Beam @ ASH 2024

December 8, 2024

Beam event participants

TOPIC	PARTICIPANT
Introduction & Beam Overview	**John Evans** Chief Executive Officer
Beam's Sickle Cell Disease Strategy	**Mr. Evans**
BEAM-101 Clinical Data Presentation	**Matthew M. Heeney, M.D.** Dana-Farber/Boston Children's Cancer and Blood Disorders Center
BEAM-101 Exploratory Biomarker Data	**Amy Simon, M.D.** Chief Medical Officer
ESCAPE Non-human Primate Data Presentation	**Giuseppe Ciaramella, Ph.D.** President
Closing Remarks	**Mr. Evans**
Q&A	**Dr. Heeney, Mr. Evans, Dr. Simon, Dr. Ciaramella**

Cautionary note regarding forward-looking statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements include statements regarding: the therapeutic applications and potential of our technology, including with respect to SCD, T-ALL/T-LL, AATD, GSD1a, and ESCAPE; our plans, and anticipated timing, to advance our programs; the clinical trial designs and expectations for BEAM-101, BEAM-201, BEAM-301, BEAM-302 and ESCAPE; our potential presentations at the ASH annual meeting; our current expectations and anticipated results of operations, including our expected use of capital; the sufficiency of our capital resources to fund operating expenses and capital expenditure requirements and the period in which such resources are expected to be available; and the therapeutic applications and potential of our technology, including our potential to develop life-long, curative, precision genetic medicines for patients through base editing, including potential safety advantages, all of which are subject to known and unknown important risks, uncertainties and other factors that may cause our actual results, performance or achievements, market trends, or industry results to differ materially from those expressed or implied by such forward-looking statements. Therefore, any statements contained herein that are not statements of historical fact may be forward-looking statements and should be evaluated as such. Without limiting the foregoing, the words "anticipate," "expect," "suggest," "plan," "vision," "believe," "intend," "project," "forecast," "estimates," "targets," “strategy,” “possibilities,” “promise,” "projections," "potential," "should," "could," "would," "may," "might," "will," and the negative thereof and similar words and expressions are intended to identify forward-looking statements.

Each forward-looking statement is subject to important risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement, including, without limitation, risks and uncertainties related to: our ability to develop, obtain regulatory approval for, and commercialize our product candidates, which may take longer or cost more than planned; our ability to raise additional funding, which may not be available; our ability to obtain, maintain and enforce patent and other intellectual property protection for our product candidates; the uncertainty that our product candidates will receive regulatory approval necessary to initiate human clinical trials; that preclinical testing of our product candidates and preliminary or interim data from preclinical studies and clinical trials may not be predictive of the results or success of ongoing or later clinical trials; that initiation and enrollment of our clinical trials may take longer than expected; that our product candidates or the delivery modalities we rely on to administer them may cause serious adverse events; that our product candidates may experience manufacturing or supply interruptions or failures; risks related to competitive products; and the other risks and uncertainties identified under the headings "Risk Factors Summary" and "Risk Factors" and elsewhere in our annual report on Form 10-K for the year ended December 31, 2023, our quarterly reports on Form 10-Q, and in any subsequent filings with the Securities and Exchange Commission (the "SEC") which are available on the SEC's website at www.sec.gov. Additional information will be made available by our annual and quarterly reports and other filings that we make from time to time with the SEC. These forward-looking statements speak only as of the date of this presentation. Factors or events that could cause our actual results to differ may emerge from time to time, and it is not possible for us to predict all of them. We undertake no obligation to update any forward-looking statement, whether as a result of new information, future developments or otherwise, except as may be required by applicable law.

OUR VISION IS TO PROVIDE LIFE-LONG CURES for patients suffering from serious diseases

POTENTIAL FOR **one-time, curative therapies**

GENE EDITING FOR **rare and common diseases**

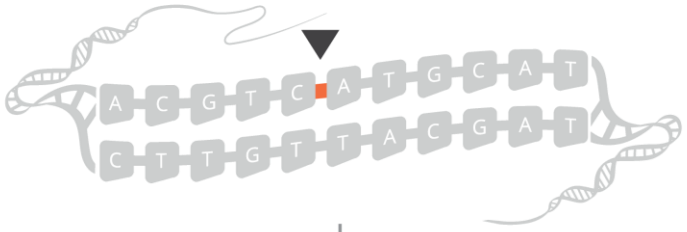
PLATFORM FOR **rapidly programmable precision medicines**

Beam THERAPEUTICS

The central hypothesis behind Beam: Base editing is more precise, efficient, predictable and versatile than nucleases

NUCLEASE CRISPR, ZFN, TALENs

Precision targeting with CRISPR



Double-stranded breaks

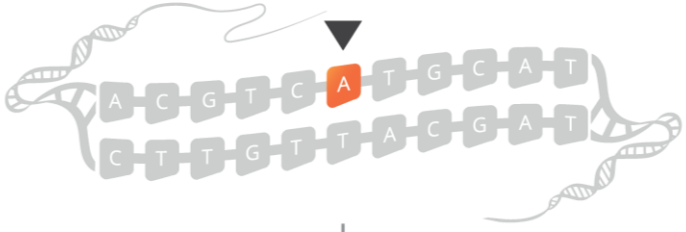
Lack of control of gene sequence outcomes

…A C G - - - - G C A T…
…A C G T C **G C T T** A T G C A T…
…A - - - - - T G C A T…
…A C G T C **T** A T G C A T…
…A C - - - - - - - A T…
…A C G T C **A A C** - - G C A T…
etc

- - - - - Deletions
A G C T Insertions

BASE EDITING BEAM THERAPEUTICS

Precision targeting with CRISPR



Enzymatic base conversion

Highly efficient with predictable gene sequence outcomes

Advancing a diversified pipeline into the clinic

PROGRAM / DISEASE		DELIVERY	EDITING APPROACH	RESEARCH	LEAD OPTIMIZATION	IND ENABLING	PHASE I/II	PIVOTAL
BEAM-101	Sickle Cell Disease (SCD)	*Ex vivo* HSC	Activation of fetal hemoglobin (HbF)					
ESCAPE (BEAM-103 & BEAM-104)	Sickle Cell Disease Beta Thalassemia	*Ex vivo* HSC	Multiplex HbF edit + CD117 edit-antibody pair					
BEAM-302	Alpha-1 Antitrypsin Deficiency (AATD)	*In vivo* LNP	Correction of E342K mutation					
BEAM-301	Glycogen Storage Disease 1a (GSD1a)	*In vivo* LNP	Correction of R83C mutation					
BEAM-201	T-ALL / T-LL and CD7+ AML	*Ex vivo* T cells	Multiplex silenced CD7 CAR-T					
Pfizer collaboration target		*In vivo* LNP	Undisclosed					
Apellis collaboration target		*In vivo* LNP	Undisclosed					

LNP = Lipid Nanoparticle; HSC = Hematopoietic Stem Cell; T-ALL / TLL = T-Cell Acute Lymphoblastic Leukemia / T-Cell Lymphoblastic Lymphoma; AML = Acute Myeloid Leukemia; ESCAPE: Engineered Stem Cell Antibody Paired Evasion

Two platforms with potential to create transformative therapies and significant value creation

Hematology

- **Best-in-class potential for BEAM-101 for sickle cell disease (SCD)**
- Increased probability of technical success for *ex vivo* gene editing and fetal hemoglobin (HbF) upregulation
- Identified FDA regulatory pathway
- **ESCAPE has potential to eliminate chemotherapy from transplant**, expanding reach of base editing to more patients
- Platform for future hematology pipeline

Initial data at ASH

Liver Genetic Diseases

- **Best-in-class potential for BEAM-302 for alpha-1 antitrypsin deficiency (AATD)**
- Increased probability of technical success for *in vivo* lipid-nanoparticle (LNP) gene editing in liver
- Potential for rapid clinical proof of concept
- Clinical-stage AATD program with potential to be a one-time treatment that benefits both lung and liver disease
- Platform for future liver-targeted pipeline

Data expected in 1H2025

Significant potential catalysts on the horizon for Beam

Recent and Anticipated Catalysts

BEAM-101
SCD

- Completed sentinel dosing and initiated expansion
- Present initial clinical data at ASH

ESCAPE
SCD & BETA-THALASSEMIA

- Initiate Phase 1-enabling preclinical studies in 2024
- Present NHP preclinical data at ASH

BEAM-302
AATD

- CTA cleared in the UK
- Initiate Phase 1/2 clinical trial
- Present initial data in 1H2025

BEAM-301
GSD1a

- Obtained U.S. IND clearance
- Dose first patient in Phase 1/2 study in early 2025

BEAM-201
T-ALL / T-LL

- Present initial clinical data at ASH

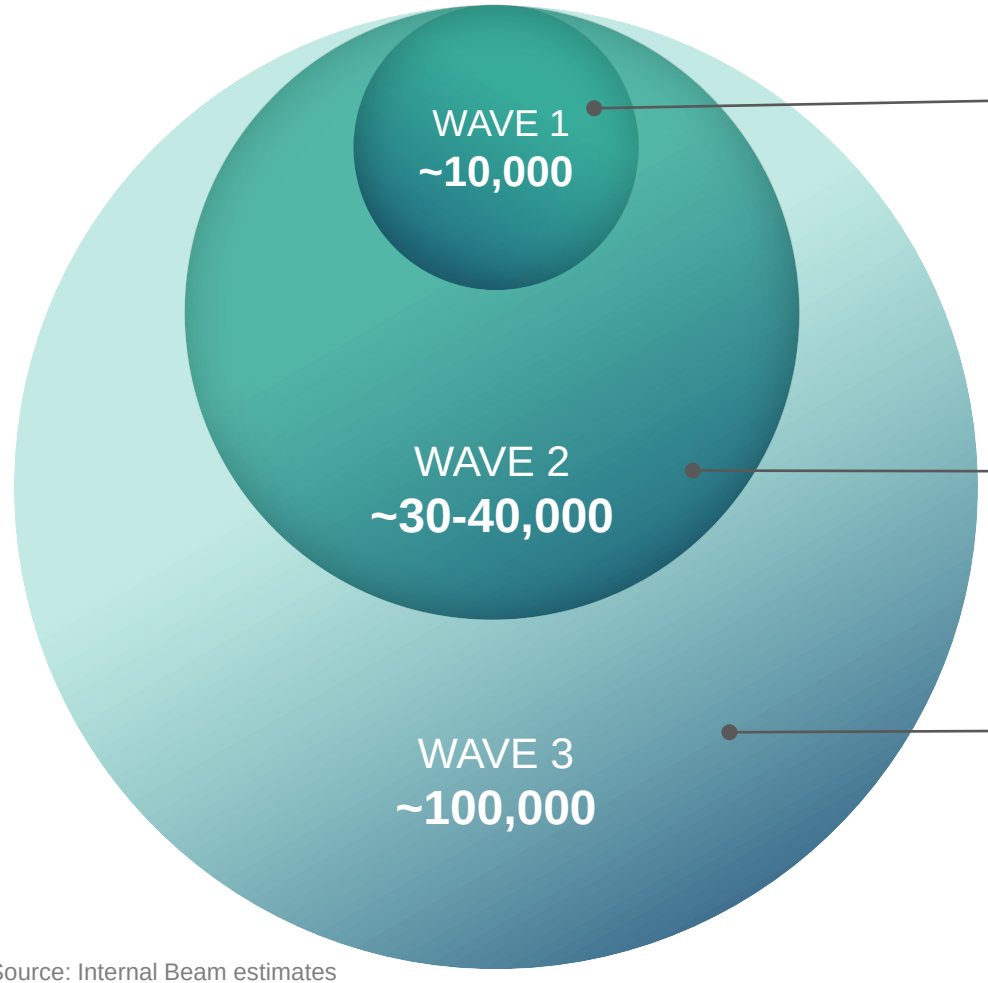
What if we could develop better one-time therapies for people living with SCD?

SICKLE CELL DISEASE

Beam THERAPEUTICS

Beam's multi-wave strategy is focused on developing safer, more effective and more accessible treatments for patients with SCD

Potential Eligible SCD Patient Population (U.S.)



BEAM-101: Precise HbF upregulation

Potentially best-in-class gene editing

Non-cutting, non-viral therapy with busulfan conditioning to address SCD with high vaso-occlusive crisis (VOC) burden

ESCAPE: Multiple edits for non-genotoxic conditioning

Designed to eliminate chemotherapy from *ex vivo* gene therapy and expand patient population with:

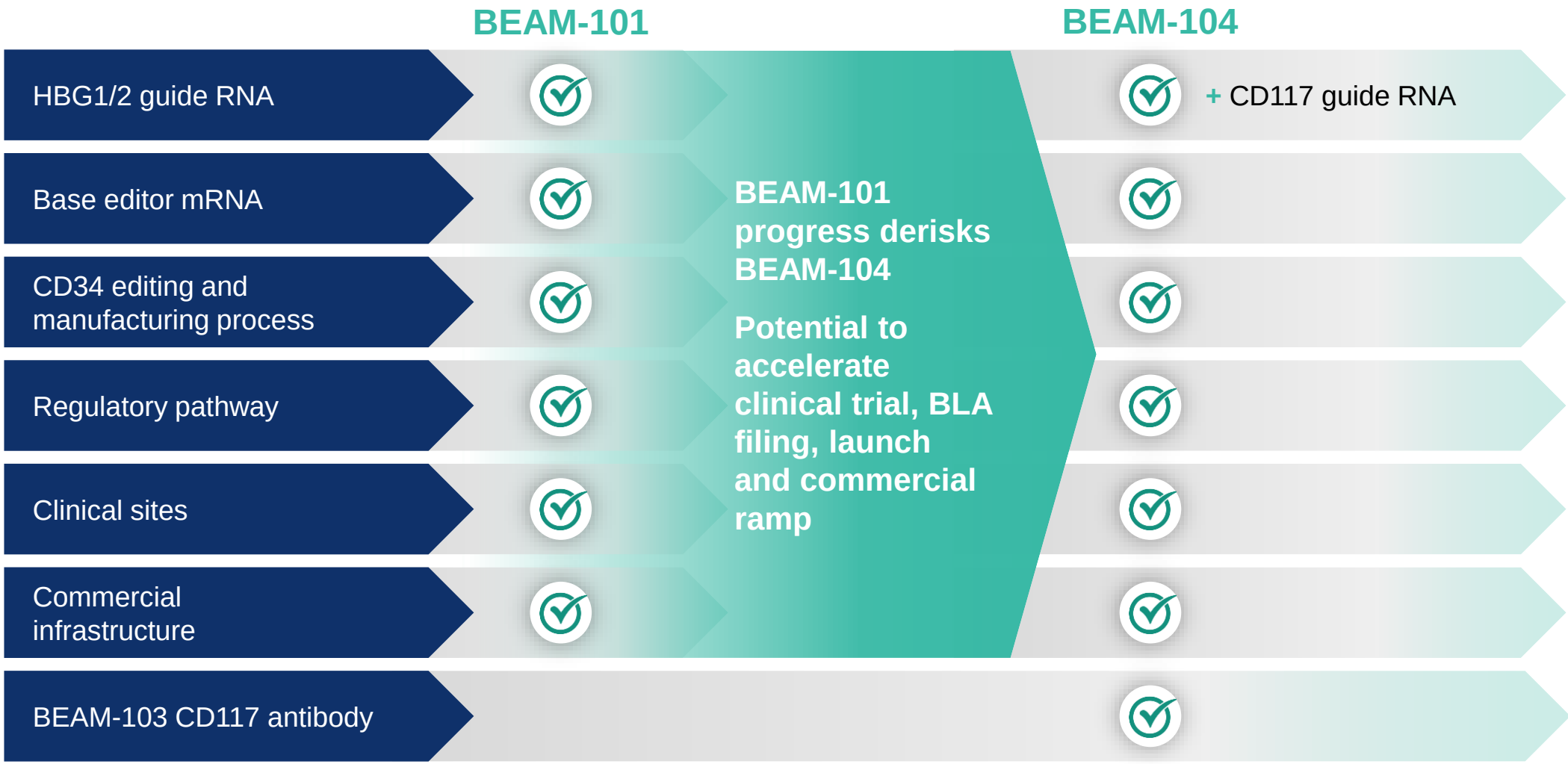
- Broader range of disease severity
- Broader age range
- Increased willingness-to-treat

In vivo: Base editing with hemopoietic stem cell (HSC)-targeted LNPs

***In vivo* delivery** would overcome need for transplantation, lower infrastructure requirements and unlock wider patient access and geographies

Source: Internal Beam estimates

Synergy between BEAM-101 and ESCAPE technology (BEAM-104 and BEAM-103) support efficient development in SCD



What would an ideal outcome for BEAM-101 look like?

