tolerance



- 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

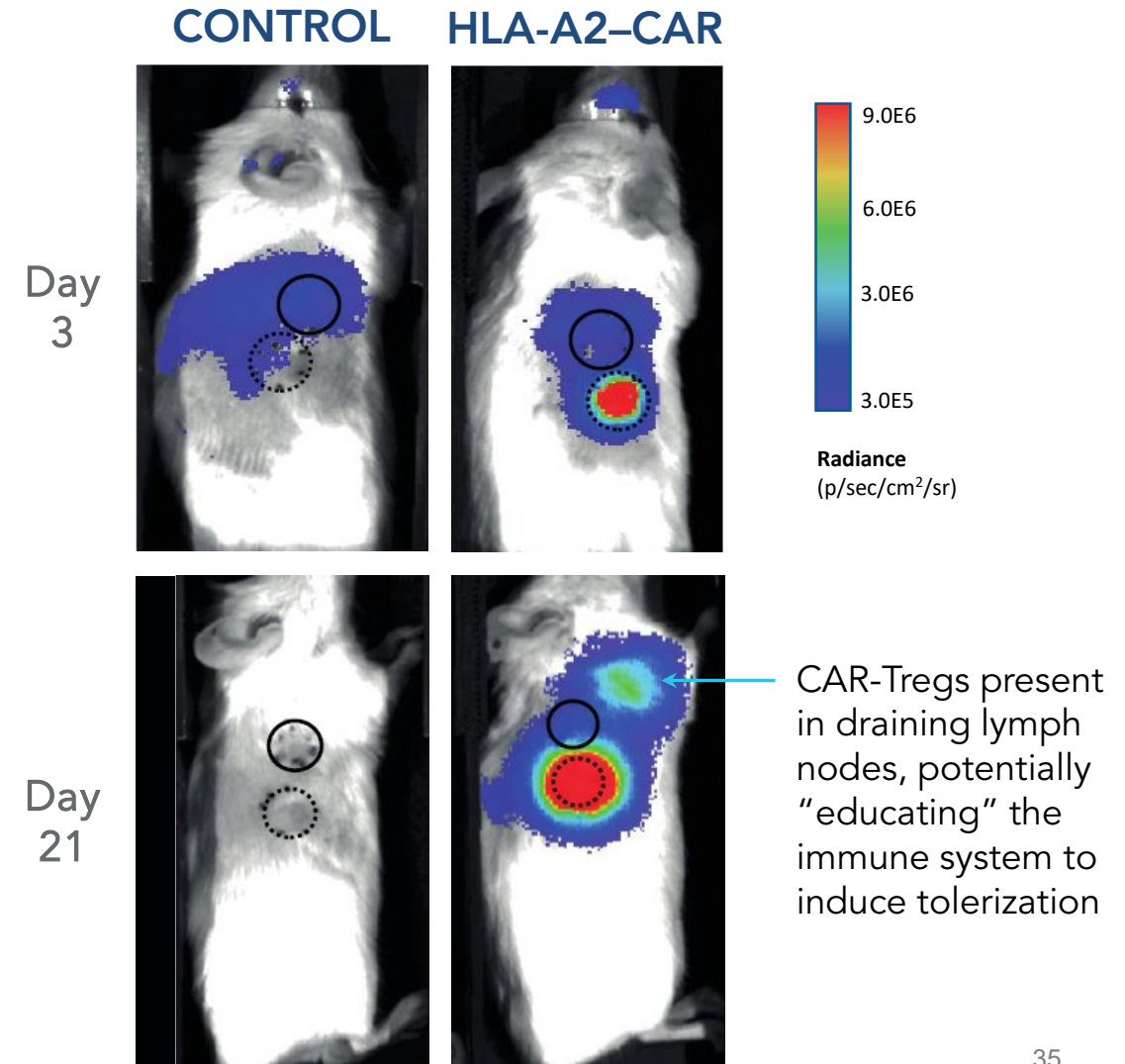
CTA filed and under review

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

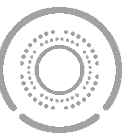


**Imaging**

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



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

