Sangamo THERAPEUTICS

Clinical data from SB-913 MPS II and SB-318 MPS I Phase 1/2 studies presented at WORLD*Symposium* 2019

February 7, 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 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; plans to conduct controlled withdrawal of weekly ERT infusions in subjects in the CHAMPIONS and EMPOWERS Studies; anticipated next steps for the CHAMPIONS and EMPOWERS Studies, and Sangamo's expectation that it will present longer-term safety and efficacy results from the CHAMPIONS and EMPOWERS Studies later in 2019. 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 the CHAMPIONS and EMPOWERS Studies will be representative of final results, whether the final results from the CHAMPIONS and EMPOWERS Studies will validate and support the safety and efficacy of SB-913 and SB-318, respectively, 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 Reports on Form 10-Q for the quarter ended September 30, 2018 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.

Agenda

Welcome
McDavid Stilwell
VP, Corporate Communications and Investor Relations

Introduction
Sandy Macrae
Chief Executive Officer

SB-913 and SB-318 Clinical Data
Ed Conner, MD
Chief Medical Officer

ZFN Gene Editing Platform
Adrian Woolfson, BM, BCh, PhD
EVP, Research & Development

Closing Remarks and Q&A

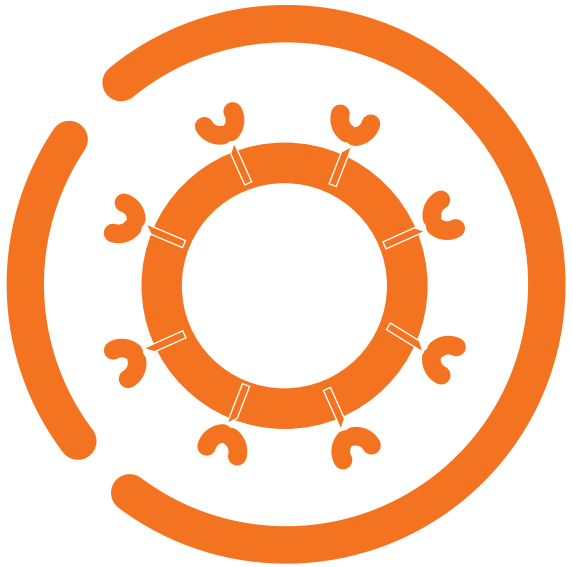
Sangamo THERAPEUTICS

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

Proprietary genomic medicines pipeline focused on three therapeutic areas

Inherited Metabolic Diseases

Rare Populations



Immunology

Rare + Large Populations

Central Nervous System

Rare + Large Populations

Partnered therapeutic areas

Hematology

Oncology

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Active clinical trials in inherited metabolic diseases and hematology

Therapeutic Area	Research	Preclinical	Phase I/II Clinical	Phase III Registrational	Collaborator
Inherited Metabolic Diseases					
MPS I (SB-318)					
MPS II (SB-913)					
Hematology					
Hemophilia A (SB-525)					Pfizer
Hemophilia B (SB-FIX)					
Hemoglobinopathies (ST-400, BIVV-003)					Bioverativ A SANOFI COMPANY

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SB-318 and SB-913 data presentations at WORLD are the first in a series of clinical readouts and updates expected in 2019

Inherited Metabolic Diseases

SB-913: MPS II (Hunter syndrome)

- ✓ Safety updates and biochemical changes
- ✓ Liver biopsy data
- ERT withdrawal
- Cohort expansion data

SB-318: MPS I (Hurler syndrome)

- ✓ Safety updates and biochemical changes
- Liver biopsy data
- ERT withdrawal
- SMC review and recommendations
- Cohort expansion data

Hematology

SB-525: hemophilia A

- SMC cohort expansion recommendation
- Safety and Factor VIII activity
- Factor replacement utilization
- Bleeding events

SB-FIX: hemophilia B

- ✓ Patient enrollment
- SMC review and recommendations
- Preliminary safety and Factor IX activity

ST-400: beta thalassemia

- Patient enrollment
- Preliminary safety and HbF production

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Advancing our proprietary and partnered preclinical programs into the clinic this year

Inherited Metabolic Diseases

ST-920: Fabry disease

Clinical trial initiation expected in 2019

Immunology

Tx200: Solid organ transplant (kidney)

Clinical trial initiation expected in 2019

Oncology

Allogeneic anti-CD19 CAR T

IND filing expected in 2H 2019 (Kite-Gilead)

Hematology

BIVV-003: Sickle cell disease

- Phase 1/2 trial is active and screening subjects (Bioverativ-Sanofi)

Clinical Data Review
SB-913 and SB-318

Ed Conner, MD
Chief Medical Officer

What are MPS I (Hurler syndrome) and MPS II (Hunter syndrome)?

About MPS I and MPS II

- Inherited, X-linked metabolic diseases caused by mutations in the genes encoding IDS enzyme (MPS II) and IDUA enzyme (MPS I)
- Mutations in IDS/IDUA gene result in loss of IDS or IDUA metabolic enzyme activity
- Accumulation of toxic waste products called glycosaminoglycans (GAGs) in lysosomes leads to tissue and organ damage
- Enzyme replacement therapy (ERT) does not address all symptoms of the disease and requires weekly infusions lasting several hours per treatment