Disease

Sickle cell disease
(two mutations)

- 0% normal Hb (HbA)
- 100% sickle Hb (HbS)
- All circulating cells with HbSS genotype

Non-disease

Sickle cell "trait" (SCT)
(carrier with one mutation, typically asymptomatic)

- 60% HbA
- 40% HbS
- No circulating cells with HbSS genotype

Normal
(no mutations)

- 100% HbA
- 0% HbS
- No circulating cells with HbSS genotype

Base editing

>60% HbF (anti-sickling)

<40% HbS

Minimize cells expressing only HbS

INITIAL RESULTS FROM THE BEACON CLINICAL STUDY

A Phase 1/2 study evaluating the safety and efficacy of a single dose of autologous CD34+ base-edited hematopoietic stem cells (BEAM-101) in patients with sickle cell disease with severe vaso-occlusive crises

66th ASH 2024

Ashish Gupta, Akshay Sharma, Haydar Frangoul, Jignesh Dalal, Julie Kanter, Asif Alavi, John DiPersio, Mary Eapen, Jennifer Jaroscak, Ernesto Ayala, Edward Ziga, Stacey Rifkin-Zenenberg, Alex Minella, Guo Chen, Yinzhong Chen, Priya S. Chockalingam, Ling Lin, Marcelyne Joseney-Antoine, Leanne Ianniello, Beth Gardner, Adam Hartigan, Giuseppe Ciaramella, Sunita Goyal, Amy Simon, Alexis A. Thompson, **Matthew M. Heeney**[1]

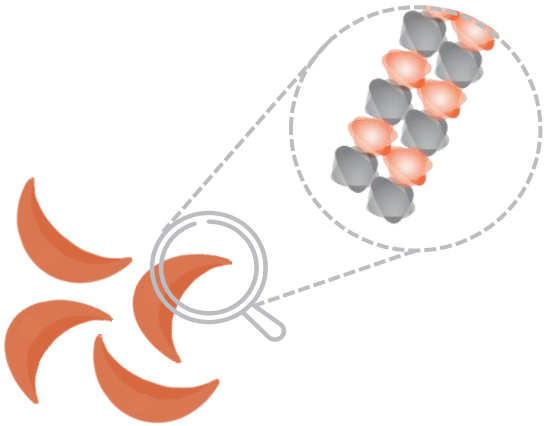
1. Dana-Farber / Boston Children's Cancer and Blood Disorders Center, Boston, MA, USA

BEAM-101 uses precise base editing to increase levels of HbF

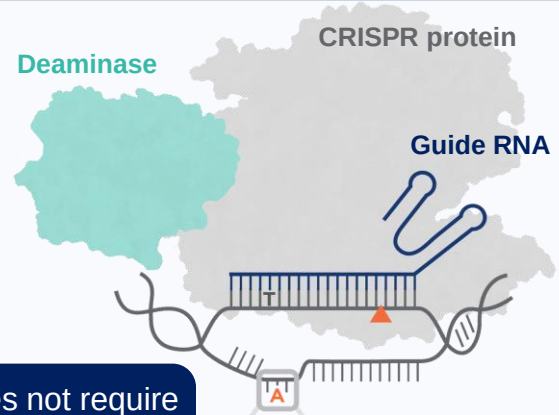
Sickle cell disease[1,2]

HbS ↓ ↑ HbF

Increased HbS leading to sickled cells

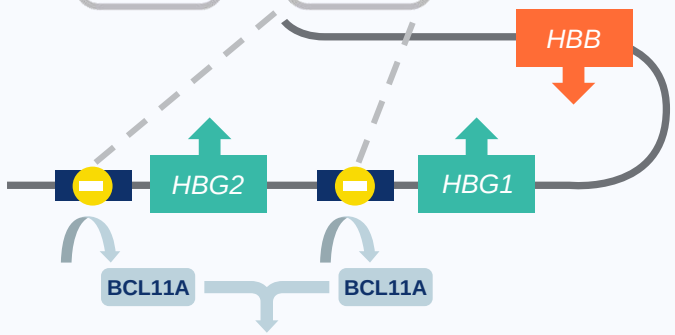


Base editing with BEAM-101[3,4]



Editing of *HBG1/2* promoters is designed to eliminate BCL11A binding sites without disrupting other BCL11A-regulated pathways

Does not require double-stranded breaks

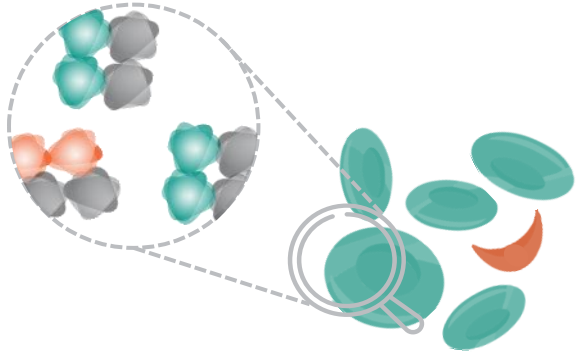


Other signaling pathways

Following treatment with BEAM-101[2,5]

Increased HbF leading to fewer sickled cells

HbF ↑ ↓ HbS



1. Eaton WA, Bunn HF. Blood 2017;129:2719–2726; 2. Akinsheye I, et al. Blood 2011;118:19–27; 3. Beam Therapeutics Inc. Protocol BTX-AUT-001; 4. Beam Therapeutics Inc. Investigator's brochure; 5. Steinberg MH, et al. Blood 2014;123:481–485. A, adenine; BCL11A, transcription factor B-cell lymphoma/leukemia 11A; CRISPR, clustered regularly interspaced short palindromic repeats; G, guanine; HBB, hemoglobin subunit beta; HBG, hemoglobin subunit gamma; HbF, fetal hemoglobin; HbS, sickle hemoglobin; RNA, ribonucleic acid

BEACON is a Phase 1/2 study evaluating safety and efficacy of BEAM-101 in patients with SCD and severe VOCs

Sentinel cohort (N=3)

- ✓Staggered start with SRC review in between
- ✓Enrollment complete
- ✓Dosing complete

DMC review

Expansion cohort

- ✓35+ patients cleared screening and enrolled
- ✓11 patients dosed with the remaining in process (as of December 2, 2024)

Key eligibility criteria

- Age ≥18 to ≤35 years
- SCD with β^S/β^S, β^S/β^0, or β^S/β^+ genotypes
- ≥4 sVOCs in 24 months pre-screening
- No available matched sibling donor
- No history of overt stroke

Key safety endpoints

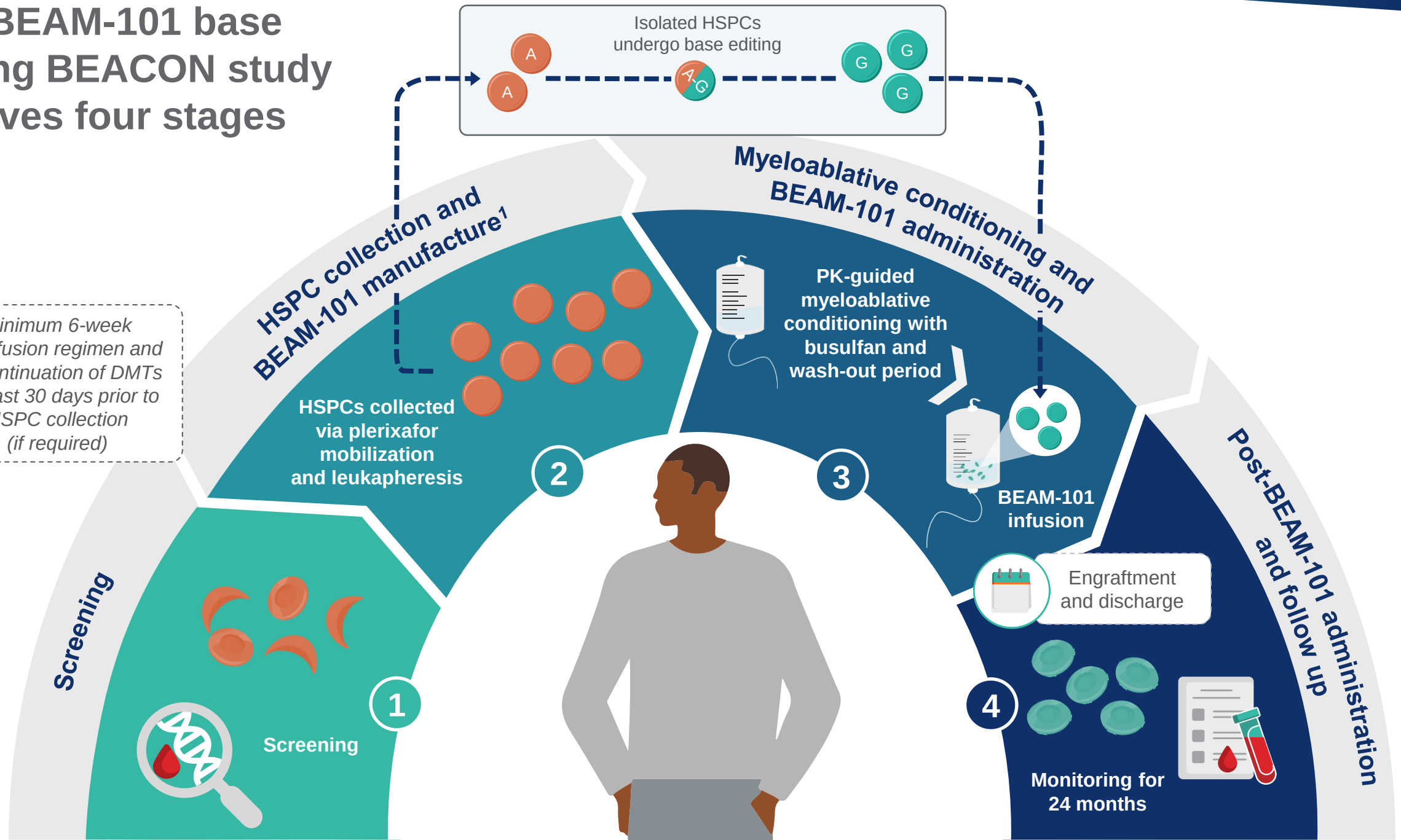
- Proportion of patients with successful neutrophil engraftment
- Time to neutrophil engraftment
- Time to platelet engraftment

Key efficacy endpoints

- Proportion of patients sVOC-free for 12 consecutive months
- Total Hb levels
- HbF and HbS levels
- Hemolysis parameters
- Patient-reported outcomes
- RBC function and organ damage

Phase 1/2, non-randomized, open-label, single-arm, multicenter, safety and efficacy study of the administration of BEAM-101 to patients with SCD (NCT05456880)
DMC, Data Monitoring Committee; HbF, fetal hemoglobin; HbS, sickle hemoglobin; RBC, red blood cell; SCD, sickle cell disease; SRC, Safety Review Committee; sVOC, severe vaso-occlusive crisis

The BEAM-101 base editing BEACON study involves four stages



1. Kopesky P, et al. Poster presented at EHA; Jun 2024; Madrid, Spain

DMT, disease-modifying therapy; HSPC, hematopoietic stem and progenitor cell; PK, pharmacokinetic

Baseline demographics and characteristics of patients treated with BEAM-101

Baseline characteristics	N=7
Age (years), mean (range)	22.6 (19–27)
Sex, n (%)	
Male	4 (57.1)
Female	3 (42.9)
Genotype, n (%)	
β^S/β^S	6 (85.7)
β^S/β^0	1 (14.3)
Race, n (%)	
Black or African American	7 (100)
Previous hydroxyurea use, n (%)	7 (100)
Alpha globin loci genotype, n (%)	
0 deletions	4 (57.1)
1 deletion	3 (42.9)
Investigator-reported severe VOCs in the 2 years prior to start of study, mean (range)	10.3 (7–13)

Safety and efficacy analysis: N=7

Length of follow up in analysis set: 11 months (range: 1–11)

Data cutoff Oct 28, 2024

To qualify as a severe VOC, the event must consist of acute episodes of pain, with no medically determined cause other than a VOC that required at least 24 hours of management in a hospital or observation unit; or a visit to an emergency department, urgent care, or outpatient facility involving therapy with an opioid or IV or IM NSAID; or ACS, as defined by the acute onset of pneumonia-like symptoms (e.g., cough, fever, shortness of breath) along with new pulmonary infiltrates; or splenic sequestration crisis, as defined by left upper quadrant pain, splenic enlargement, and a decrease in Hb of ≥2 g/dL; or priapism episode, defined as a sustained, unwanted, painful erection requiring evaluation and treatment at a medical facility. ACS, acute chest syndrome; Hb, hemoglobin; IM, intramuscular; IV, intravenous; NSAID, nonsteroidal anti-inflammatory drug; VOC, vaso-occlusive crisis