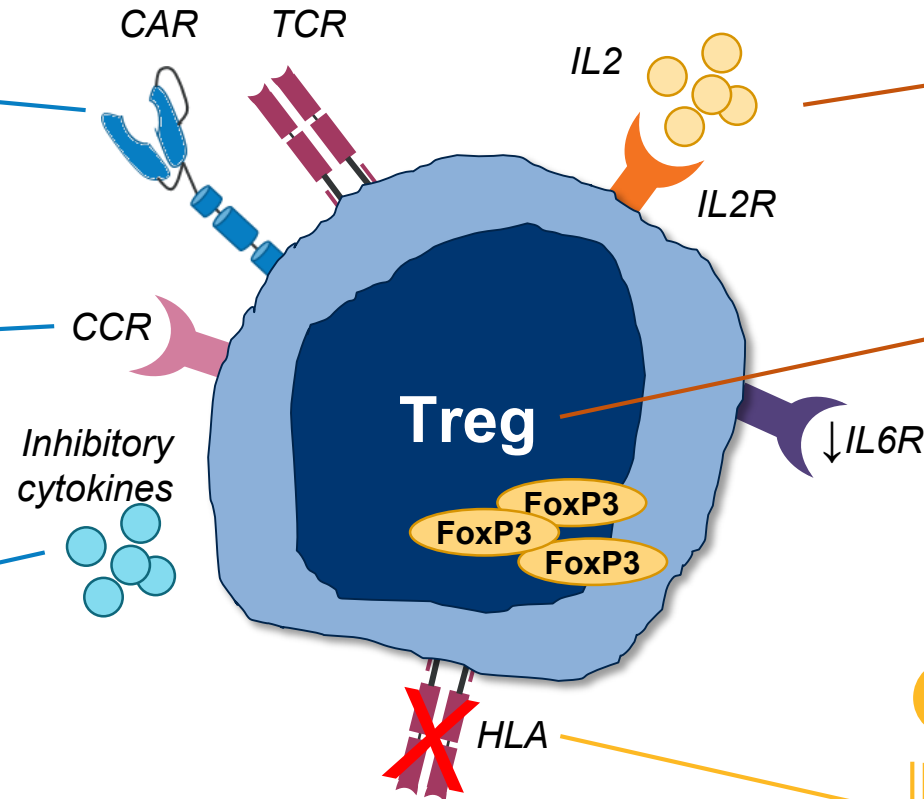


## ⚡ Increase Efficacy + Potency

Target tissue-specific antigen(s) w/CAR

Promote localization to disease site(s) with chemokine receptors

Bolster immunosuppressive function



## 🕒 Increase Persistence + Stability

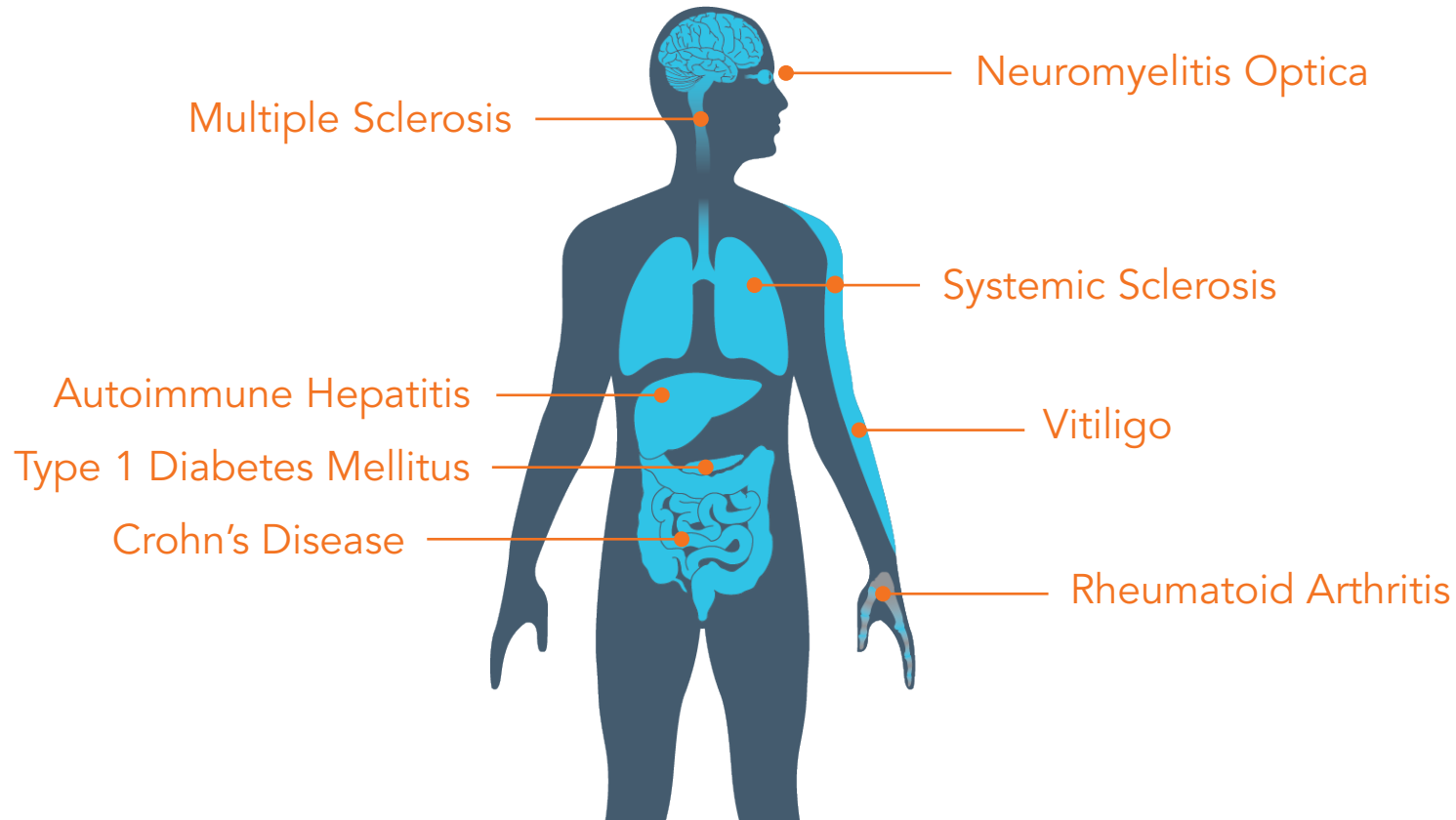
Increase Treg proliferation and durability