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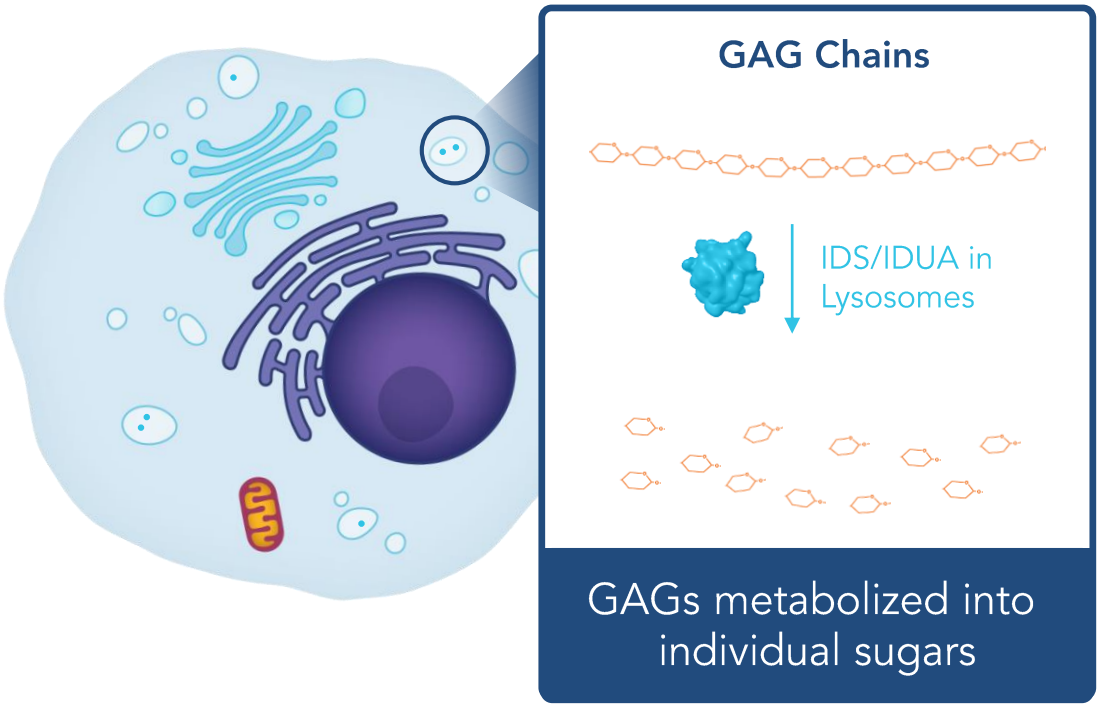
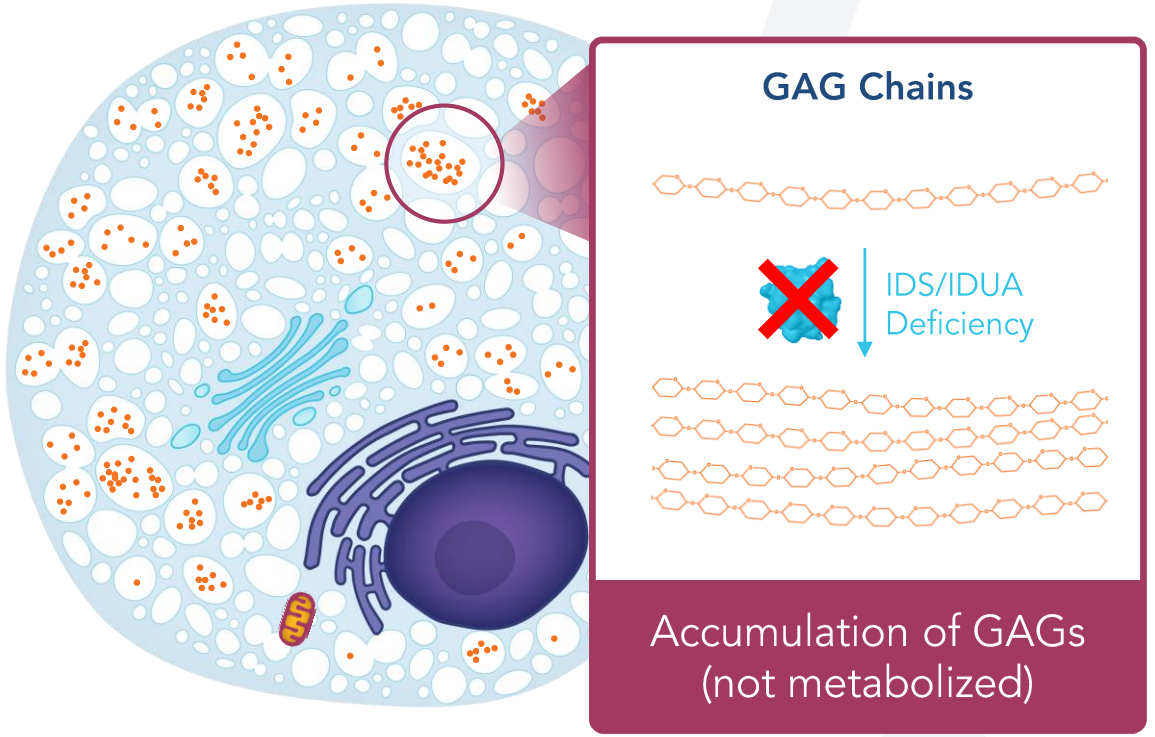
A lack of active enzyme results in accumulation of GAGs in the lysosomes, leading to loss of cellular function and organ damage

Normal Cell



MPS Cell



Toxic build up enlarges lysosomes, crowds critical organelles and engorges the cell

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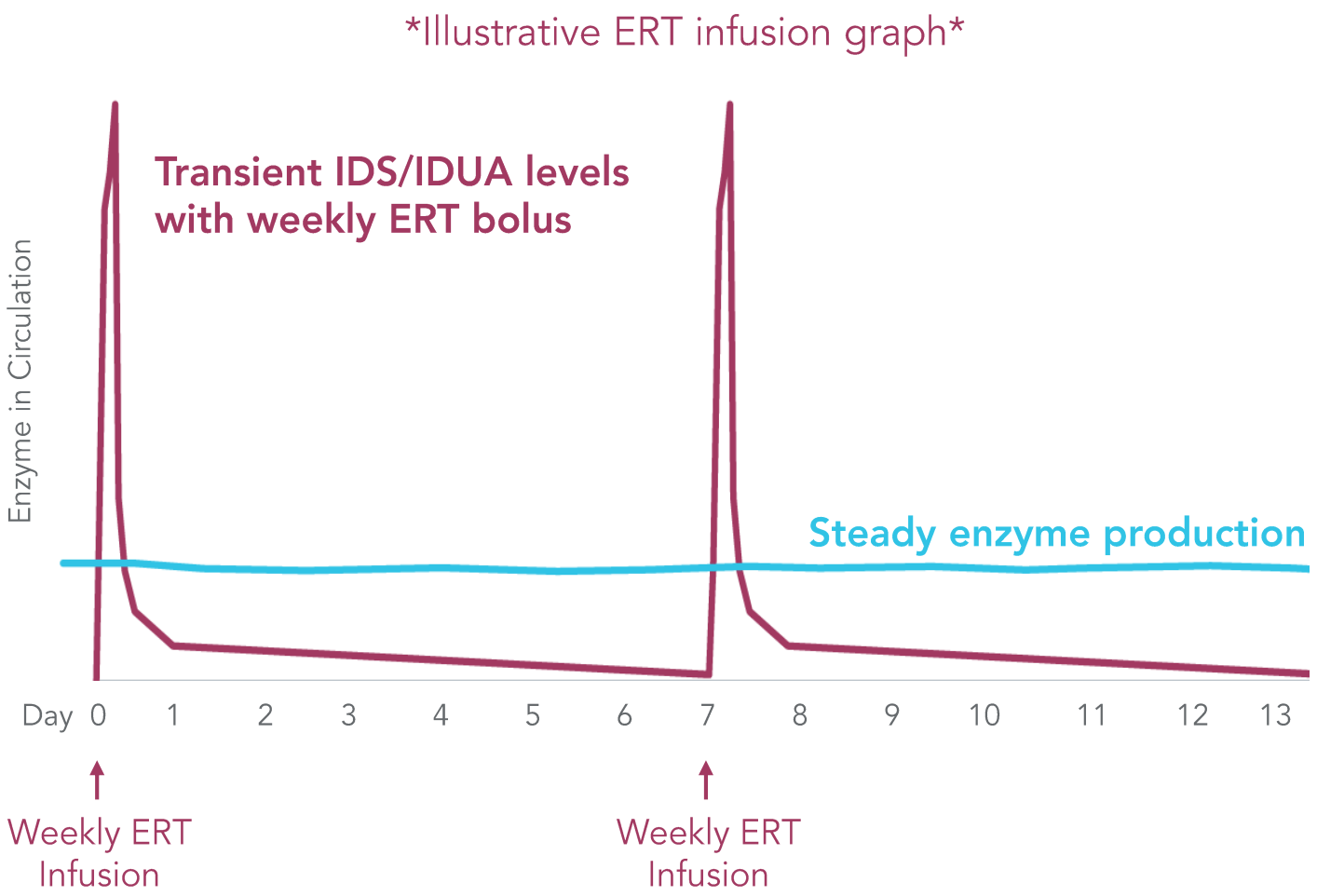
ERT infusions do not provide sustained exposure of enzyme to the tissues



- Large amount of enzyme is taken up by the liver due to high-capacity, low-specificity receptors on liver cell surface
- For significant period of time (i.e. 5-6 days out of the week), patients' enzyme levels are very low or absent
- PK modeling: steady enzyme production allows for longer interaction of IDS / IDUA with uptake receptor, leading to GAG reduction

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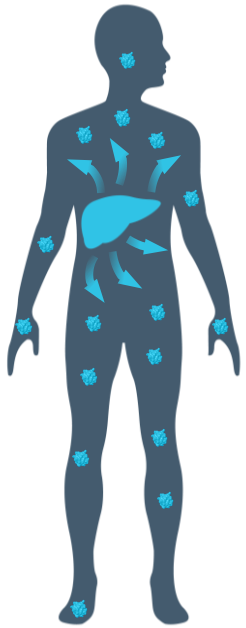
The goal of genome editing is to continuously produce enzyme in order to stabilize or reduce GAG accumulation