BEAM-101 treatment characteristics

Dosing	N=7
Number of mobilization and apheresis cycles, mean (range)	1.4 (1–2)
Busulfan cumulative AUC (µg*h/mL), mean (range)	73.9 (61.8–83.2)
BEAM-101 dose infused ($\times 10^6$ CD34+ cells/kg) mean (range)	10.7 (3.2–23.4)
Duration (months) of follow up after BEAM-101 dosing, mean (range)	5.6 (1.4–11.0)
Day of last RBC transfusion, median (range)	15 (7–122*)

BEAM-101's efficient manufacturing process contributed to patients requiring few collection cycles

Data cutoff Oct 28, 2024

Therapeutic drug monitoring for busulfan was performed and dosing was adjusted based upon plasma busulfan concentrations to maintain a daily target busulfan AUC of 20 µg*h/mL with a cumulative AUC target of 80 µg*h/mL

*One patient required blood transfusions up to Day 122 as part of ongoing management of critical illness; excluding this patient, the mean (range) last day of RBC transfusion is 11.8 (7–17)

AUC, area under the curve; RBC, red blood cell

BEAM-101 treatment and engraftment characteristics

Dosing	N=7
Number of mobilization and apheresis cycles, mean (range)	1.4 (1–2)
Busulfan cumulative AUC (µg*h/mL), mean (range)	73.9 (61.8–83.2)
BEAM-101 dose infused (×10^6 CD34+ cells/kg) mean (range)	10.7 (3.2–23.4)
Duration (months) of follow up after BEAM-101 dosing, mean (range)	5.6 (1.4–11.0)
Day of last RBC transfusion, median (range)	15 (7–122*)
Time to neutrophil engraftment (days), mean (range)	17.1 (15–21)
Duration of neutropenia (ANC <500 cells/µL), (days), mean (range)	6.3 (4–9)
Time to platelet engraftment (days), mean (range)	19.1 (11–34)

Patients had rapid neutrophil and platelet engraftment with a low number of neutropenic days

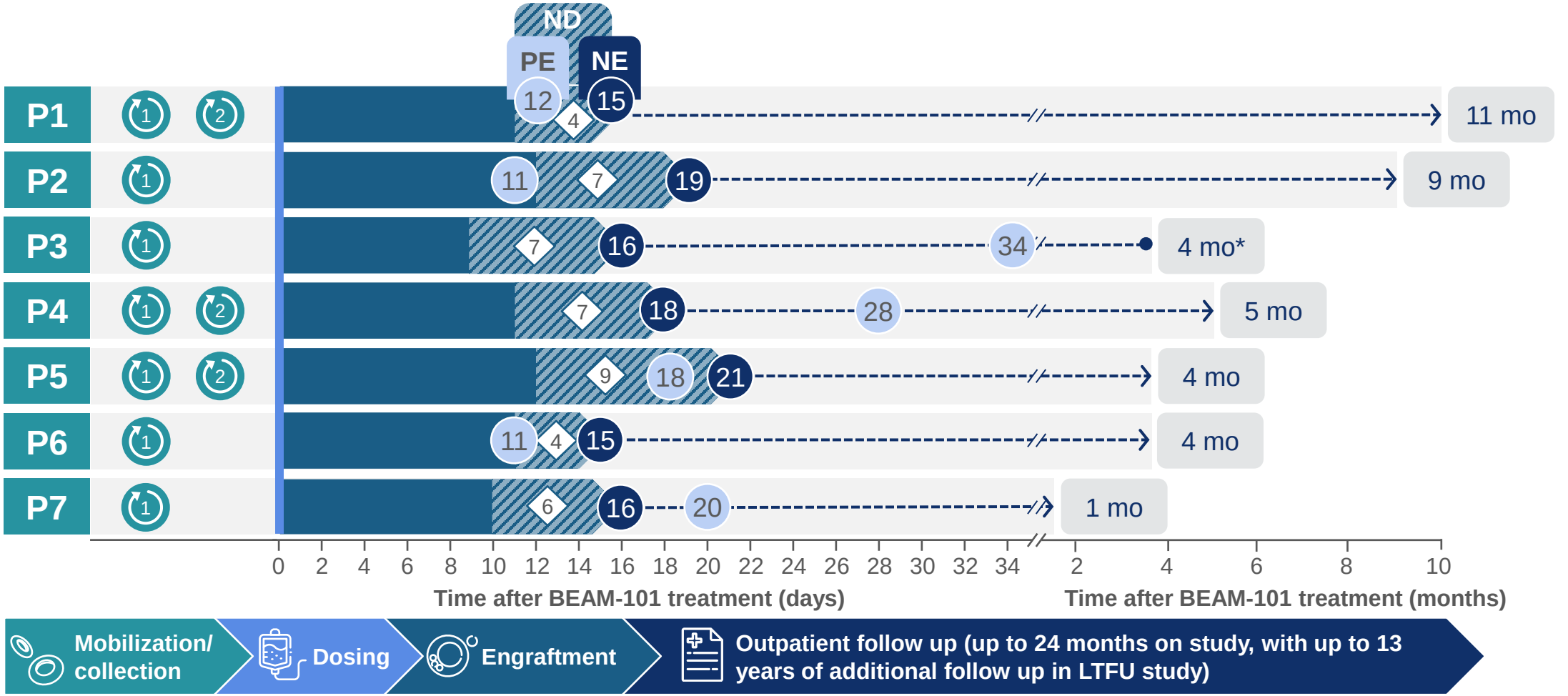
Data cutoff Oct 28, 2024

Neutrophil engraftment defined as ANC ≥500 cells/µL for 3 consecutive days independent of growth factor support. Platelet engraftment defined as post-nadir platelet count ≥50,000 per µL on 3 separate days without receiving a platelet transfusion for at least 7 days prior to the first of the 3 measurements through to the last measurement

*One patient required blood transfusions up to Day 122 as part of ongoing management of critical illness; excluding this patient, the mean (range) last day of RBC transfusion is 11.8 (7–17)

ANC, absolute neutrophil count; AUC, area under the curve; RBC, red blood cell

BEAM-101 and its treatment process aim to minimize mobilization and engraftment burden



Data cutoff Oct 28, 2024. Patients remain as inpatients until neutrophil engraftment has occurred, and the patient is deemed clinically stable for discharge and outpatient management. Patients assessed at daily intervals to evaluate engraftment success status. Patients will be discharged home after neutrophil engraftment. Platelet engraftment may be monitored in the outpatient setting on a weekly basis. *P3 died due to refractory respiratory failure 4 months after infusion. LTFU, long-term follow up; mo, month; ND, neutropenic days; NE, neutrophil engraftment; P, patient; PE, platelet engraftment

Day of neutrophil engraftment
Day of platelet engraftment
Mobilization cycle
Daily monitoring
Neutropenic days
Follow up

BEAM-101 initial safety data are consistent with busulfan conditioning and autologous HSCT

Patients with, n (%)	N=7
Any TEAEs	7 (100)
Related to BEAM-101	1 (14.3)
Any TEAEs ≥Grade 3	7 (100)
Related to BEAM-101	0
AEs leading to discontinuation	0
Serious TEAEs	4 (57.0)
Related to BEAM-101	0
Death	1
Related to BEAM-101	0

- Most common TEAEs (≥3 patients) included febrile neutropenia*, stomatitis*, skin hyperpigmentation, pharyngeal inflammation, anemia*, edema peripheral, decreased appetite*, headache, hypervolemia, hypokalemia
- All but 1 non-serious TEAE (Grade 1 dizziness) were assessed as not related to BEAM-101
- No serious TEAEs occurred in >1 patient

No patients have experienced any VOCs post-engraftment

Data cutoff Oct 28, 2024

Related events include events where investigator has assessed relationship as possibly or definitely related to BEAM-101

*Includes events that were ≥Grade 3 in at least 3 patients

AE, adverse event; HSCT, hematopoietic stem-cell transplantation; TEAE, treatment-emergent adverse event

One patient died due to respiratory failure, likely related to busulfan conditioning, 4 months after infusion

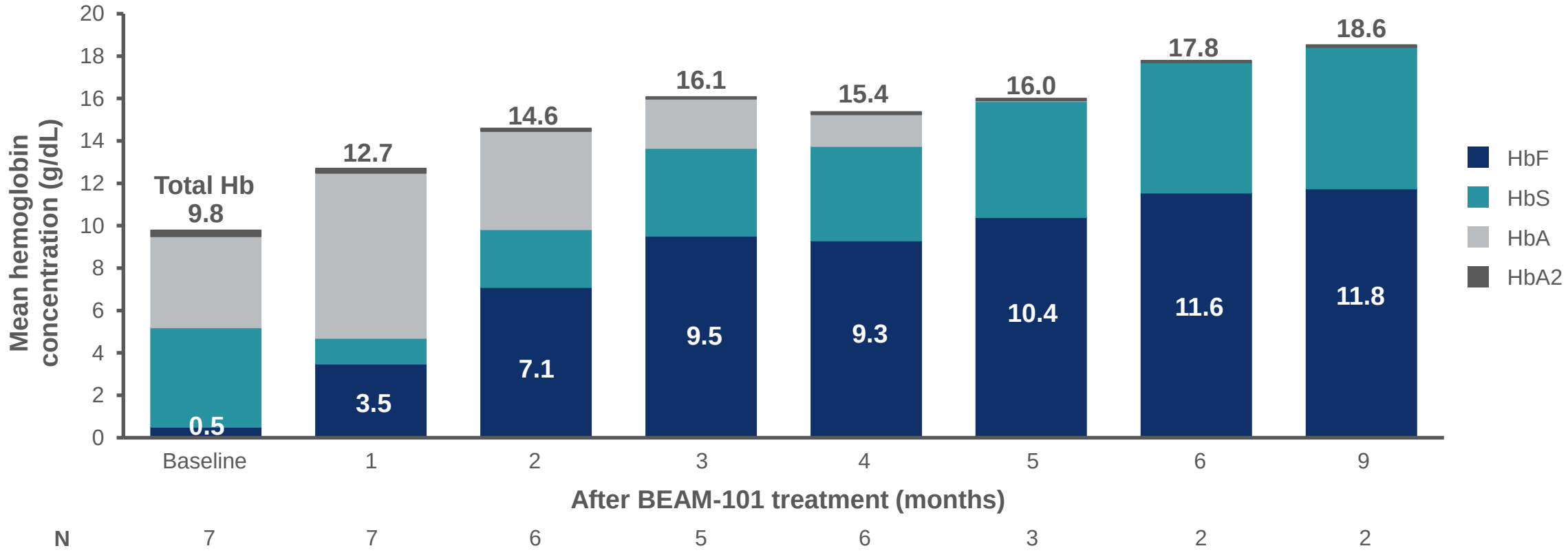
P3 medical history	• Female / 21 yrs / β^S/β^S with history of SCD with ACS, severe VOCs, obstructive sleep apnea, and e-cigarette use
Conditioning and dosing	• Conditioned with busulfan dose of 0.8 mg/kg Q6H x 4 days, cumulative AUC of 74.2 µg•h/mL • Busulfan dose and AUC within protocol target • Cell dose: 6.2 $\times 10^6$ CD34+ cells/kg • Neutrophil engraftment on Day 16, platelet engraftment on Day 34
Event course	• Admitted Day 58 with fever, vomiting, diarrhea; then developed respiratory distress with multiple pulmonary infiltrates • Infection or hemorrhage ruled out, patient discharged home on Day 82 with steroids and nocturnal BiPAP • Readmitted 4 days later with progressive respiratory distress, acute lung injury and pneumomediastinum consistent with idiopathic pneumonia syndrome (IPS)*, requiring mechanical ventilation • Patient died due to refractory respiratory failure, at 4 months after BEAM-101 infusion
Investigator assessment	• **Event was not related to BEAM-101** • Fatal event of respiratory failure likely related to busulfan conditioning, which has known pulmonary toxicity, resulting in IPS • Possible contributing factor was e-cigarette use (vaping)

The DMC concluded:
'The occurrence of severe pulmonary toxicity is in keeping with known risks with busulfan'

*Defined as diffuse alveolar injury with multi-lobar pneumonia, absence of infection or other etiology (cardiac, etc.), along with hypoxemia
ACS, acute chest syndrome; AUC, area under the curve; BiPAP, bilevel positive airway pressure; DMC, data monitoring committee; e-cigarette, electronic cigarette; ICU, intensive care unit; P, patient; Q6H, every 6 hours; SCD, sickle cell disease; VOC, vaso-occlusive crises

Patients achieved rapid and robust HbF induction with corresponding HbS reduction

All patients achieved endogenous HbF >60% and HbS <40% by 1 month after BEAM-101 treatment



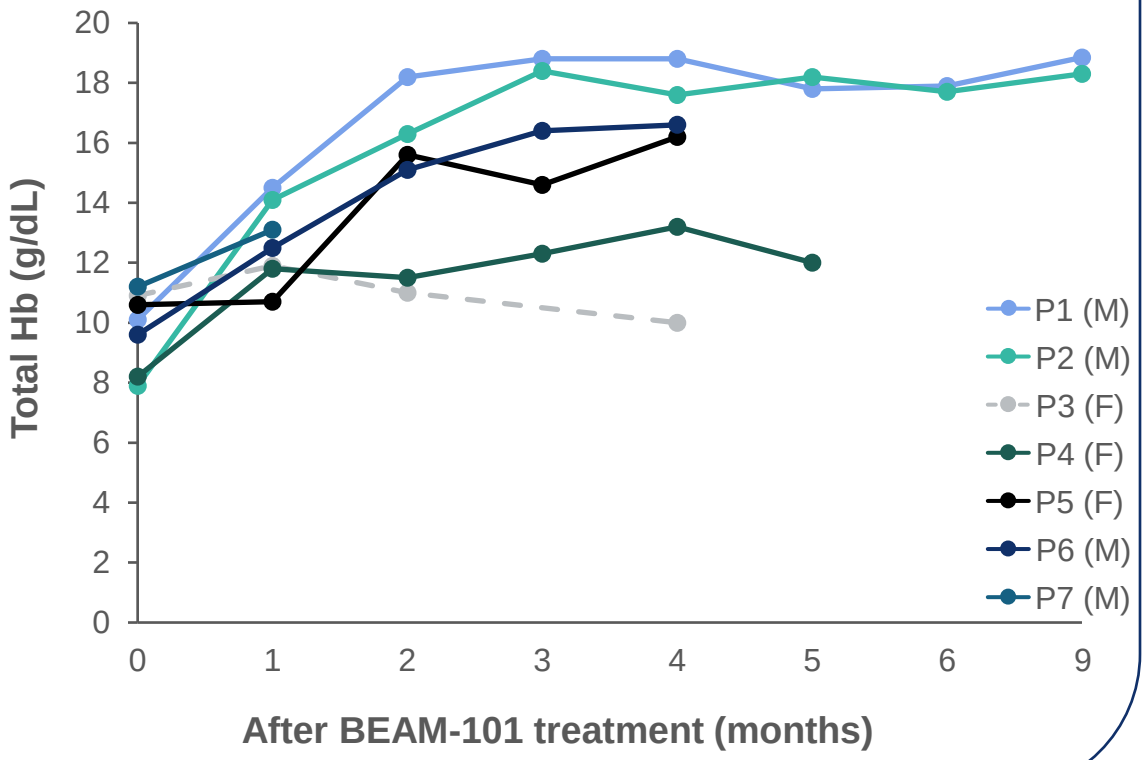
N	7	7	6	5	6	3	2	2
%HbF (HbF/HbF+HbS)	10%	74%	72%	70%	67%	65%	65%	64%