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

# *In Vivo* Genome Editing

SB-913: MPS II

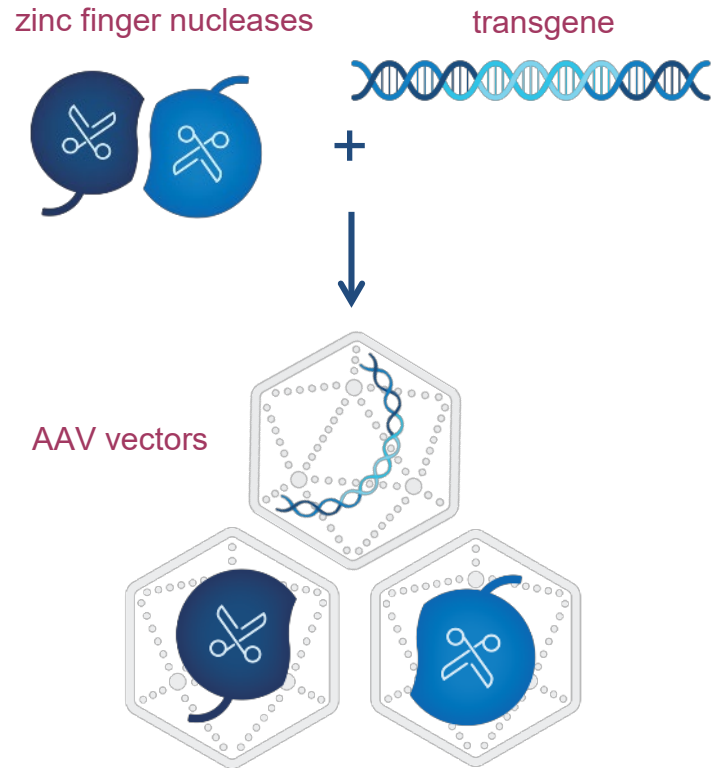
SB-318: MPS I

SB-FIX: hemophilia B

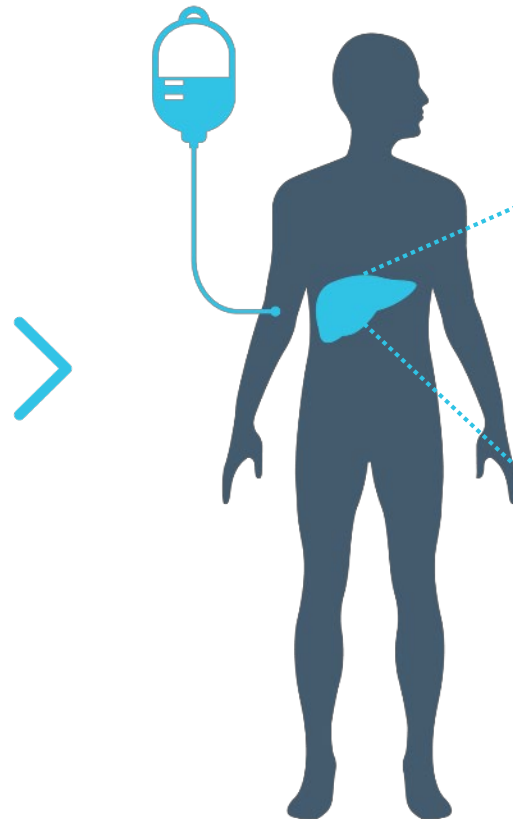
# *In Vivo* genome editing: harnessing the albumin locus in the liver



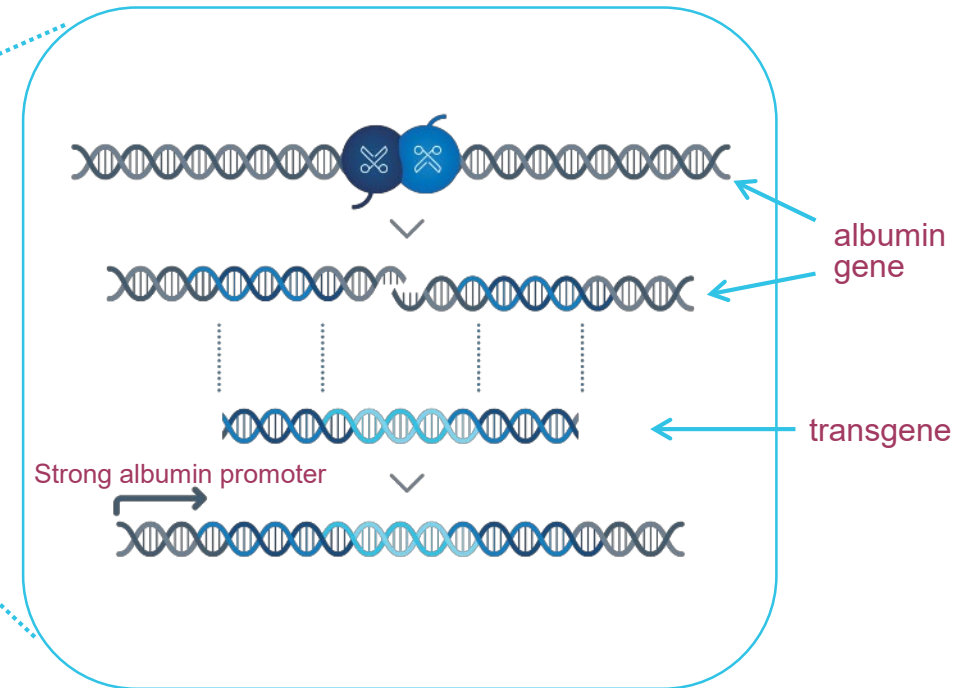
## Packaging into AAV vectors



## Delivery



## In the liver



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

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- As previously announced, Phase 1/2 clinical trials evaluating these programs are ongoing and data will continue to accumulate throughout 2019. No additional patients will receive first-generation ZFNs
- Next *in vivo* genome editing clinical trial is expected to be initiated by year-end 2020
  - Next-generation albumin locus construct with updated ZFNs to improve precision, efficiency, and specificity
  - Delivery enhancements to increase intra-cellular concentration of ZFNs





CNS

Tauopathies  
C9ORF72-linked ALS/FTLD  
Huntington's disease

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



## Potential CNS applications of ZFP-TF gene regulation

### Pan-Allele

ZFP-TFs can be engineered for potent and specific single gene repression

- Tauopathies
- $\alpha$ -synuclein

### Allele-Selective

Repeat-targeted ZFP-TFs repress disease isoforms while preserving normal protein expression