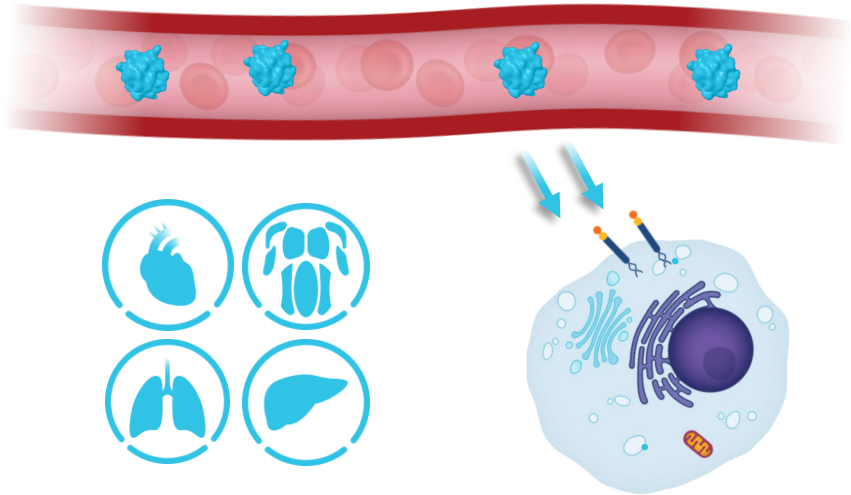
1

Edited liver cells steadily release enzyme into the circulation



2

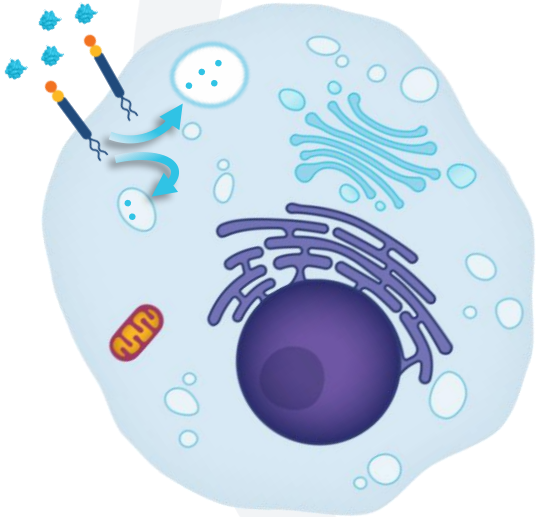
Stable enzyme levels in circulation increase exposure in tissues throughout the body, facilitating receptor-mediated uptake of enzyme



Continuous enzyme exposure may also facilitate uptake in tissues with limited vascularization

3

Enzyme is transported to lysosomes to metabolize GAGs



SB-913, *in vivo* genome editing for MPS II

Expanding high dose cohort, initiating adolescent screening and ERT withdrawal

Phase I/II Open Label Study

9 Adults (18+ yrs), 2+ adolescents (12-17 yrs) and 2+ children (5-11 yrs) with MPS II

Dose Escalation Complete

Cohort 1	Cohort 2	Cohort 3
5e12 vg/kg	1e13 vg/kg	5e13 vg/kg

October SMC Review / Recommendations

- **Adult Cohort Expansion (5e13 vg/kg)**
- **Initiate Adolescent Dosing (12-17 years)**
- **Initiate ERT withdrawal**

Adult Cohort Expansion and Adolescent Screening Underway

5e13 vg/kg

Next steps

- **Interim data update from cohorts 1-3 at WORLD*Symposium* 2019**
- **Completed enrollment of adult expansion cohort**
- Complete ERT withdrawal
- Initiate 2nd generation ZFN study

FDA

- Orphan Drug
- Fast Track
- Rare Pediatric Disease

- Orphan Medicinal Product

IND open

CTA granted

Goals

Patient safety | Reduction in GAGs | IDS enzyme production | ERT withdrawal

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SB-913-1602: Serious Adverse Events (SAEs)

- Three serious adverse events (SAEs) were reported, one in each cohort
- All 3 SAEs were assessed as *not related* to the study drug by the site investigator, and considered secondary to the subject's MPS II disease
- All 3 subjects have recovered and remain on study

MedDRA Preferred Term	Cohort/ (Dose)	Study Day	Toxicity Grade	Outcome	Relationship to Study Drug	
Bronchitis	1 (5e12vg/kg)	20	3	Resolved	Not related	Secondary to subject's medical history of chronic pulmonary disease from MPS II
Atrial fibrillation	2 (1e13vg/kg)	52	2	Resolved	Not related	Secondary to subject's medical history of cardiac valve disease from MPS II
Umbilical hernia, obstructive	3 (5e13vg/kg)	121	3	Resolved*	Not related	Secondary to subject's underlying MPS II disease, medical history of hernias, and obesity

**per PI communication 30 JAN 2019*

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Data cut-off date: 20 DEC 2018

SB-913-1602: Study Drug-Related Adverse Events (AEs)

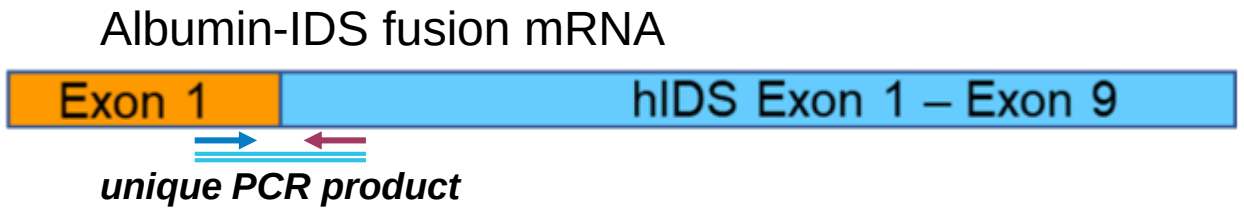
- Study drug-related AEs were mild or moderate and all resolved

MedDRA Preferred Term Severity	Cohort 1 (N=2) n [T]	Cohort 2 (N=2) n [T]	Cohort 3 (N=4) n [T]	Overall (N=8) n [T]
Any Event	2 [5]	1 [5]	2 [8]	5 [18]
Grade 1-Mild	2 [5]	1 [5]	2 [6]	5 [16]
Grade 2-Moderate	-	-	1 [2]	1 [2]
Pruritus	1 [2]	-	1 [1]	2 [3]
Flushing	-	1 [1]	1 [1]	2 [2]
Erythema	-	1 [2]	-	1 [2]
Transaminases increased	-	-	1 [3]	1 [3]
Alanine aminotransferase increased	-	1 [1]	-	1 [1]
Aspartate aminotransferase increased	-	1 [1]	-	1 [1]
Asthenia	1 [1]	-	-	1 [1]
Cold sweat	1 [1]	-	-	1 [1]
Dizziness	1 [1]	-	-	1 [1]
Dysgeusia	-	-	1 [1]	1 [1]
Headache	-	-	1 [1]*	1 [1]
Pyrexia	-	-	1 [1]*	1 [1]

N= Total number of subjects in each treatment group, n= number of subjects in each SOC, [T]= total number of adverse events.
*Grade 2 event reported

Data cut-off date: 20 DEC 2018

SB-913-1602: Liver Biopsy to Assess Genome-Editing



- An RT-qPCR assay has been developed to identify the unique albumin-IDS mRNA transcript in liver biopsy tissue that is made after integration of the IDS gene into the targeted albumin locus
- Results were positive in both Cohort 2 subjects who received 1e13vg/kg dose, Cohort 3 results are pending

Week 24 Results	Cohort 1		Cohort 2		Cohort 3	
Subject	**1**	**2***	**3**	**4**	**5***	**6**
Integration Assay	-	*n/a*	+	+	*n/a*	pend

*no results available as liver biopsy procedure contraindicated due to anticoagulation therapy

- A less sensitive genomic DNA assay using MiSeq to detect insertions/deletions (“indels”) at target site in the albumin gene was negative in all samples tested (lower limit of quantitation ~ 1 in 1,000 genomes)