Data cutoff Oct 28, 2024

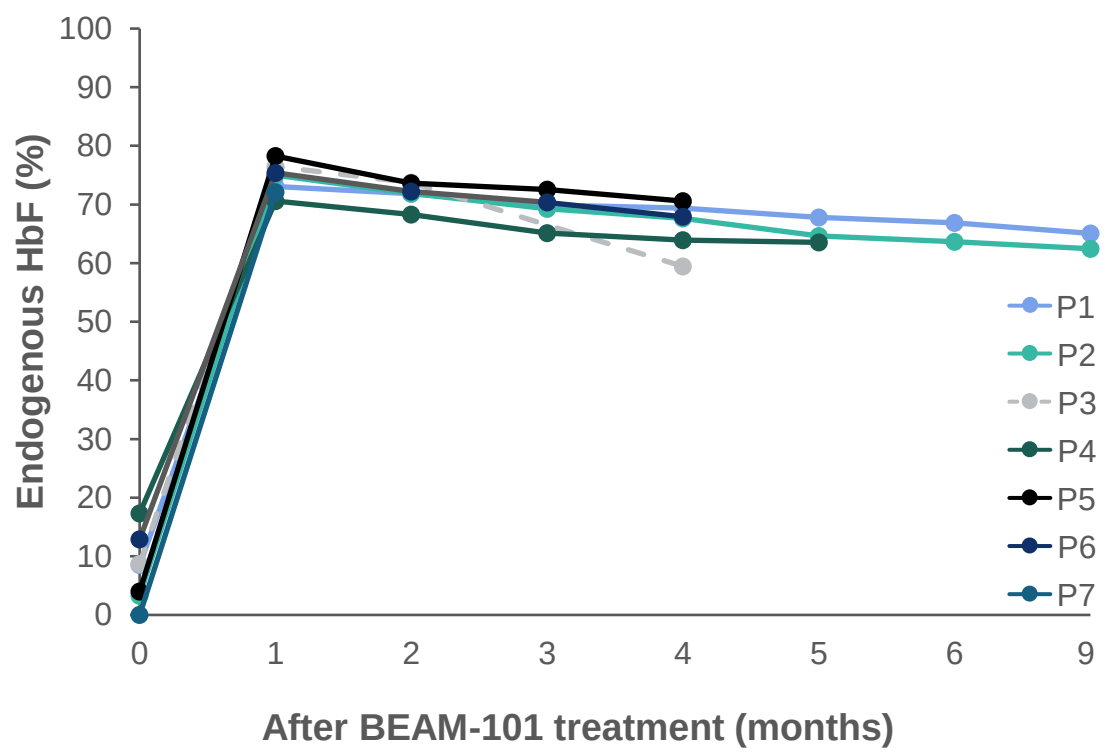
Female total Hb LLN-ULN: 11.5-15 g/dL; Male LLN-ULN: 13-17 g/dL. Hb, hemoglobin; HbA, adult hemoglobin; HbF, fetal hemoglobin; HbS, sickle hemoglobin; LLN, lower limit of normal; ULN, upper limit of normal

All patients had rapid and robust increases in total Hb and HbF that were sustained through follow up

Robust increase in total Hb that is stable through follow up



Rapid and robust increase in % endogenous HbF that remained >60% through follow up



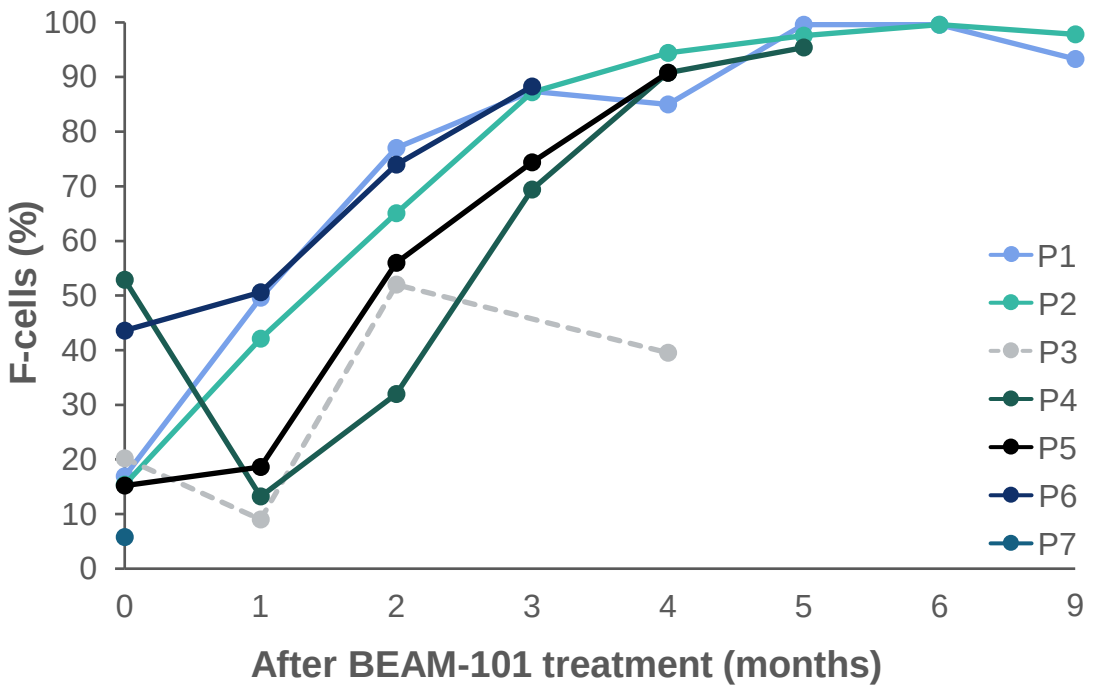
Data cutoff Oct 28, 2024

Female total Hb LLN-ULN: 11.5-15 g/dL; Male LLN-ULN: 13-17 g/dL

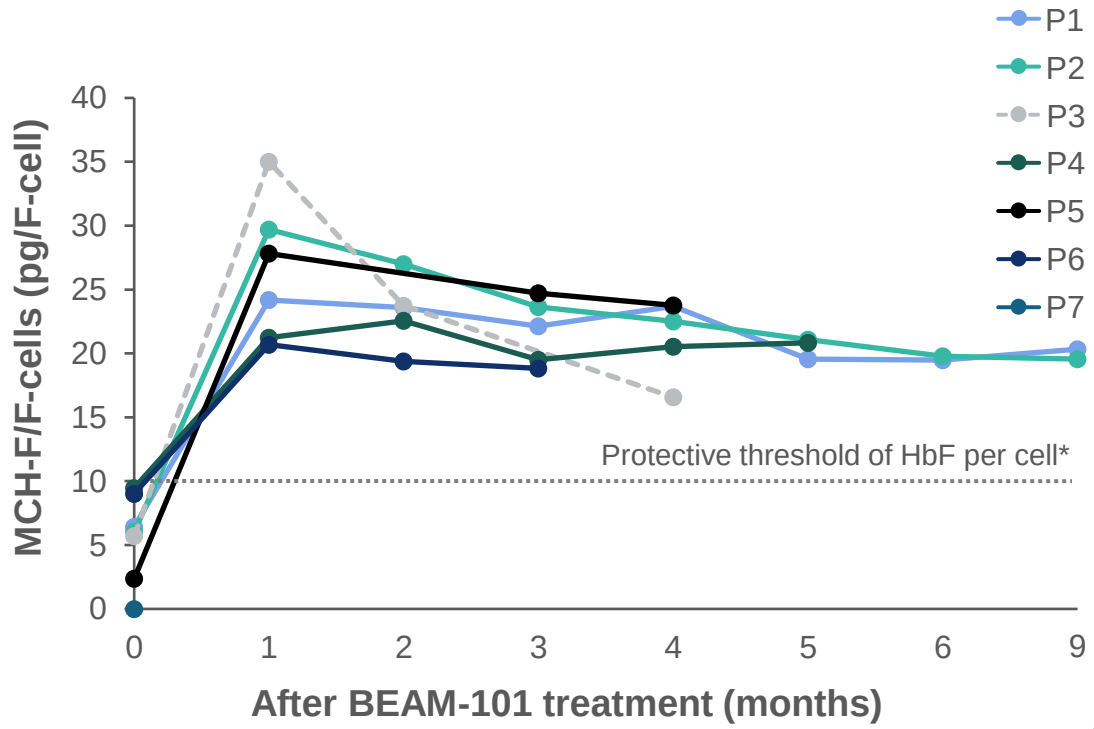
Hb, hemoglobin; HbF, fetal hemoglobin; F, female; M, male

Pancellular distribution of HbF observed through follow up

Pancellular HbF expression observed following elimination of transfused blood



Mean HbF (pg/cell) reached the protective threshold by M1 and were sustained through follow up



Visit Poster 4957 on Dec 9th for further details on HbF and HbS expression and biomarker analyses exploring RBC health and function from the BEACON study

Data cutoff Oct 28, 2024

*Defined as the level of HbF that inhibits deoxyHbS polymerization; Steinberg MH, et al. Blood 2014;123:481–485

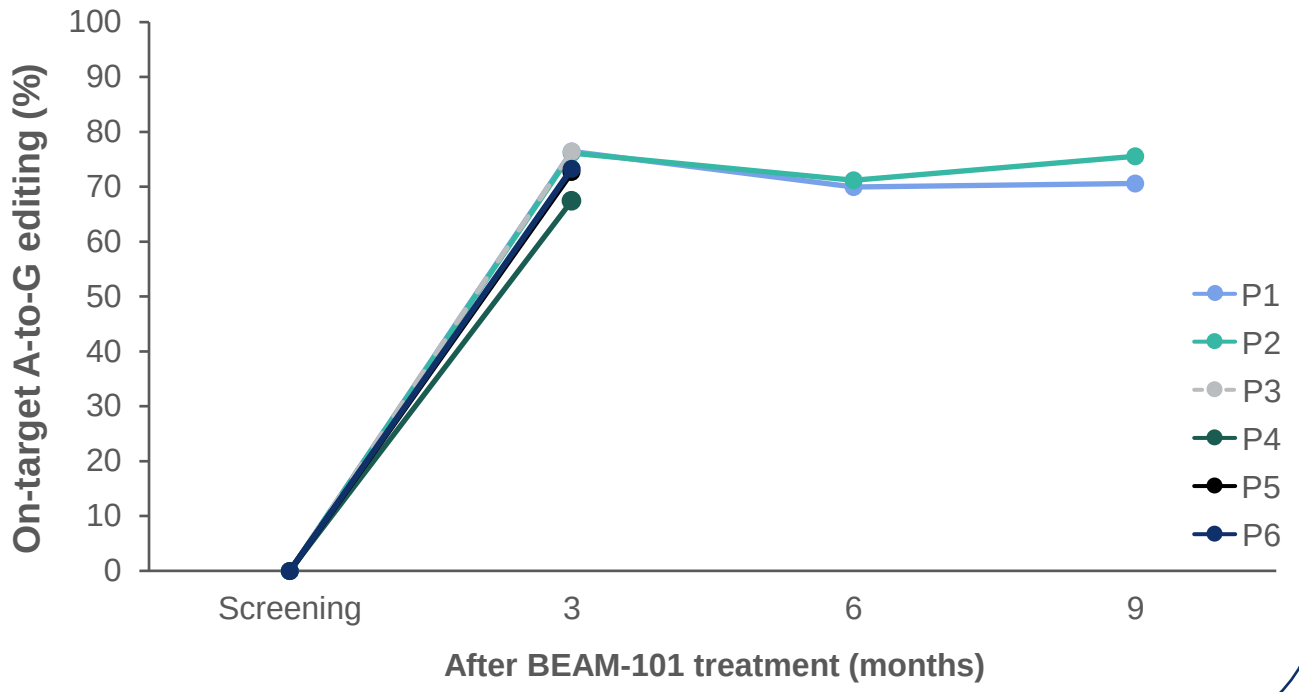
F-cell, HbF-containing cell; HbF, fetal hemoglobin; HbS, sickle hemoglobin; M, month; MCH, mean corpuscular hemoglobin; P, patient

High editing rates in peripheral blood following BEAM-101 treatment indicate successful engraftment and persistence of gene-edited cells

High % editing in BEAM-101 drug product

Patient	On-target A-to-G editing (%)
1	93
2	92
3	90
4	93
5	92
6	94

Early data show consistent high levels of persistent editing in peripheral blood after BEAM-101 treatment



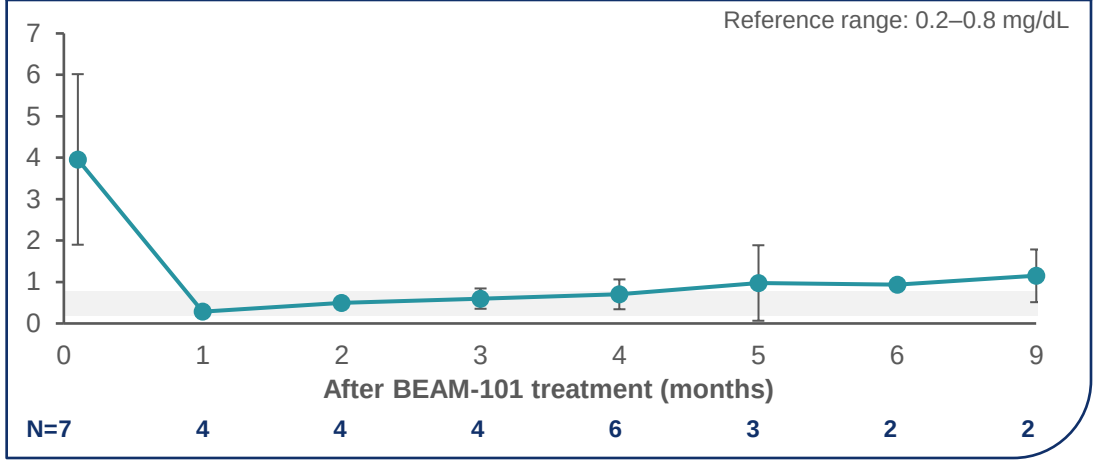
Data cutoff Oct 28, 2024

Percent of target bases that undergo A-to-G edit; Percent of editing from the drug product release is measured at day 14 of in vitro erythroid differentiation by NGS

