

Corporate Presentation

September 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, 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-Treas 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 forwardlooking 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 guarter ended June 30, 2019 that it filed on August 7, 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









Gene therapy provides tractable, valuable nearterm opportunities





Gene therapy provides tractable, valuable nearterm opportunities Continue to advance *ex vivo* editing to create cell therapies





Gene therapy provides tractable, valuable nearterm 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



SB-525: Hemophilia A ST-920: Fabry disease Undisclosed targets ST-400: Beta thalassemia BIVV003: Sickle cell disease TX200: Solid organ transplant KITE-037: Allo-CD19 CAR-T Undisclosed targets SB-913: MPS II SB-318: MPS I SB-FIX: Hemophilia B Undisclosed targets Tauopathies C9ORF72-linked ALS/FTLD Huntington's disease Undisclosed targets



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)					Pfizer
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 (Multiple)					Kite
In Vivo Genome Editing					
MPS I (SB-318)					
MPS II (SB-913)					
Hemophilia B (SB-FIX)					
In Vivo Gene Regulation					
Tauopathies					
ALS/FTD					Pfizer
Huntington's Disease					Takeda



Gene Therapy

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

SB-525, gene therapy for hemophilia A





Factor VIII activity: Chromogenic



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

Konkle BA et al. ISTH 2019 Melbourne, AU, 6 July 2019

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
- 1	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

Data cut-off date: 30 MAY 2019

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 [§]

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

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

Data cut-off date: 30 MAY 2019

Konkle BA et al. ISTH 2019 Melbourne, AU, 6 July 2019

Safety Summary

- Treatment-related SAEs of hypotension (grade 3) and fever (grade 2) in one Cohort 4 subject occurred 6 hrs following SB-525 infusion. Fully resolved with treatment within 24 hrs
 - Based on the temporal association, assessed as related to study treatment
 No similar hypotension observed in subsequent 3 subjects dosed
- In the 3e13 vg/kg cohort two subjects experienced a transient grade 1 alanine aminotransferase elevation (>1.5 x baseline) managed with a tapering course of oral steroids. Neither resulted in a loss of FVIII activity levels

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



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
- ST-920 clinical trial initiated (STAAR). First patient enrollment expected by year-end 2019

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 a-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) <u>KITE-037: Allogeneic anti-</u>CD19 CAR-T

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

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

Sangame

SANOFI 5

22

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

Apheresis (Healthy Donor) Isolate T-cells from a healthy donor's blood

Sangame

universal CAR-T cells via single-

step, multiplexed gene editing

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

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 <u>activated</u>: better controlled cell product and dosing

Robust and scalable processes

tissue cell antigen variable fragment of a relevant antibody spacer **CD28** co-stimulatory domain CD3C antigen-specific human antibody signaling domain FoxP3 Treg CAR-Treg (Genetically modified Treg)

Antigen-specific CAR-Treg

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

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

Radiance $(p/sec/cm^2/sr)$

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

Day

3

Day

21

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 longterm protection of graft

Phase 1/2 clinical trial initiation expected in 2019

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 (

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

- 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

Gene regulation

C9ORF72-linked ALS/FTLD Tauopathies and Huntington's disease

Sangamo's zinc finger protein transcription factors (ZFP-TFs): gene regulation technology for CNS diseases

>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

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 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

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

Sanaamo

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

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

Normal Allele: ~2–30x

Operations

Manufacturing

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

Conclusions

Milestones and catalysts

Gene therapy	SB-525: hemophilia A ST-920: Fabry disease	 present longer-term patient data (4Q 2019) complete regulatory and manufacturing preparations for Phase III first patient enrolled by year end 2019
<i>Ex Vivo</i> gene-edited cell therapy	ST-400: beta thalassemia BIVV003: sickle cell disease TX200: solid organ transplant KITE-037: Allo-CD19 CAR-T	 complete patient enrollment present additional preliminary data (4Q 2019) complete patient enrollment (Sanofi) file CTA in 2019 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 <i>in vivo</i> genome editing clinical study before year end 2020

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