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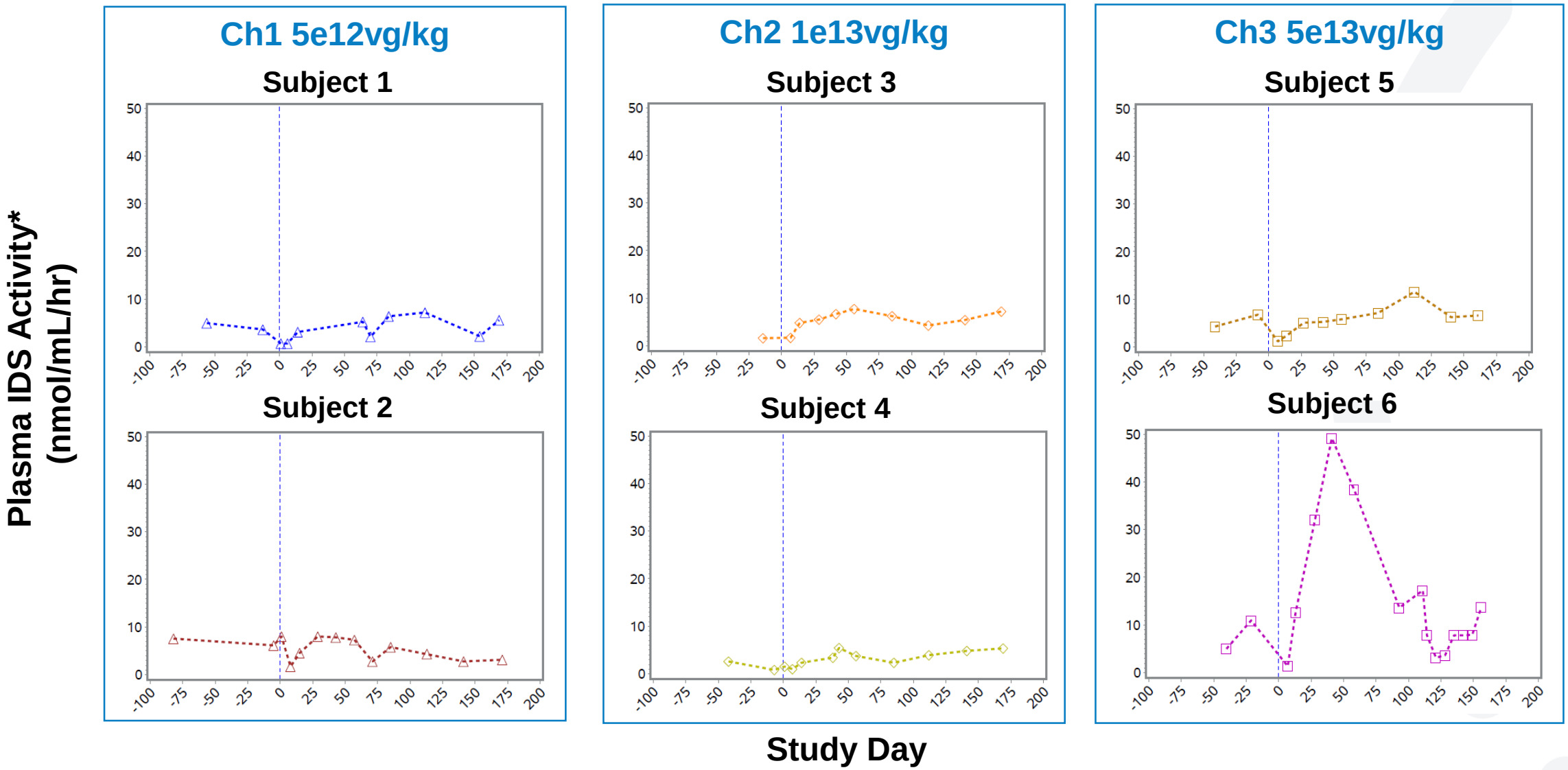
Data cut-off date: 10 JAN 2019

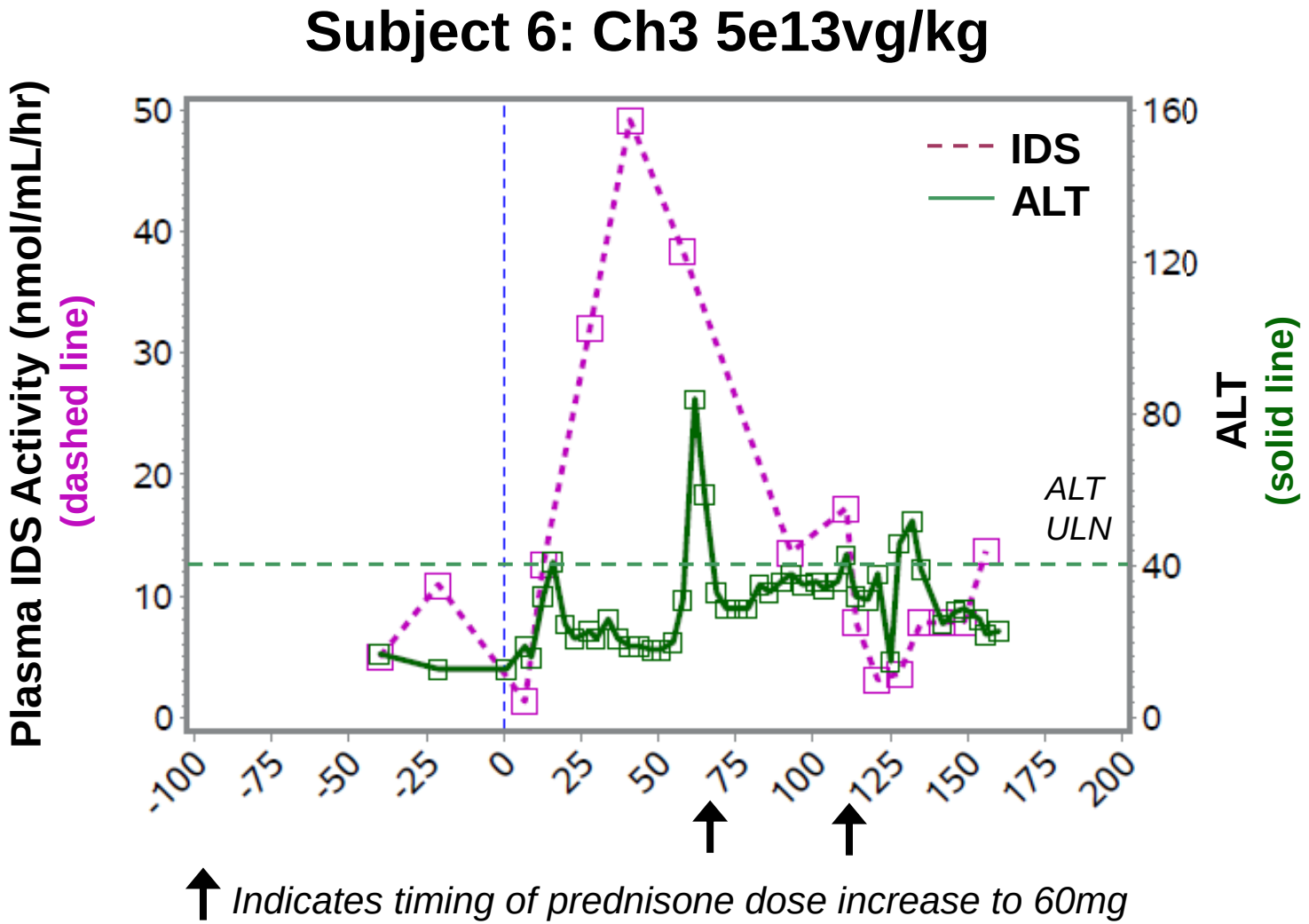
SB-913-1602: Plasma IDS Activity up to Week 24



*Highly-sensitive qualified fluorometric assay with lower limit of quantitation=0.78, samples obtained <96h post-ERT excluded
Reference ranges (nmol/mL/hr): Unaffected: 82-200 Baseline MPS II (>96h post-ERT): estimated 0-10