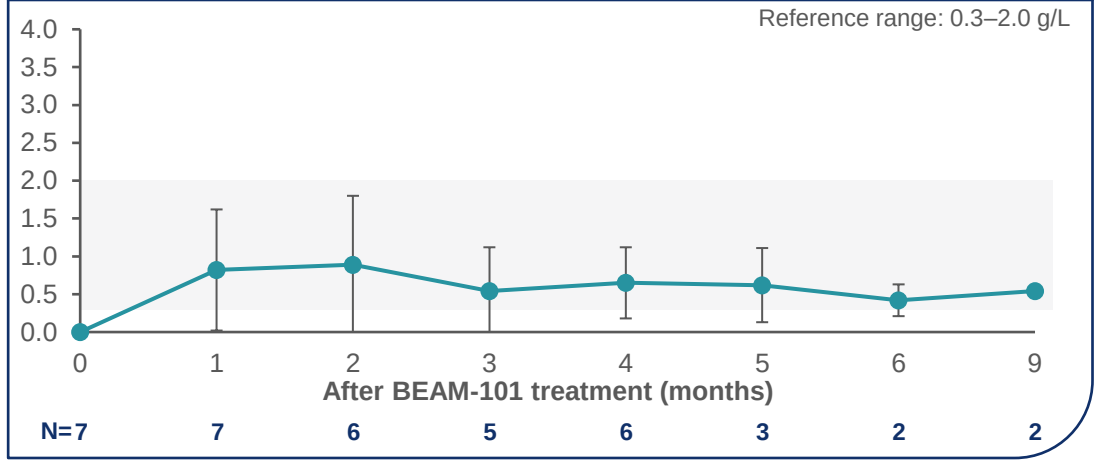
NGS, next-generation sequencing; P, patient

Hemolysis markers normalized or improved following BEAM-101 treatment

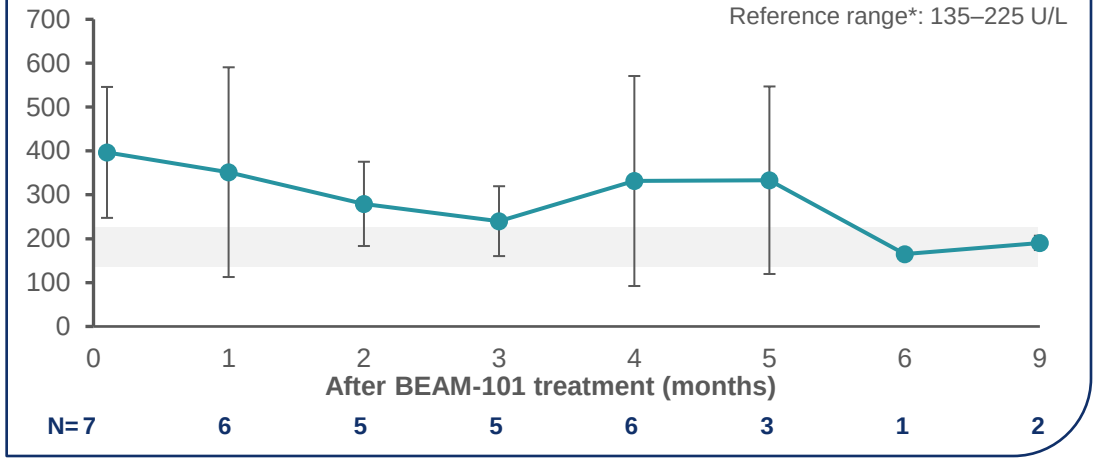
Indirect bilirubin (mg/dL ± SD)



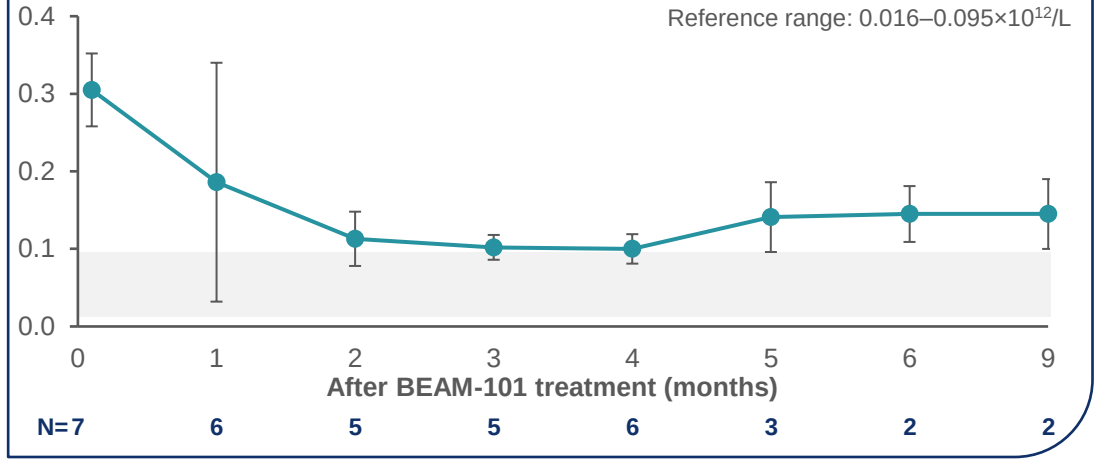
Haptoglobin (g/L ± SD)



Lactate dehydrogenase (U/L ± SD)



Reticulocytes (×10^{12}/L ± SD)



Data cutoff Oct 28, 2024

*Reference range shows lower limit of normal for male/female; higher limit of normal for male. SD, standard deviation

Conclusions

- Patients treated with BEAM-101 required a **low number of mobilization cycles**, and achieved **rapid neutrophil and platelet engraftment** with low number of neutropenic days
- **Initial safety data with BEAM-101 are consistent with busulfan conditioning and autologous HSCT**, with **no VOCs reported** by investigators post-engraftment
- All patients achieved **rapid and robust increases in total Hb and HbF**; **pancellular** distribution of HbF was **maintained above protective thresholds** through follow up
- All patients achieved **rapid and robust decrease in HbS**, and markers of hemolysis were **normalized or improved**

Initial data from the BEACON study demonstrate the potential of base editing and show that treatment with BEAM-101 results in robust and sustained **increases in HbF expression** and **resolution of anemia** in SCD patients

Data cutoff Oct 28, 2024

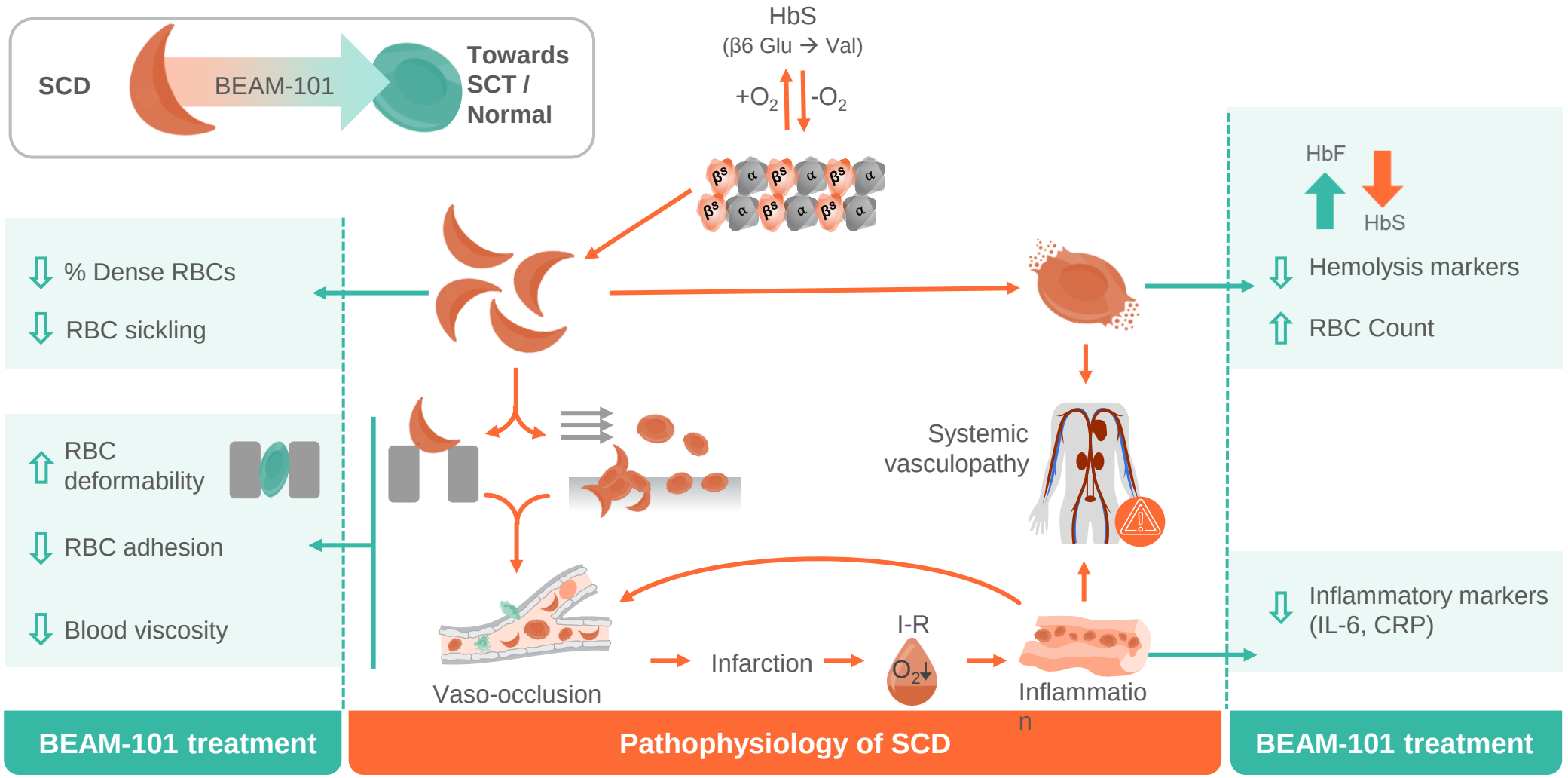
HbF, fetal hemoglobin; HbS, sickle hemoglobin; HSCT, hematopoietic stem-cell transplantation; SCD, sickle cell disease; VOC, vaso-occlusive crisis

BEAM-101 Clinical Exploratory Biomarkers

AMY SIMON, M.D., CHIEF MEDICAL OFFICER

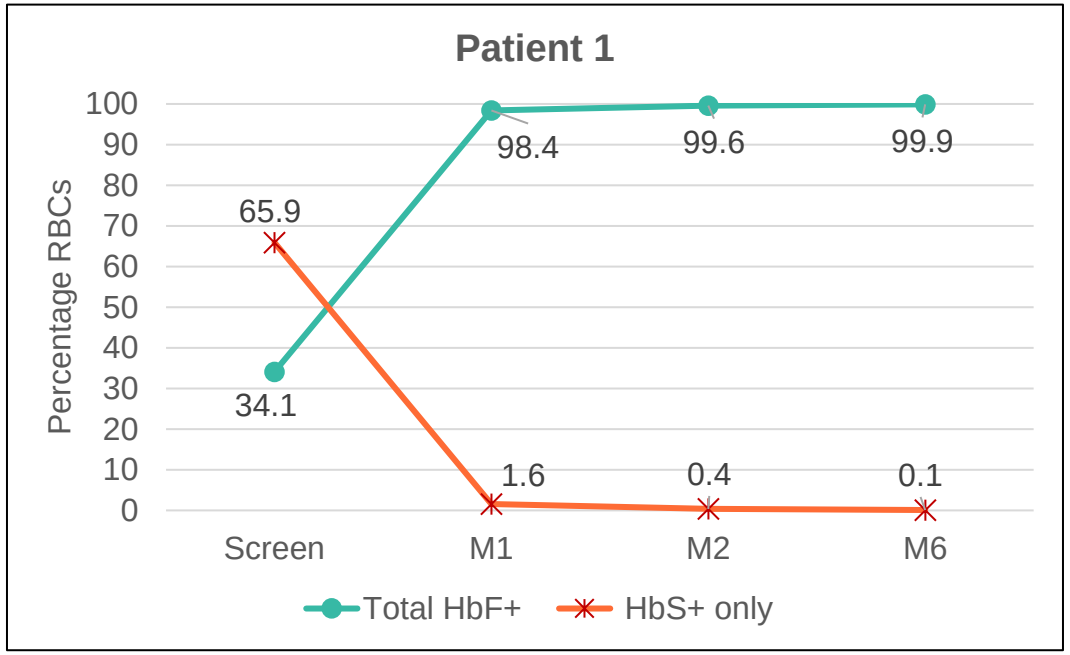
Beam THERAPEUTICS

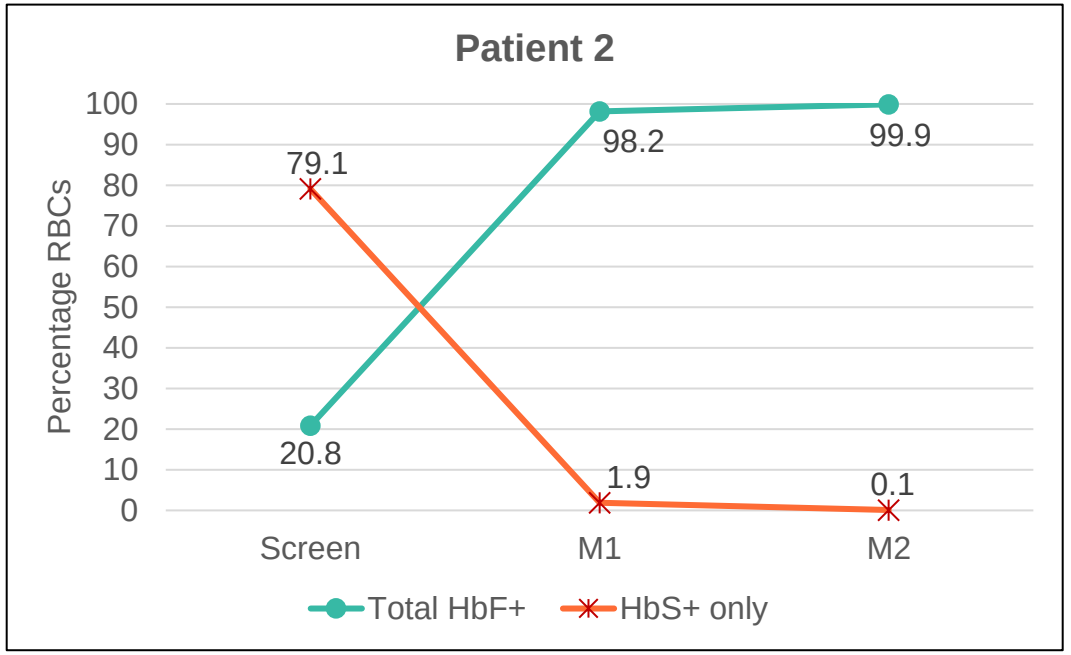
What would improved RBC health and function look like post BEAM-101 treatment?