- Huntington's Disease
- C9ORF72-linked ALS

### X Reactivation

Target DNA demethylase domain locally to precisely and specifically reverse X inactivation

- Rett Syndrome
- Fragile X

## Potential CNS applications of ZFN genome editing

### Inflammation based targets

ZFN modified Treg cells for inhibition of neuroinflammation and remyelination

- Multiple Sclerosis
- ALS

### Mitochondrial

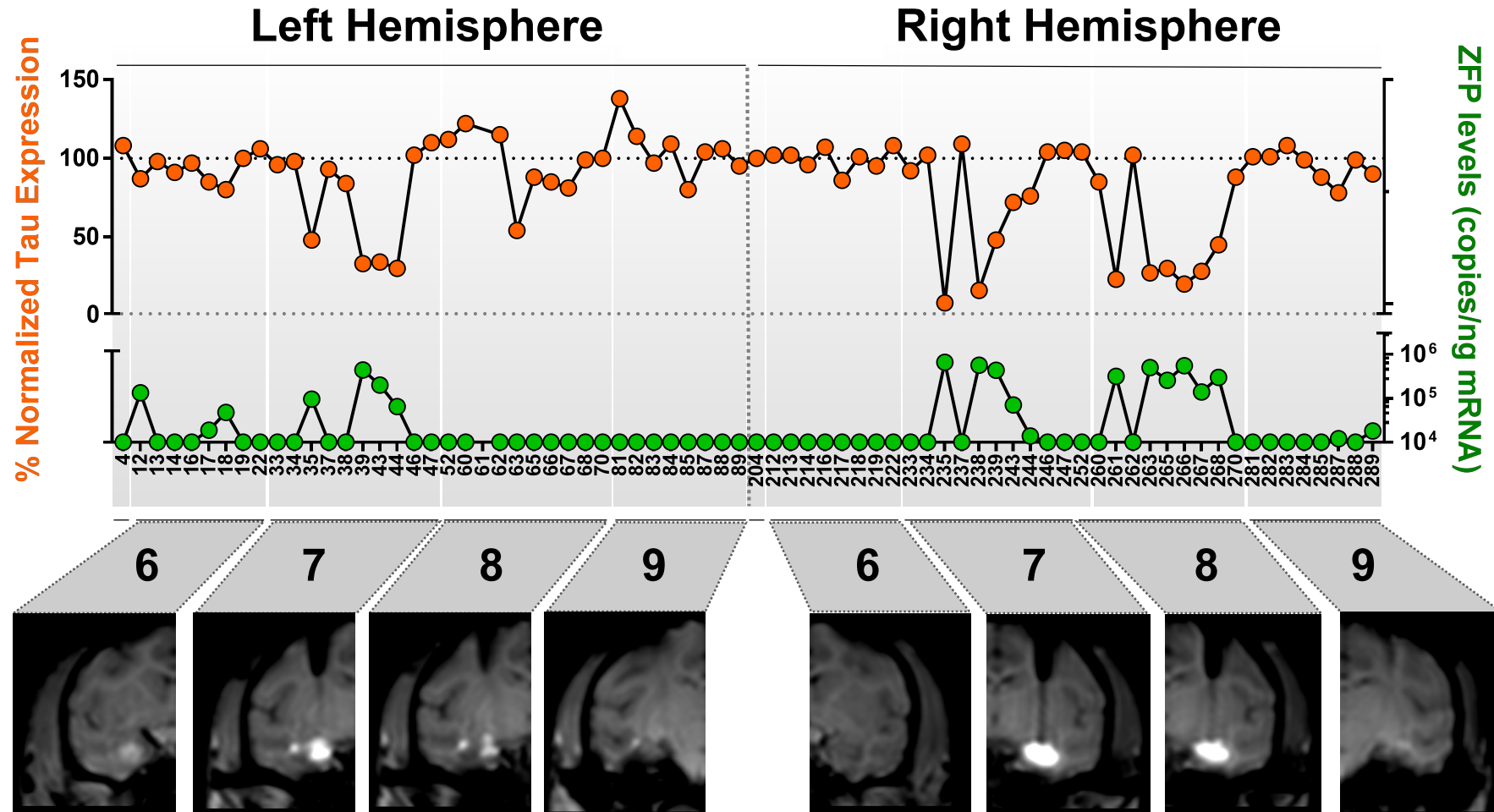
ZFNs for selective clearance of mutant mitochondrial genomes in heteroplasmic cells