Data cut-off date: 10 JAN 2019

SB-913-1602: Subject 6 Development of Transaminitis



- Mild (Grade 1) increases in liver function tests reported on study Day 62, 111, and 128
- Prednisone dose increased to 60mg PO daily and then tapered
- Subject also had SAE of incarcerated umbilical hernia on Day 121 unrelated to study drug

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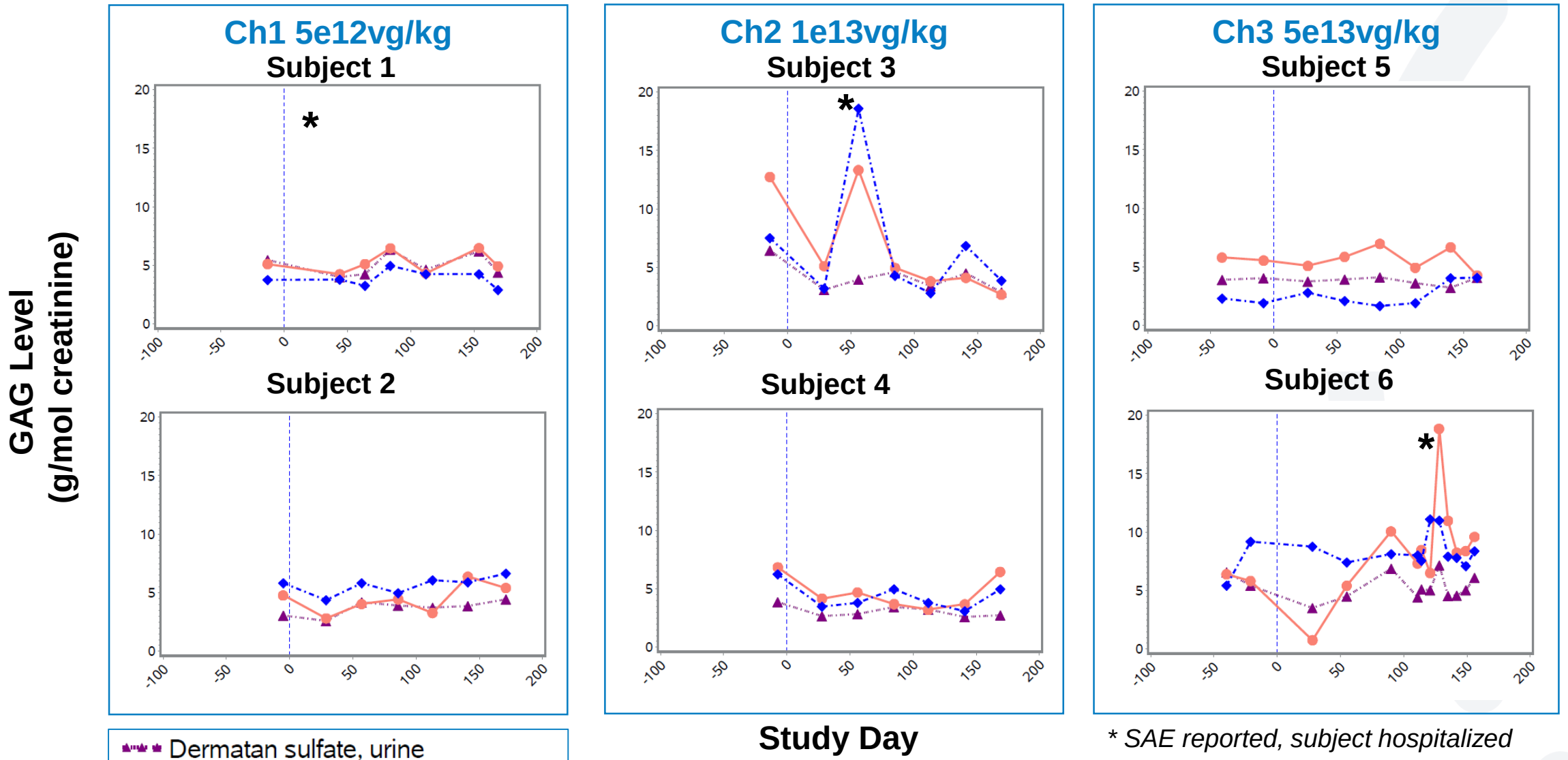
Data cut-off date: 10 JAN 2019

SB-913-1602: Urine GAG Results up to Week 24



* *SAE reported, subject hospitalized*

Normal reference ranges (g/mol creatinine):
Dermatan sulfate: 0 - 4.59 *Heparan sulfate: 0 - 1.07* *Total GAG: 0 - 6.5*

Data cut-off date: 10 JAN 2019

SB-913-1602: ERT Withdrawal

- ERT withdrawal has been initiated under protocol-specified schedule with monitoring of safety, IDS/GAG biochemical markers, and functional measures
- Three subjects (2 in Ch2 and 1 in Ch3) have started ERT withdrawal, 1 subject in Ch2 is planning to restart ERT after approximately 3 months due to fatigue and concurrent increase in GAGs *(per PI communication on 02 FEB 2019)*
- ERT withdrawal will begin in other subjects and analysis of data is ongoing

SB-913-1602: Summary of Results

- SB-913 was administered to 8 subjects with attenuated MPS II at a dose of up to 5e13 vg/kg and was generally well-tolerated
- Adverse events related to study drug were mild or moderate and resolved. No serious adverse events related to the study drug were reported
- Analysis of liver tissue showed evidence of albumin-IDS mRNA transcript in both subjects at the 1e13vg/kg dose after 24 weeks, suggesting that genome editing had occurred (analysis of the 5e13vg/kg dosed subject is pending)
- A substantial increase in plasma IDS activity was observed in 1 subject at the 5e13vg/kg dose, however this decreased after development of mild transaminitis
- Expansion with 3 additional subjects at the 5e13 vg/kg dose is complete and a trial of ERT withdrawal for all subjects is planned

SB-318, *in vivo* genome editing for MPS I

High dose cohort enrollment complete

Phase I/II Open Label Study

Up to 9 adults (18+ yrs) with MPS I

Dose Escalation Complete

Cohort 1	Cohort 2	Cohort 3
5e12 vg/kg	1e13 vg/kg	5e13 vg/kg

October SMC Review / Recommendations

Advance Enrollment to the 5e13 vg/kg Dose Cohort

Next steps

- **Preliminary data from first 3 patients at WORLD*Symposium* 2019**
- SMC review and recommendations

FDA

- Orphan Drug
- Fast Track
- Rare Pediatric Disease

- Orphan Medicinal Product

IND open

CTA granted

Goals

Patient safety | Reduction in GAGs | IDS enzyme production | ERT withdrawal

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SB-318-1502: Adverse Event (AE) Summary