HbF, Fetal hemoglobin; HbS, Sickle hemoglobin; RBC, Red blood cell; SCD, Sickle cell disease; SCT, Sickle Cell Trait; I-R, Ischemia Reperfusion
Data cutoff 28 Oct 2024 for the biomarker data presented here.

Exploratory red blood cell (RBC) function assays





After BEAM-101 treatment:

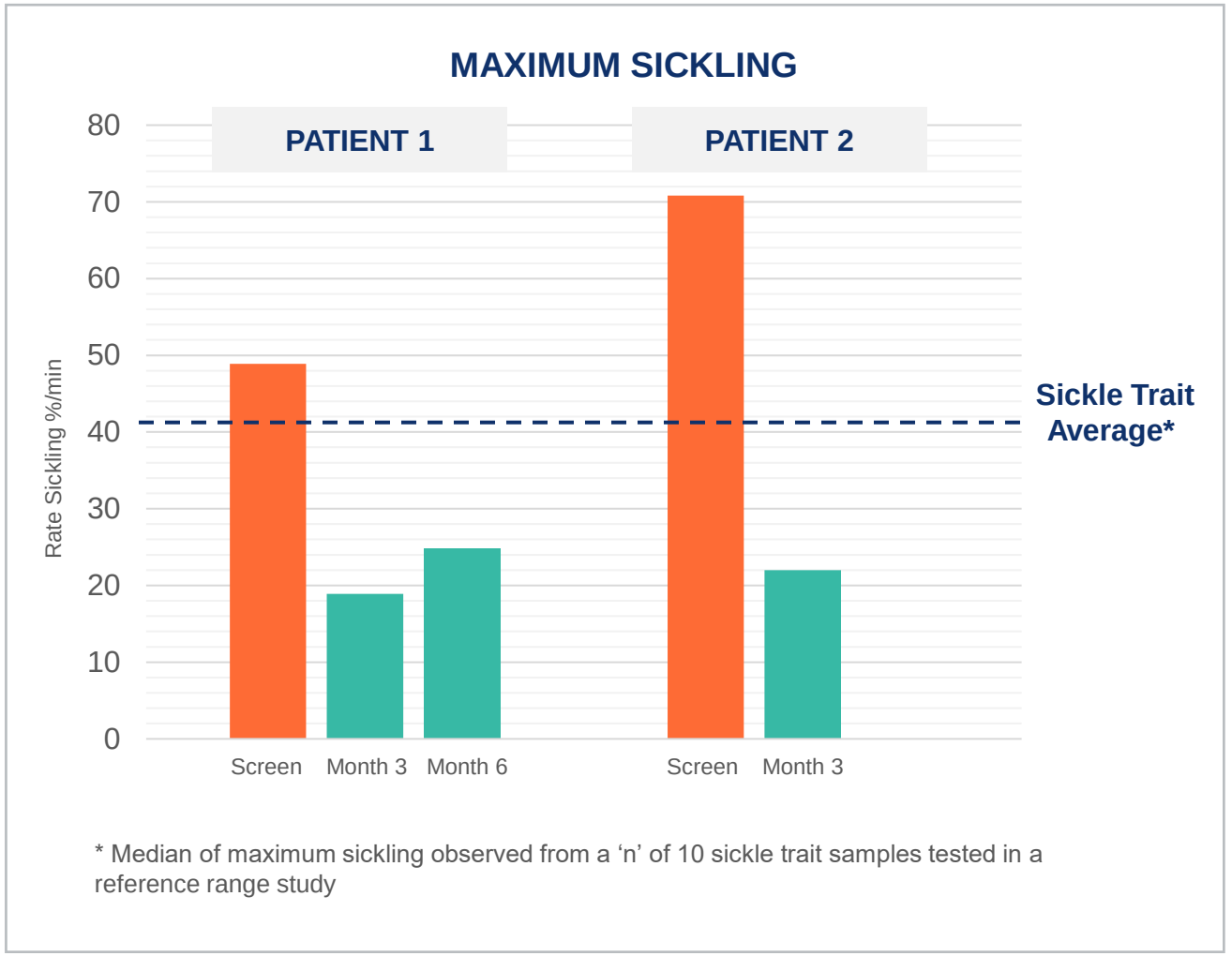
- Nearly all RBCs were expressing HbF by Month 1
- Nearly all RBCs expressing solely HbS were eliminated by Month 2

Duplex flow cytometry performed on untransfused RBCs

Data cut as of July 2, 2024

Exploratory red blood cell (RBC) function assays

- Reduction in RBC sickling (see graph) and cell adhesion to levels comparable to SCT samples (N=2)
- Other RBC function improvements include increased deformability and decreased density (N=1 at Month 6)
- Resolution of abnormal cell morphology and sickle cells by Month 6 and 4 in patients 1 and 2, respectively



* Median of maximum sickling observed from a 'n' of 10 sickle trait samples tested in a reference range study

Data cut as of July 2, 2024

Poster presentation on exploratory biomarkers in up to 6 patients suggest that BEAM-101 restored RBC health and function

- >98% of non-transfused RBCs express HbF at Month 1 with near complete elimination of RBCs expressing solely HbS post BEAM-101
- Percentage dense RBCs, blood viscosity, oxygen affinity, and RBC deformability improved post BEAM-101
- Cell adhesion reduced to significantly below the critical SCD threshold post BEAM-101 indicating a reduced risk for VOCs
- Increase in RBC cell number and resolution of abnormal RBC morphology observed post BEAM-101
- Changes in multiple sickling parameters & reduction in sickling of RBC were comparable to HbAS post BEAM-101 treatment
- **Visit poster presentation (abstract #4957) on Monday, Dec. 9, 6-8 p.m.**

Rapid advancement of the BEACON Phase 1/2 study of BEAM-101

35+

Adult sickle cell disease patients **cleared screening and enrolled**

20+

Patients with **manufactured drug product**

11

Patients **dosed with BEAM-101**

DMC + FDA

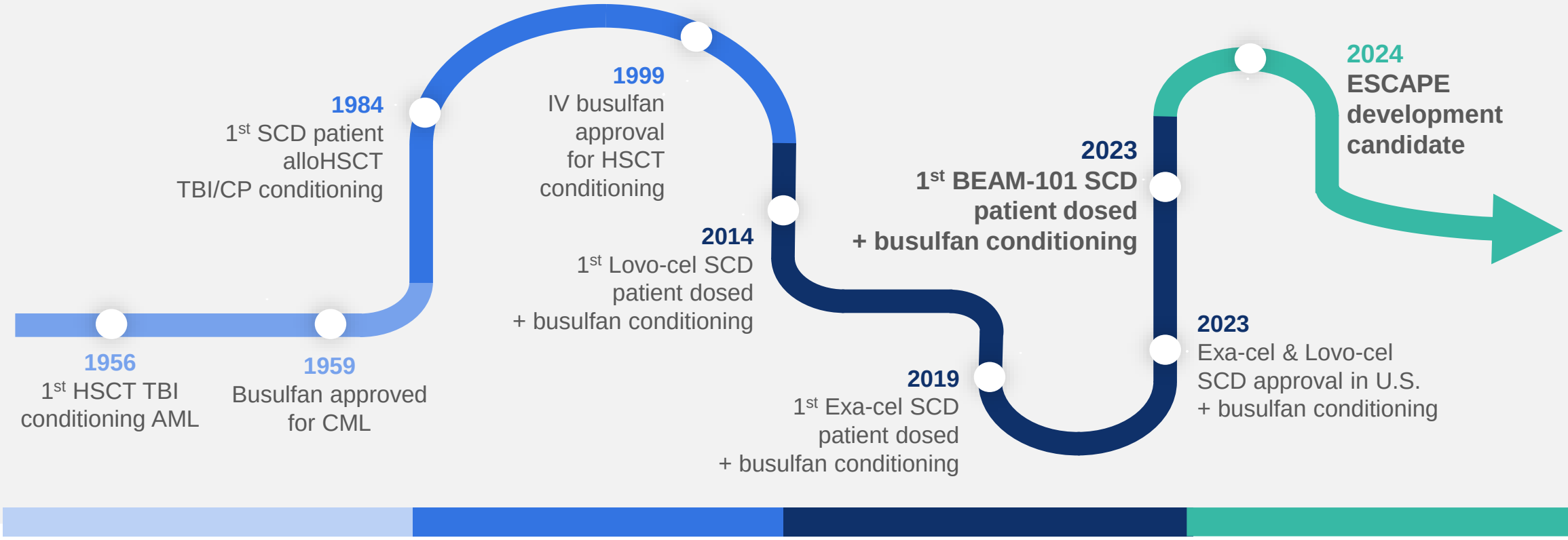
approved **enrollment of adolescents** (ages 12-17 years old) in BEACON

ESCAPE Program

GIUSEPPE CIARAMELLA, PH.D., PRESIDENT

Beam THERAPEUTICS

ESCAPE technology designed to bring a paradigm shift to transplant conditioning for the first time in nearly 70 years



68 years of genotoxic conditioning:

- Infertility
- Secondary malignancy
- Organ toxicities
- Infection complications
- Inpatient

Promise of non-genotoxic conditioning

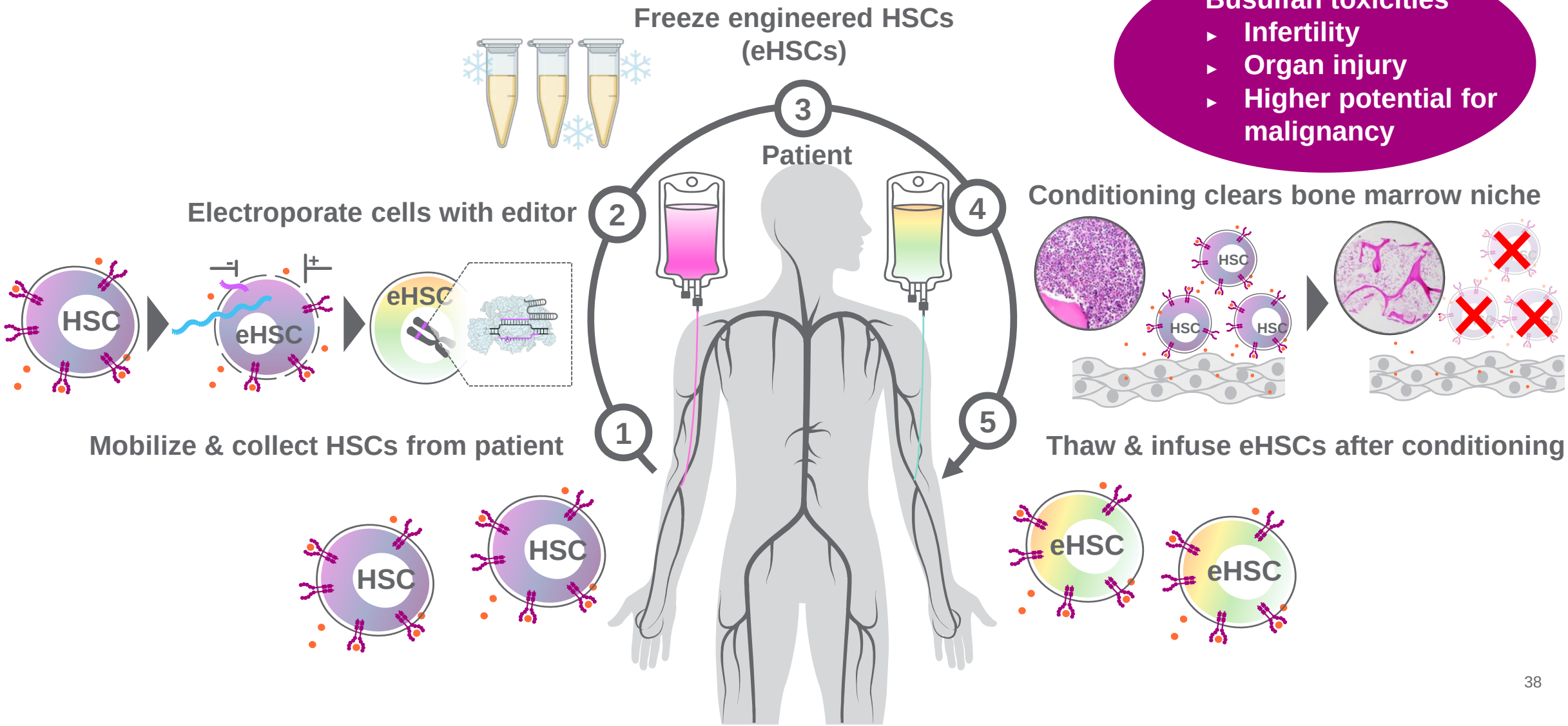
- Prevent acute and chronic toxicities
- Preserve fertility
- Potential to be outpatient

CD117 antibody conditioning and multiplex base editing enable rapid and robust fetal hemoglobin reactivation in a rhesus autologous transplantation model

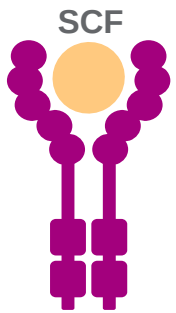
66th ASH Annual Meeting
Session: 801
December 8, 2024

Curative gene therapies for SCD currently require myeloablative genotoxic conditioning with busulfan prior to transplant, which have significant toxicities

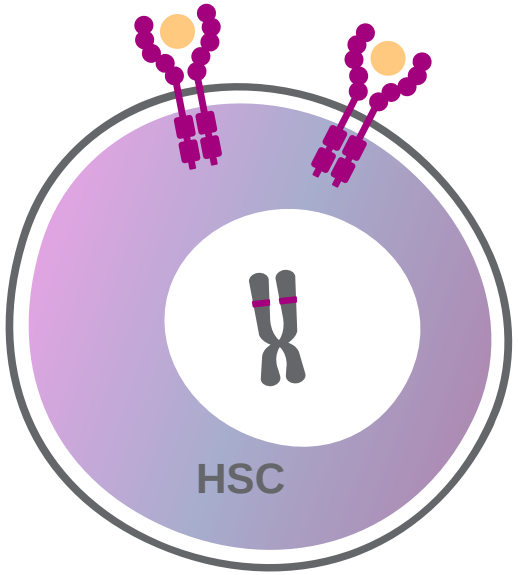
Busulfan toxicities
- Infertility
- Organ injury
- Higher potential for malignancy