- Ataxia
- Leigh Syndrome

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

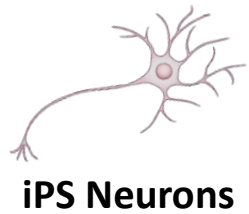


qRT-PCR:  
All Punches  
for 1 NHP



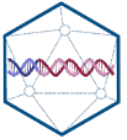
ZFP expression and tau reduction are closely correlated

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



iPS Neurons

+

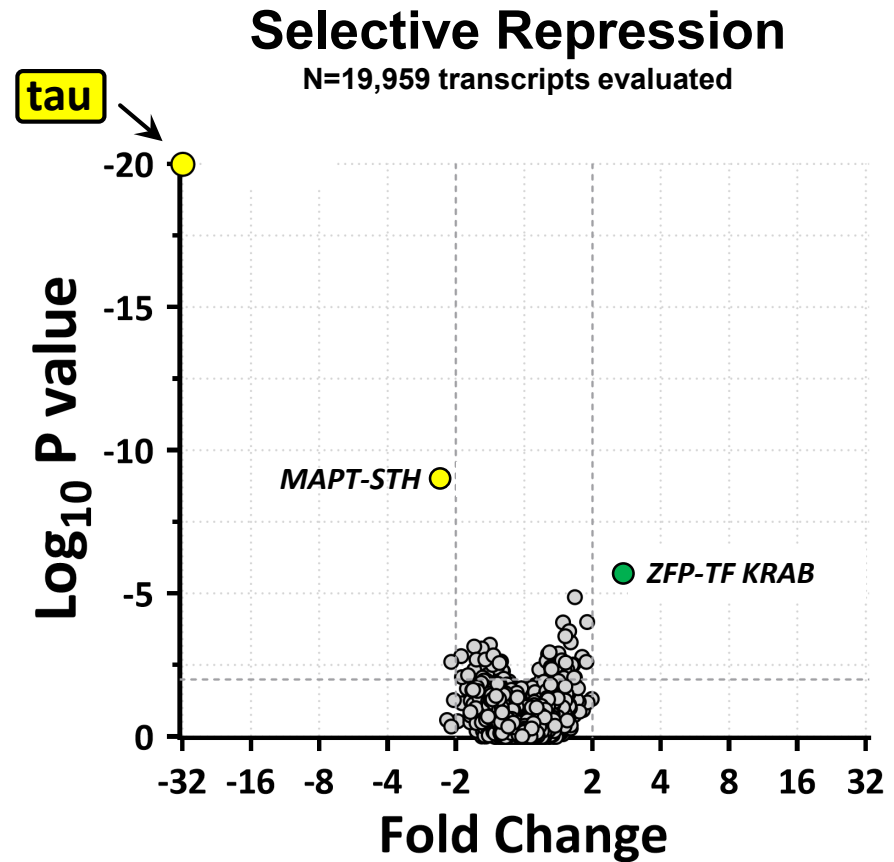
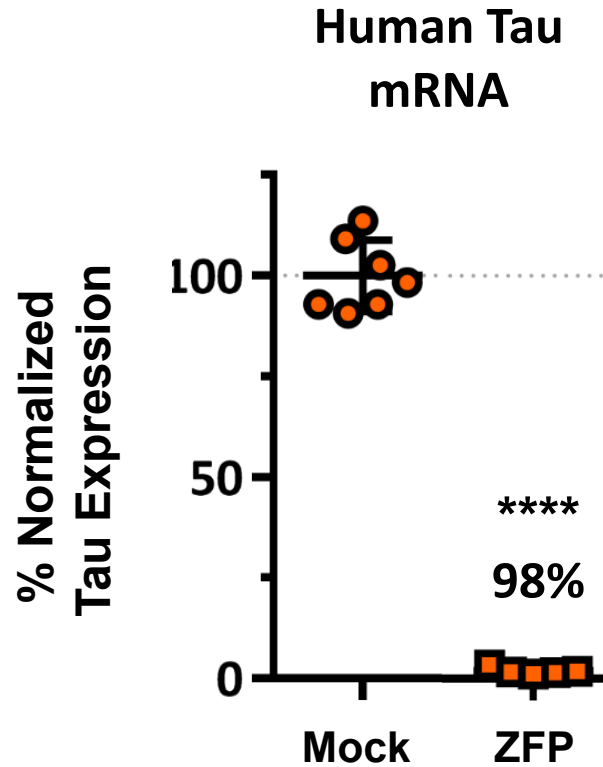