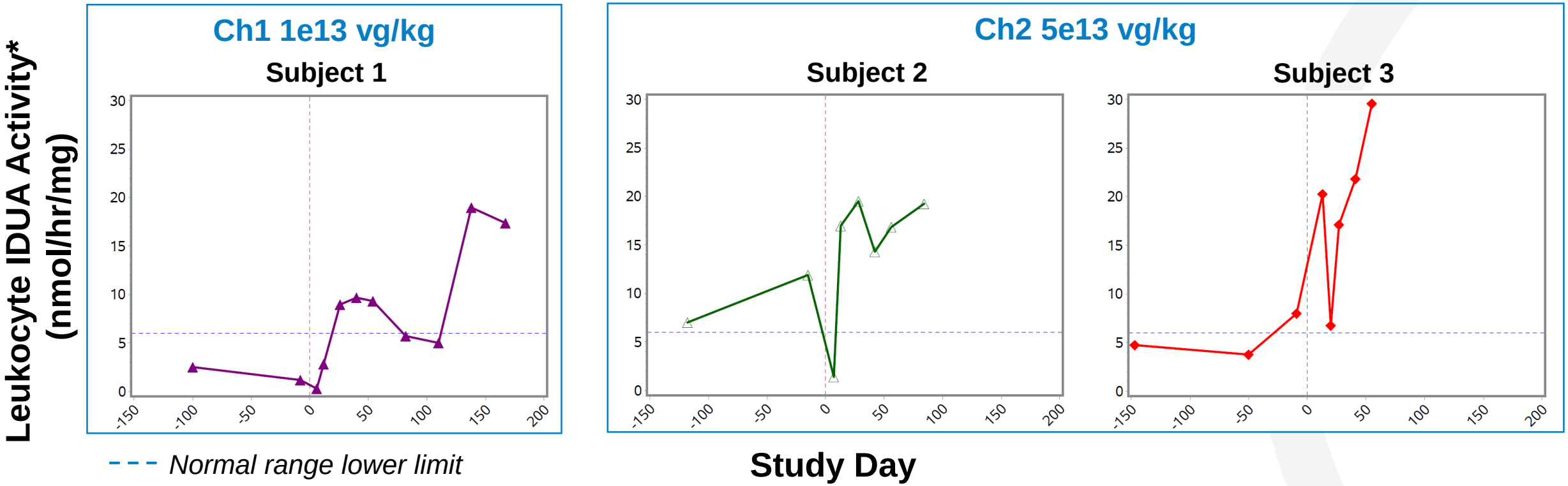
- All subjects reported mild or moderate AEs, consistent with ongoing MPS I disease
- No AEs related to the study drug were reported and no serious AEs were reported
- No AEs of elevated liver function tests were reported

MedDRA Preferred Term (PT)	Cohort 1 (N=1) n [T]	Cohort 2 (N=2) n [T]	Overall (N=3) n [T]
Any TEAE	1 [2]	2 [4]	3 [6]
Grade 1-Mild	1 [1]	2 [3]	3 [4]
Grade 2-Moderate	1 [1]	1 [1]	2 [2]
Acne	-	2 [2]*	2 [2]
Headache	1 [1]	-	1 [1]
Musculoskeletal stiffness	-	1 [1]	1 [1]
Oropharyngeal pain	-	1 [1]	1 [1]
Upper respiratory tract infection	1 [1]*	-	1 [1]

N= Total number of subjects in each treatment group, n= number of subjects in each SOC, [T]= total number of adverse events.
*Grade 2 event reported

Data cut-off date: 20 DEC 2018

SB-318-1502: Leukocyte IDUA Activity Results

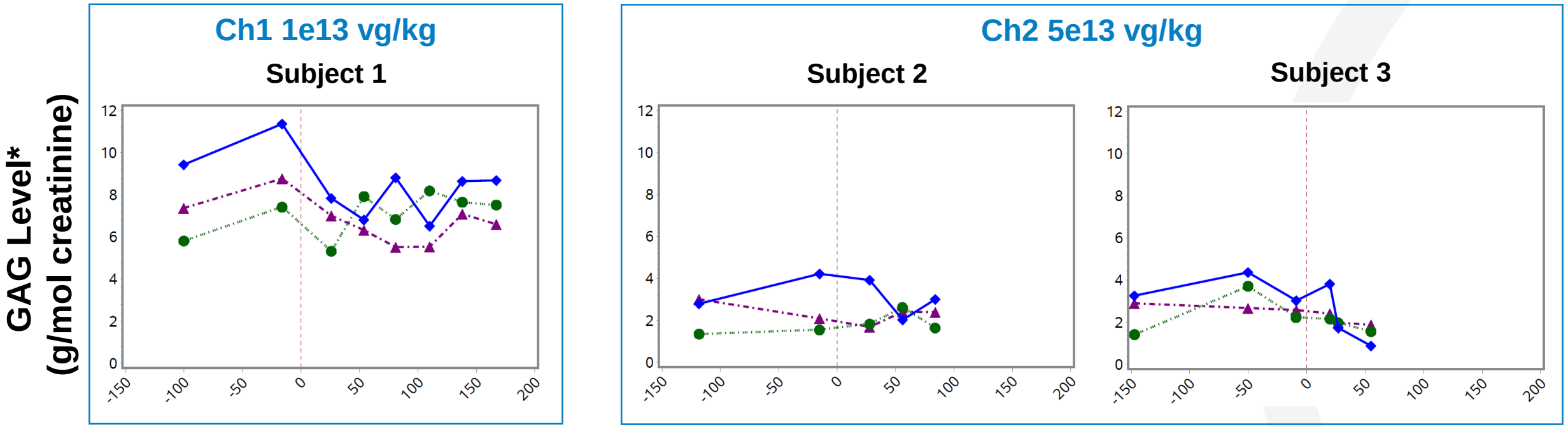


Greenwood Genetics validated diagnostic assay, samples obtained <96h post-ERT excluded
Reference ranges: Normal: 6.0-71.4 nmol/hr/mg MPS I (ERT-naïve): 0-1.0 nmol/hr/mg

- Plasma IDUA activity was also measured and was not significantly changed from pre-treatment values

Data cut-off date: 10 JAN 2019

SB-318-1502: Urine GAG Results



Normal reference ranges:
Dermatan sulfate: 0 - 4.59 g/mol creatinine
Heparan sulfate: 0 - 1.07 g/mol creatinine
Total GAG: 0 - 6.5 g/mol creatinine

**Total GAG measured by validated 1,9-dimethylene blue (DMB) colorimetric assay, dermatan sulfate and heparan sulfate measured by validated mass spectrometry assay*

Data cut-off date: 10 JAN 2019

SB-318-1502: Summary of Results

- SB-318 was administered to 3 subjects with attenuated MPS I at a dose of up to 5e13 vg/kg and was generally well-tolerated
- No adverse events related to the study drug were reported
- Increases in leukocyte IDUA activity were observed in all three treated subjects at both the 1e13 and 5e13 vg/kg dose
- Plasma IDUA activity was not significantly changed from pre-treatment values
- Analysis of liver biopsy tissue obtained at week 24 is planned to assess for evidence of genome editing
- ERT withdrawal is planned under a protocol-specified schedule with monitoring of safety, IDUA/GAG biochemical markers, and functional measures