Epitope engineering via base editing enables eHSCs to selectively ESCAPE mAb binding

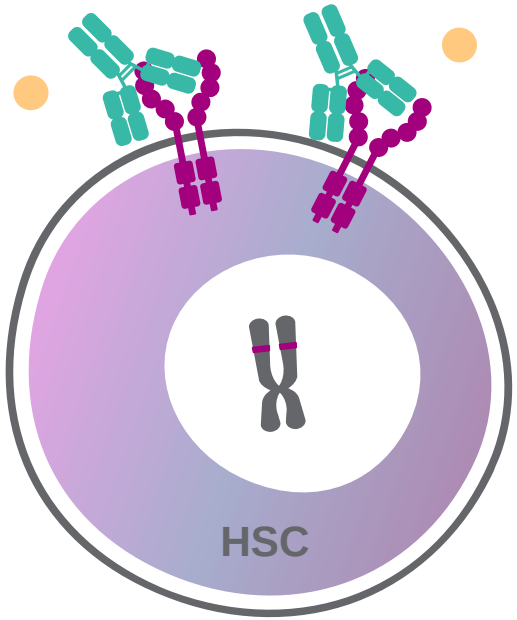


High expression in the long-term and short-term HSCs make CD117 an attractive target for immunologic conditioning



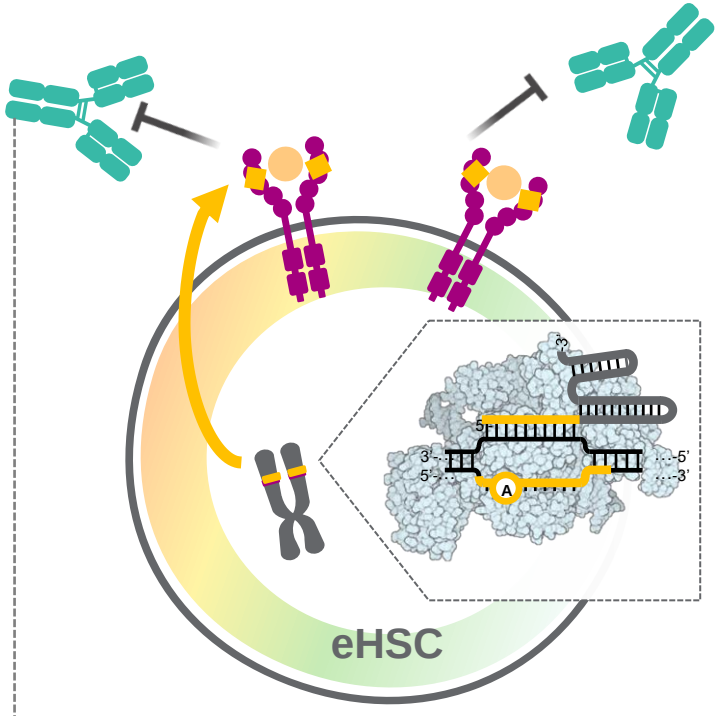
Unedited CD34 cell
No BEAM-103
Normal signaling

Cell Survives



Unedited CD34 cell
BEAM-103 blocks SCF
BEAM-103 blocked signaling

Cell Dies



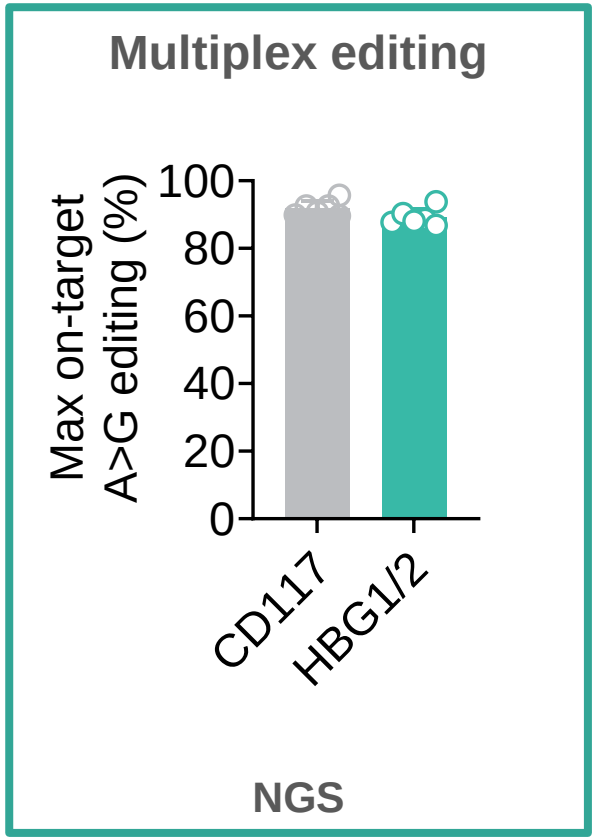
Edited CD34 cell (BEAM-104)
Escapes BEAM-103
Normal signaling

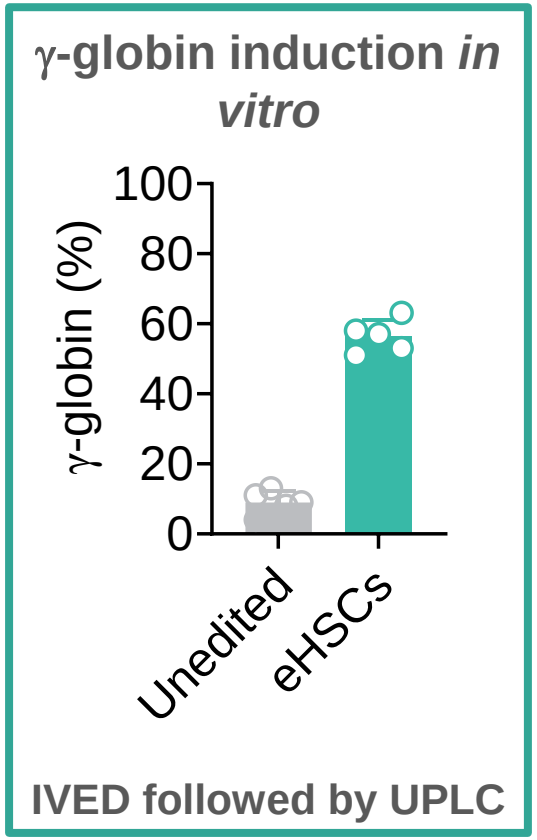
Cell survives
HBG1/2 editing leads to HBG induction

BEAM-104 = Multiplex edited eHSC
BEAM-103 = Anti-CD117 mAb

ESCAPE: Engineered Stem Cell Antibody Paired Evasion

Multiplex editing and γ-globin induction achieved *in vitro*



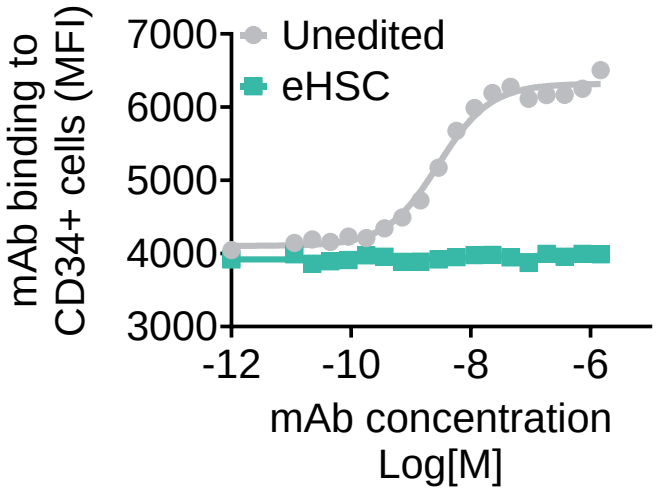


- >90% bulk CD117 and HBG1/2 editing
- Comparable to single-plex editing rates for each target site
- Single clonal analysis showed majority (>90%) of the clones harbored CD117 edit
- No CD117 only edited cells were identified
- *In vitro* differentiated (IVED) multiplex edited erythroid cells yielded >50% γ-globin

- Multiplex editing led to similar editing outcomes as single-plex editing for each target site
- >50% γ-globin by *in vitro* differentiated erythroid cells

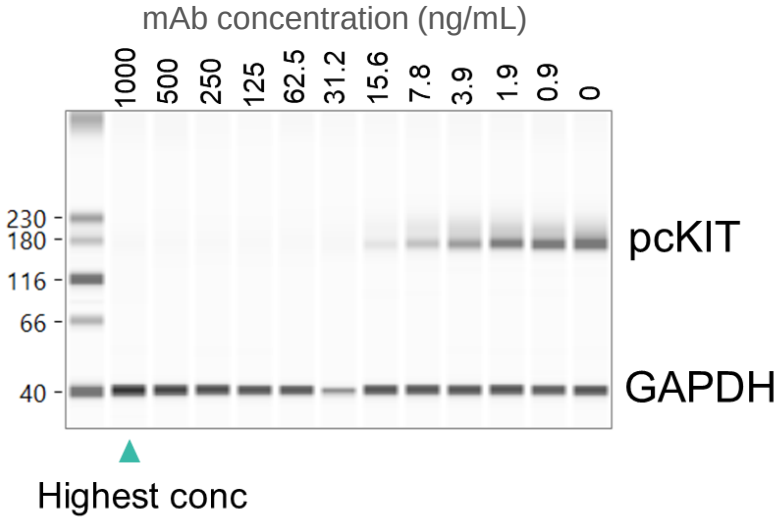
Anti-CD117 mAb selectively bound with high affinity and depleted WT CD117 expressing HSCs

Anti-CD117 mAb bound to unedited HSPCs but not to eHSCs



Flow cytometry of CD34s

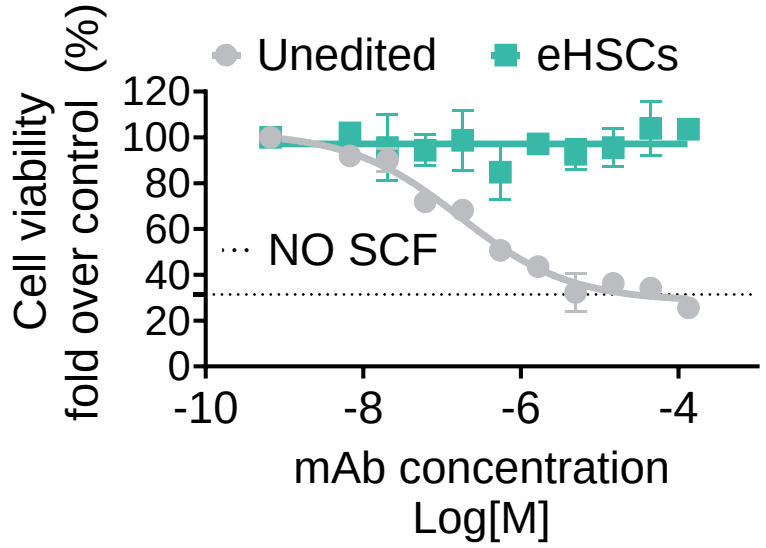
Anti-CD117 mAb abrogated CD117 phosphorylation



cKIT, CD117
pcKIT, phosphorylated CD117 (cKIT)
GAPDH, glyceraldehyde 3-phosphate dehydrogenase, used as loading control

Western blot

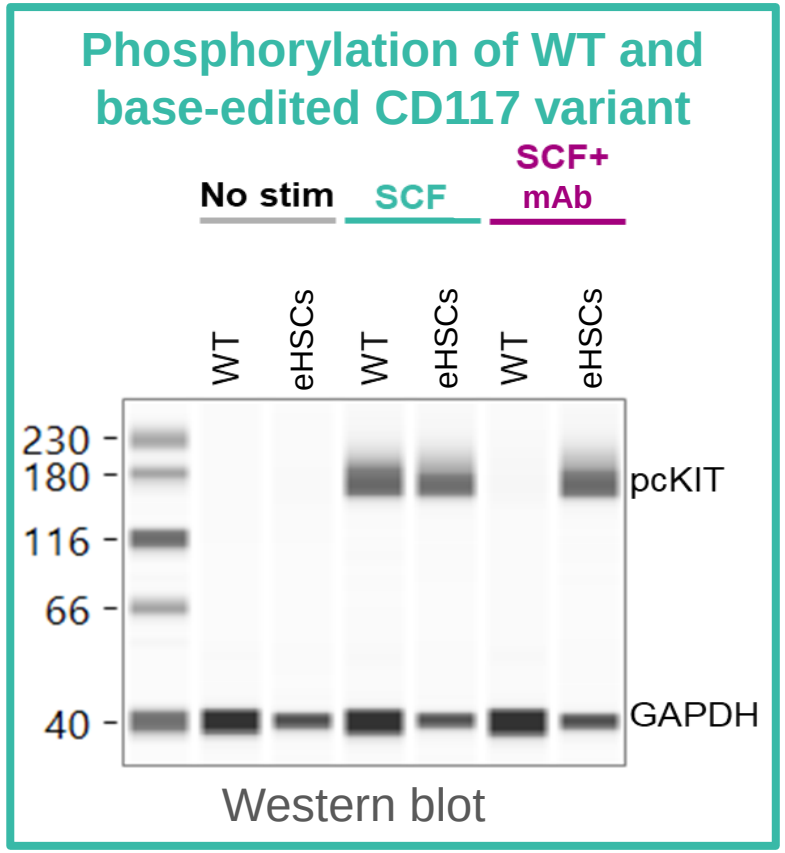
Anti-CD117 mAb selectively depleted unedited cells while eHSCs escaped depletion



***In vitro* treatment of CD34s**

- Anti-CD117 mAb showed selective binding to WT CD117 and no binding to multiple edited eHSCs
- mAb binding led to complete abrogation of WT CD117 signaling
- Multiplex edited eHSCs were protected from mAb mediated depletion *in vitro*

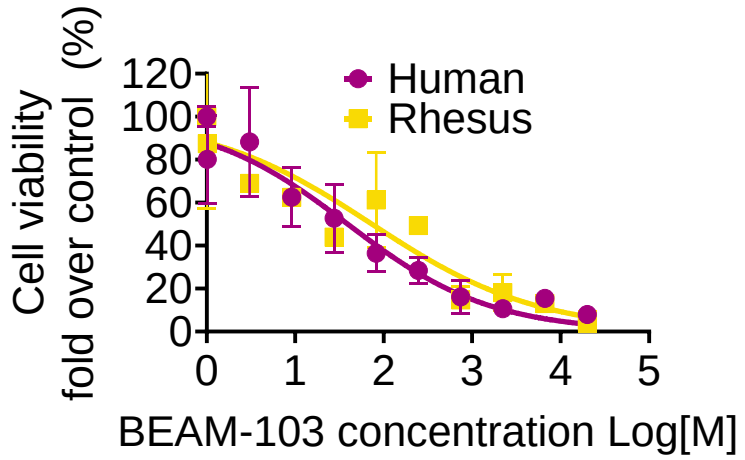
Base-edited CD117 variant retained comparable receptor binding and function to wild-type