AAV6 + ZFP

19d



qRT-PCR  
microarray



# Engineered allele-selective ZFP-TFs for treatment of Huntington's Disease (HD)

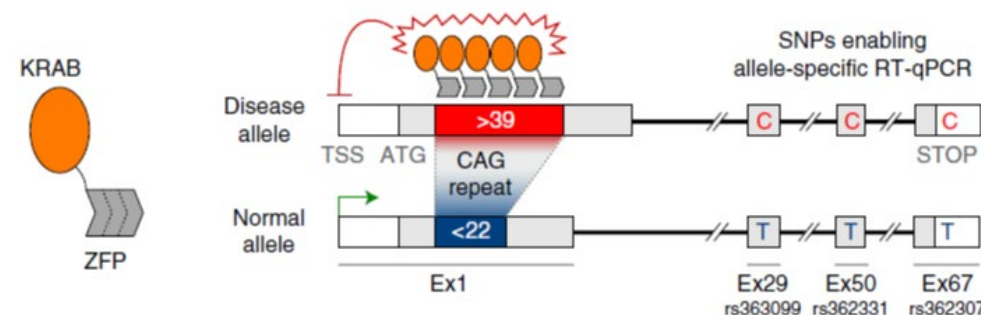
- HD - caused by a CAG trinucleotide expansion coding the mutant HTT (mHTT) protein
- Therapeutic strategy: Allele-selective ZFP-TFs targeting pathogenic CAG repeats without disrupting normal HTT expression
- In patient-derived fibroblasts and neurons, ZFP-TFs repressed >99% of mutant alleles while preserving expression of >86% of normal alleles
- Virally delivered ZFP-TFs are well tolerated and active in neurons >100 days in culture and at least nine months in the mouse brain
- Improvements in molecular, histopathological, electrophysiological and functional endpoints

nature  
medicine

ARTICLES

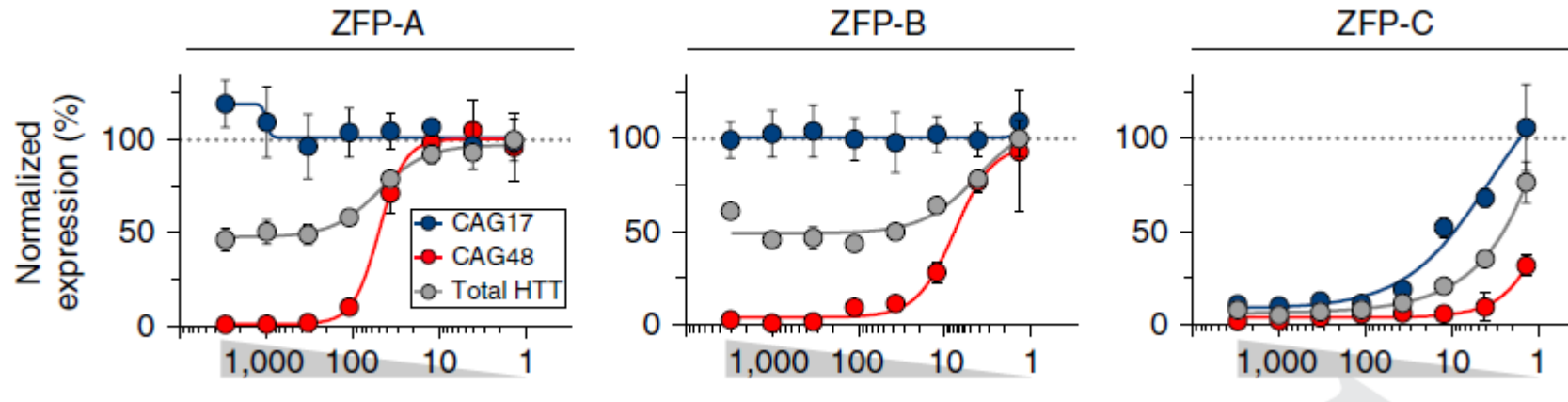
<https://doi.org/10.1038/s41591-019-0478-3>