ZFN Gene Editing Platform

Adrian Woolfson, BM, BCh, PhD
EVP, Research & Development

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

ZFN mRNA Transcription

ZFN Protein Translation

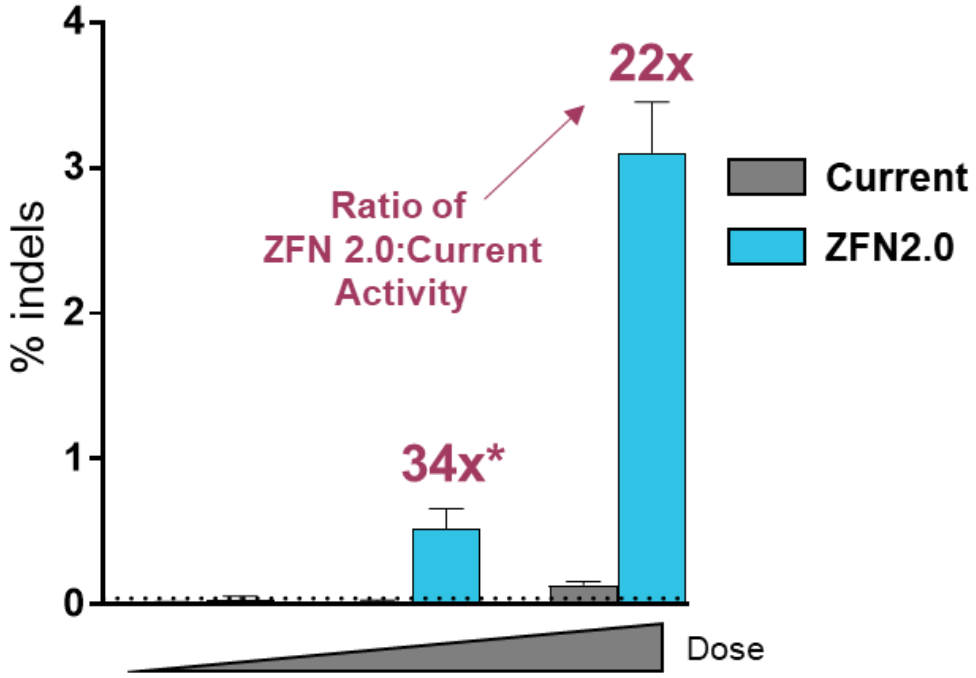
ZFN Protein Nuclear Import

ZFN Binding and Cleavage

Transgene Integration

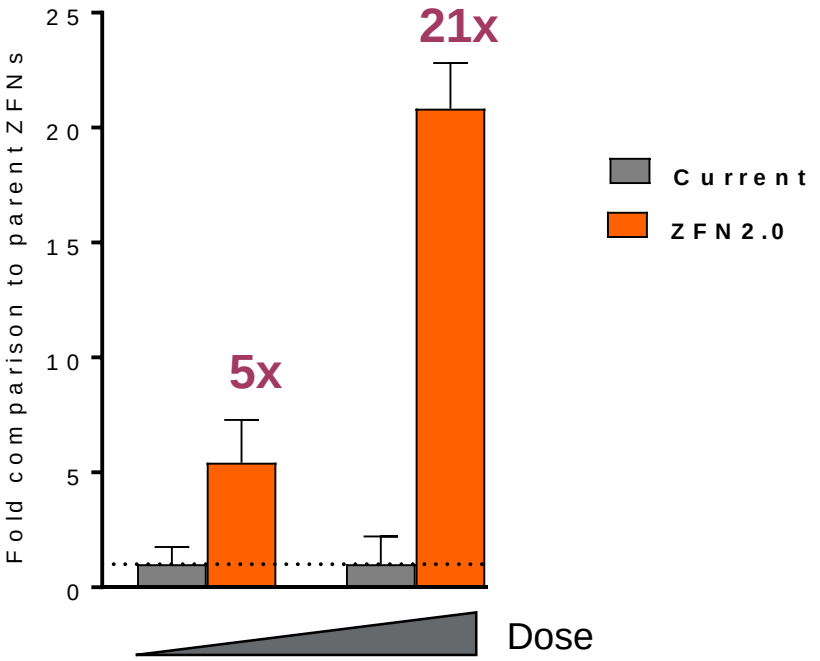
Second-generation ZFNs improve editing efficiency up to 30-fold and significantly increase IDS production in preclinical models

ZFN activity (% indels) in primary human hepatocytes



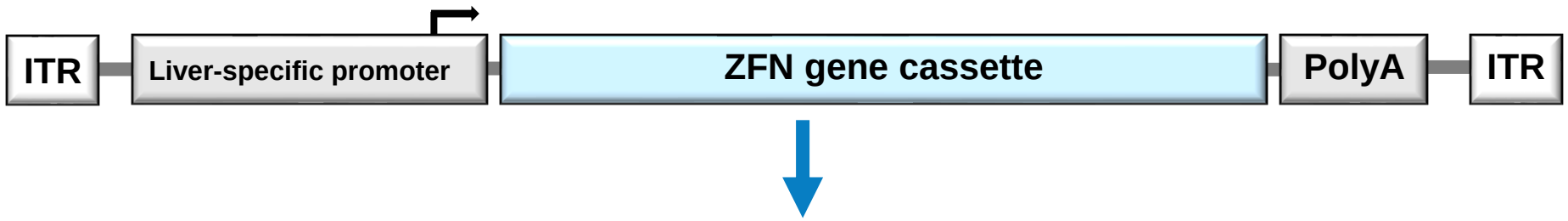
* = 'Current' sample contains no ZFN activity above background

IDS activity in primary human hepatocytes



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

Efficiency

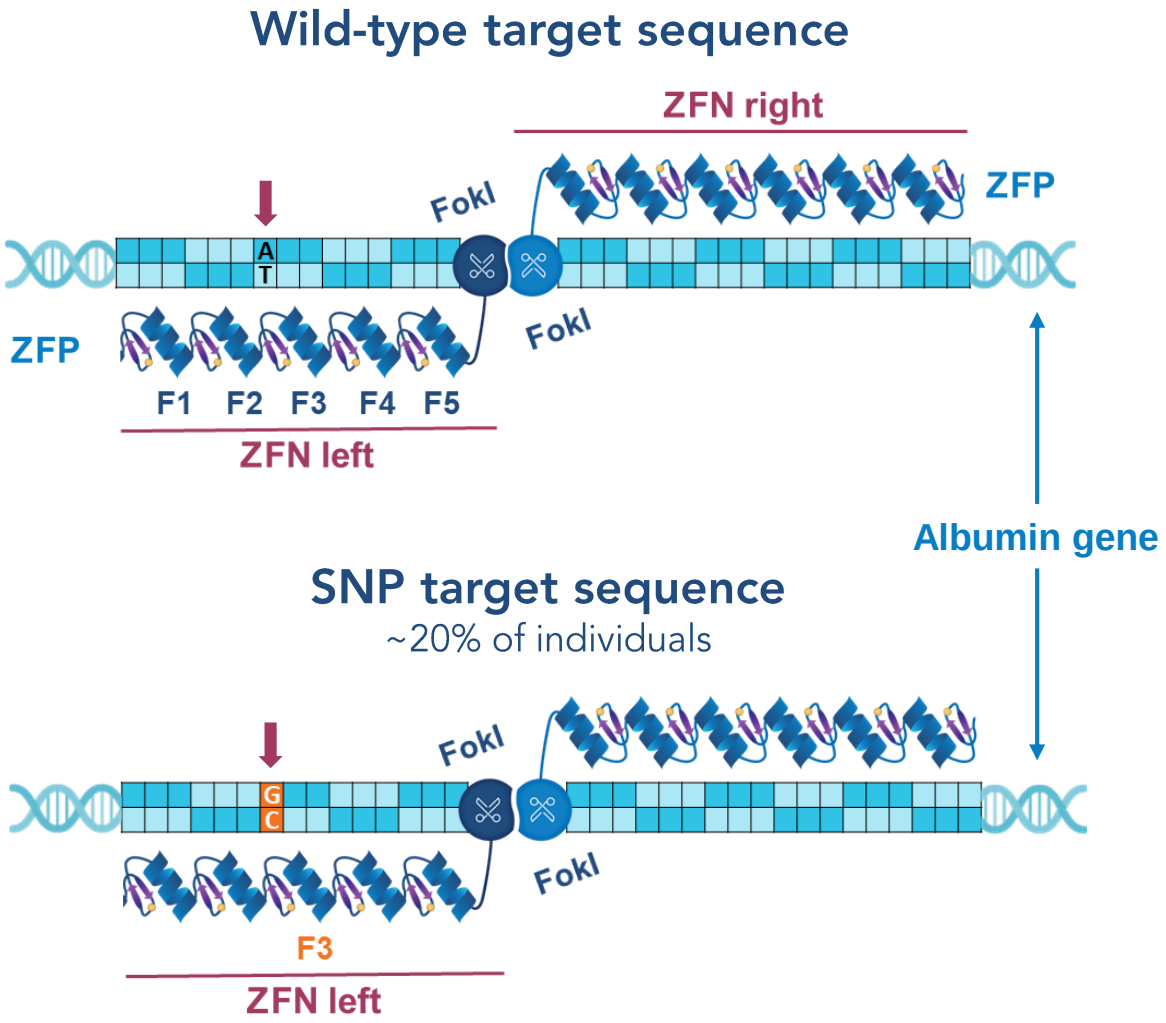


Transgene Modifications

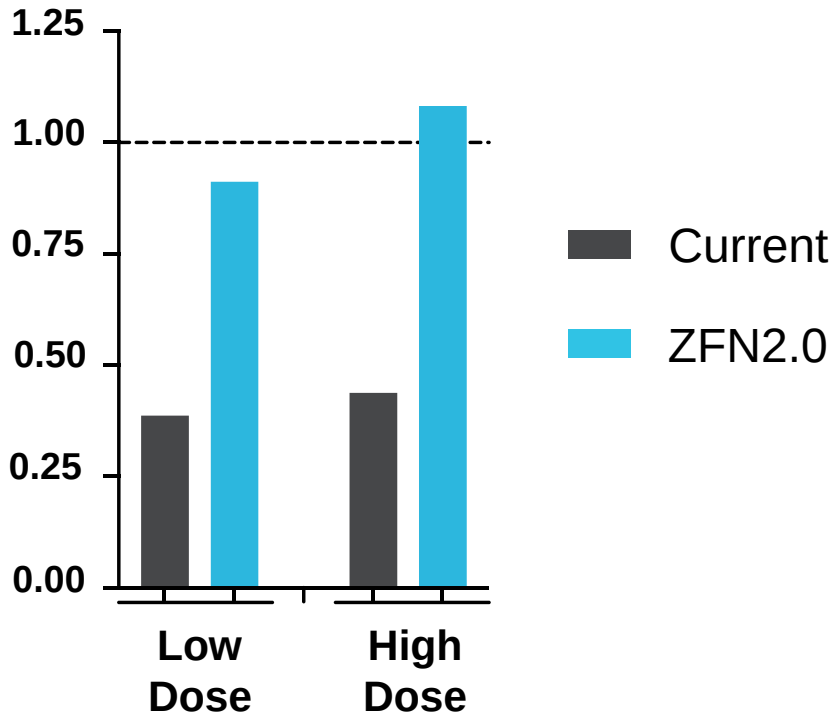
- Addition of a 5'UTR enhances translation
- Addition of an N-terminal peptide increases expression levels
- Addition of an expression enhancer increases ZFN mRNA stability and translation

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

Architectural changes enable editing of wildtype and SNP target sequences of albumin gene equally

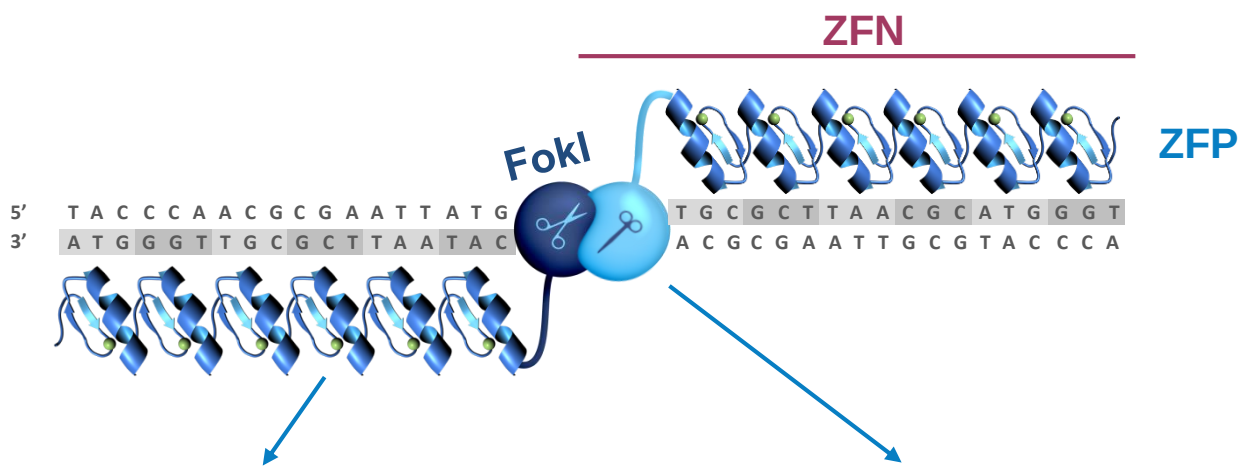


Ratio of ZFN activity (% indels) at SNP vs WT loci

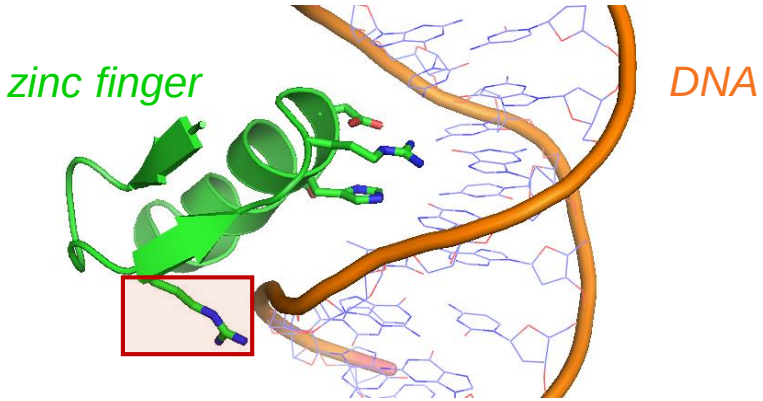


Tuning of amino acid residues improves specificity while maintaining high levels of gene modification

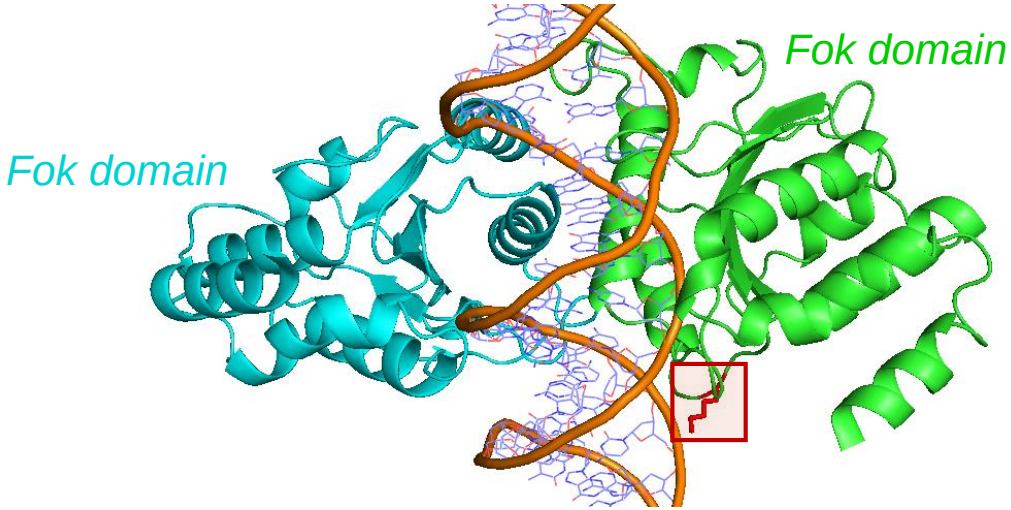
Specificity



1) Remove Arg-phosphate contacts
→ to tune affinity



2) Substitute key FokI residues
→ to adjust cleavage rate



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Elrod-Erickson *et al.*, *Structure* 1996 – 1AAY.pdb

Closing Remarks

Sandy Macrae
Chief Executive Officer

SB-318 and SB-913 data presentations at WORLD are the first in a series of clinical readouts and updates expected in 2019

Inherited Metabolic Diseases

SB-913: MPS II (Hunter syndrome)

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- SMC cohort expansion recommendation
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- Factor replacement utilization
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- ✓ Patient enrollment
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ST-400: beta thalassemia

- Patient enrollment
- Preliminary safety and HbF production

Sangamo THERAPEUTICS

Advancing our proprietary and partnered preclinical programs into the clinic this year

Inherited Metabolic Diseases

ST-920: Fabry disease

Clinical trial initiation expected in 2019

Immunology

Tx200: Solid organ transplant (kidney)

Clinical trial initiation expected in 2019

Oncology

Allogeneic anti-CD19 CAR T

IND filing expected in 2H 2019 (Kite-Gilead)

Hematology

BIVV-003: Sickle cell disease

- Phase 1/2 trial is active and screening subjects (Bioverativ-Sanofi)

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Q&A