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

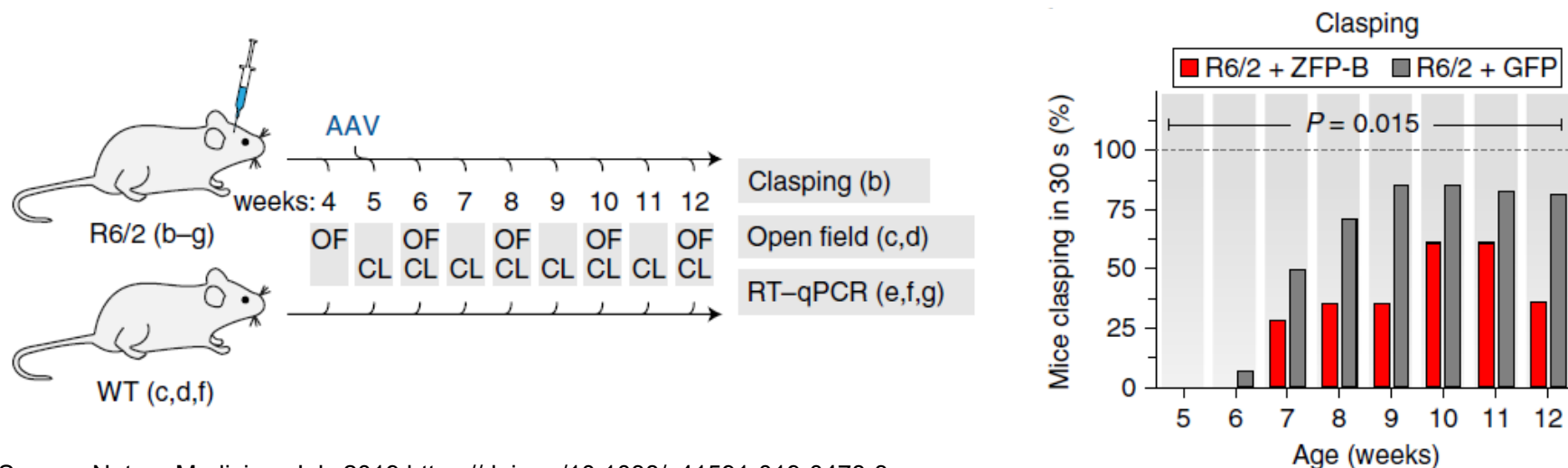


# ZFP-TFs repressed mHTT expression in neurons and improved motor abnormalities in mice

Three ZFPs tested in neural stem cells: two repress the disease allele only; a third represses both



Reduced clasping in mice suggests potential for improvements in HD motor abnormalities



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# Finance and Operations

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Financial results  
Manufacturing

# 3Q 2019 financial results and 2019 guidance

\$ in Millions, except per share data	Q3 2019	Q3 2018
Revenues		
	\$22.0	\$23.6
Operating Expenses		
R&D	36.3	28.8
G&A	14.9	11.0
Total Operating Expenses	51.2	39.8
Operating Loss	(29.2)	(16.2)
Net Loss	(27.3)	(12.8)
Net Loss per Share	(\$0.24)	(\$0.13)
Cash Position		
Ending Cash Balance	\$408.3	\$459.3

Amounts have been rounded for presentation purposes

## 2019 Guidance

Operating  
expenses:  
**\$210-220M**

Cash runway:  
**Through  
year-end  
2021**



# 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

- In-house phase 1/2 cGMP manufacturing by 2021
  - Gene therapy: Brisbane, California
  - Cell therapy: Brisbane, California and Valbonne, France
- 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
  - Enables seamless transition from early to late stage development and manufacturing
  - Sangamo and Brammer have worked together for more than a decade

# Conclusions



# Milestones and catalysts

## Gene therapy



SB-525: hemophilia A

- present longer-term patient data at ASH 2019
- IND transfer to Pfizer in 1Q 2020

ST-920: Fabry disease

- first patient enrolled by year end 2019

## *Ex Vivo* gene-edited cell therapy



ST-400: beta thalassemia

- complete patient enrollment
- present additional preliminary data at ASH 2019

BIVV003: sickle cell disease

- complete patient enrollment (Sanofi)

TX200: solid organ transplant

- CTA filed and under review

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 next *in vivo* genome editing clinical study before year end 2020

# Key takeaways

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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