- Base-edited CD117 retained normal ligand binding, phosphorylation and internalization properties
- Anti-CD117 mAb blocked phosphorylation of WT CD117 but not of base-edited CD117

Anti-CD117 mAb is cross-reactive to and led to depletion of Rhesus HSPCs *in vitro*

Anti-CD117 mAb similarly depleted WT human and Rhesus HSPCs

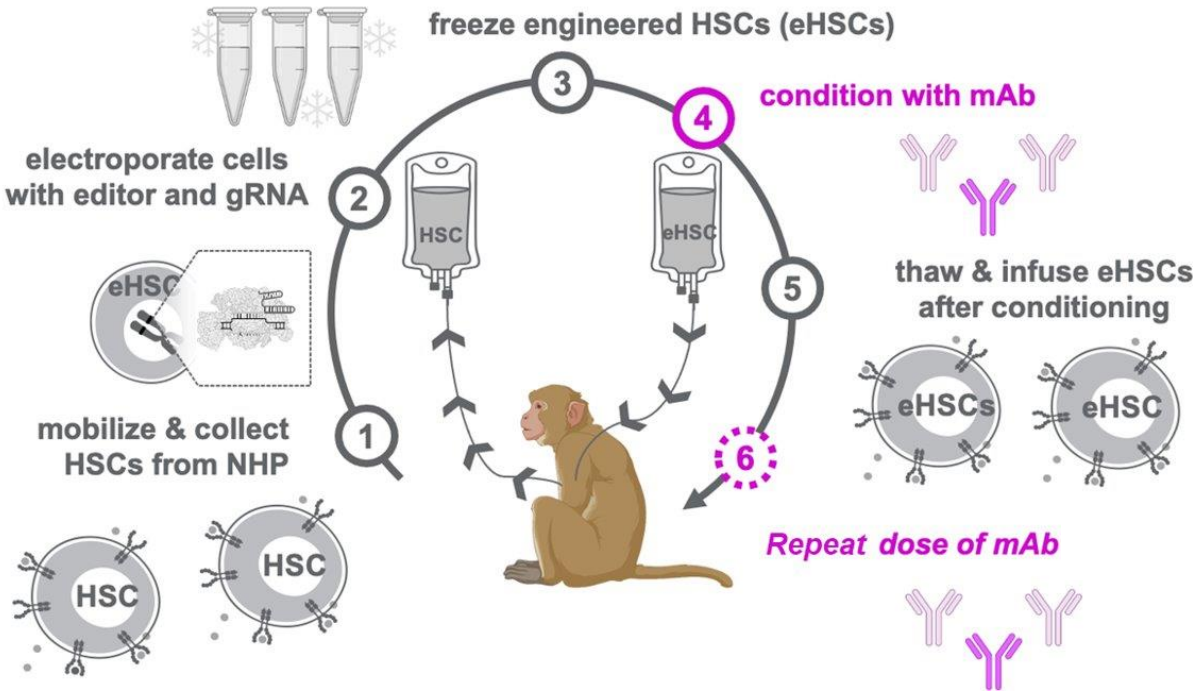


***In vitro* treatment of CD34s**

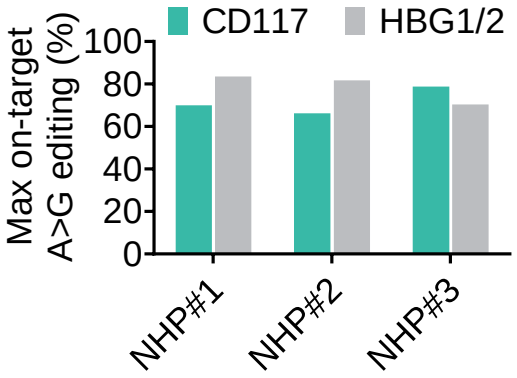
BEAM-104 = Multiplex edited eHSC
BEAM-103 = Anti-CD117 mAb

NHP autologous transplant model for our ESCAPE conditioning approach

Multiplex base-editing and erythroid differentiation of Rhesus CD34+ cells

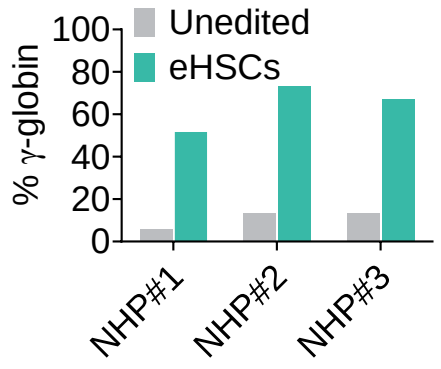


Multiplex editing in Rhesus HSPCs



Next generation sequencing

Potential for therapeutic levels of HBF upon multiplex editing



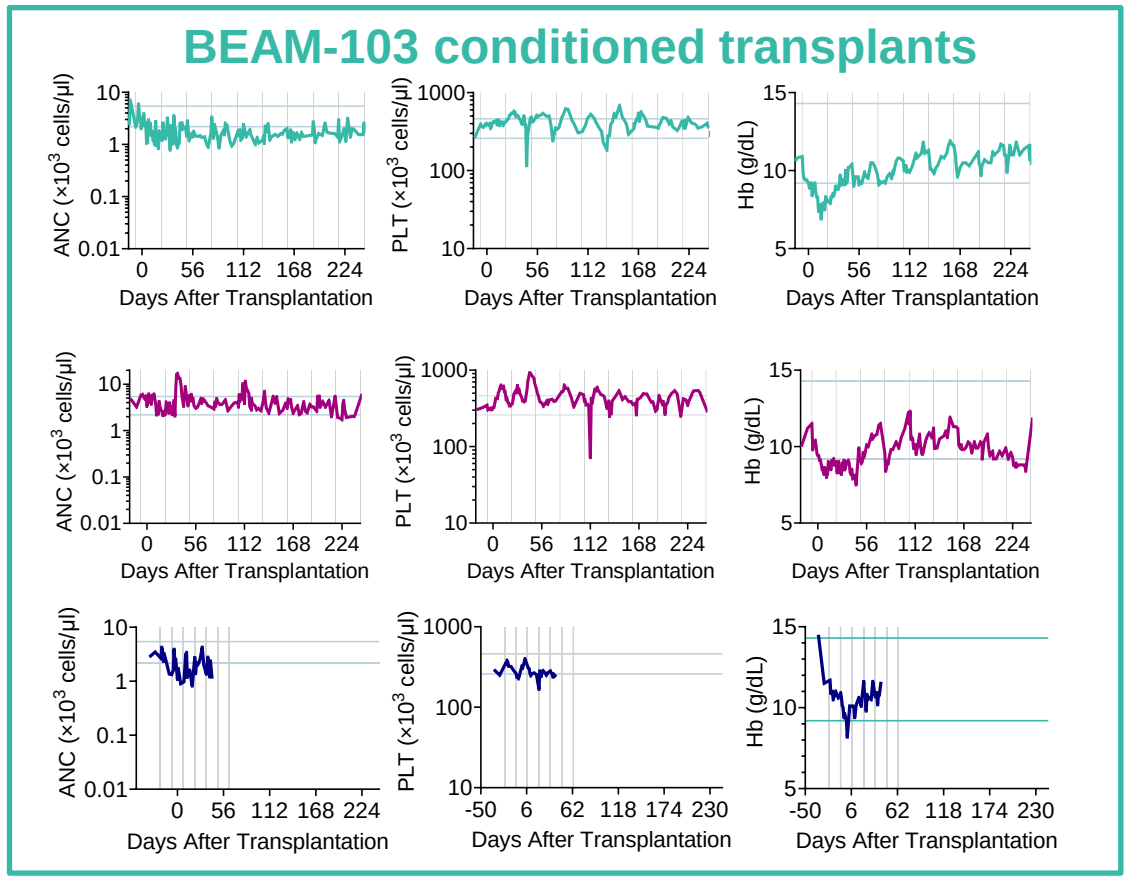
In vitro erythroid differentiation

Infusion product was manufactured with priority for maximizing total CD34+ cell dose for transplant

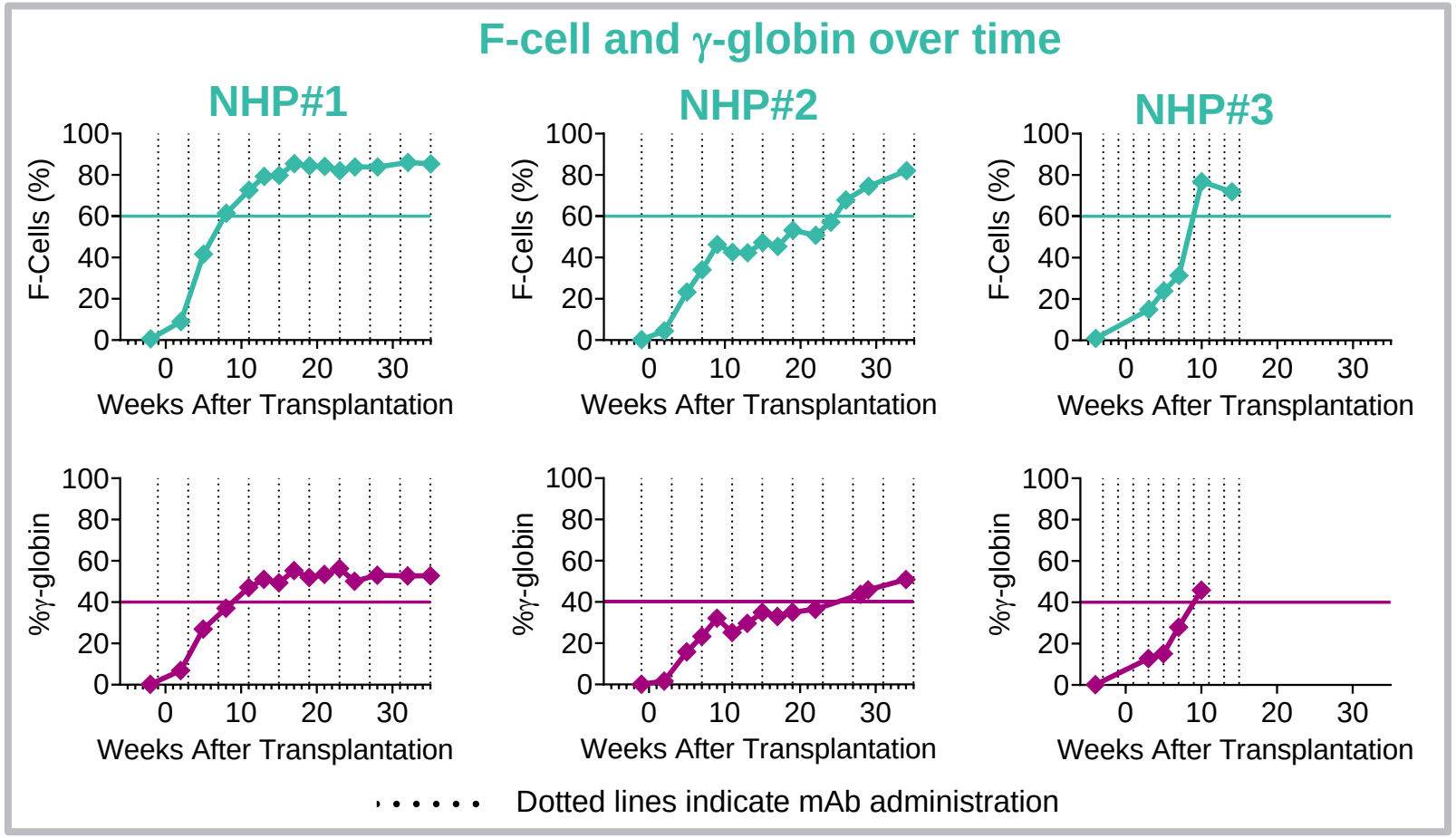
mAb dosing was well tolerated with no use of transfusions/antibiotic support

- In contrast with busulfan conditioning, NHPs dosed with mAb demonstrated only minor dips in neutrophil counts
- Although platelet counts dropped after each mAb dose, levels recovered quickly
- Minor drops in hemoglobin upon mAb dosing recovered post-transplant
- **The ESCAPE transplant strategy presented sharp contrast with busulfan conditioning as the animals remained healthy without the need for transfusion/ antibiotics or additional supportive care**

Repeat dosing of anti-CD117 mAb was well tolerated



NHPs dosed with mAb demonstrated rapid turnover of unedited erythroid cells and early induction of therapeutic γ-globin levels



- Rapid and complete replacement of erythroid cells by edited cells
- F-cell levels reached ~60% as early as 8-weeks post-transplant
- Earliest time to achieve ~40% γ-globin was ~8 weeks post-transplant

BEAM-104 = Multiplex edited eHSC
BEAM-103 = Anti-CD117 mAb

Rapid reactivation of fetal hemoglobin post-transplant shows promise of potential early therapeutic benefit in SCD patients

Summary

- Busulfan-associated toxicity continues to be a major obstacle to expanding the use of autologous HSCT-based gene therapies for SCD
- The ESCAPE strategy can potentially address this unmet need by enabling HSC-targeted non-genotoxic naked anti-CD117 mAb conditioning
- The CD117 base-edit showed normal receptor function *in vitro,* and the multiplex edited eHSCs produced durable engraftment and multi-lineage reconstitution in an autologous transplant model with busulfan conditioning
- Here we present non-human primate data demonstrating proof-of-concept for ESCAPE non-genotoxic conditioning, potentially removing the requirement for toxic, myeloablative conditioning for autologous HSCT
  - We observed rapid and complete replacement of host erythroid cells by edited cells leading to early induction of therapeutically relevant levels of fetal hemoglobin (60% F-cells and 40% γ-globin as early as 8-weeks post-transplant), providing potential early therapeutic benefit in SCD patients
  - The ESCAPE transplant strategy presents a sharp contrast to busulfan-based conditioning as the animals remained healthy without the need of transfusion, antibiotics or additional supportive care

Anticipated next steps for ESCAPE

1

- Follow-up NHP studies to optimize antibody dose regimen, dose response and chimerism
  - Additional data expected in 2025

2

- GMP manufacturing initiated
- Initiate Phase 1-enabling tox studies by YE 2024

3

- Phase 1 study of BEAM-103 antibody to evaluate PK/PD and safety in heathy volunteers

4

- Efficacy study of BEAM-103 and BEAM-104 in SCD and beta-thalassemia patients

Beam presentations at the ASH Annual Meeting

ORAL

Initial Results from the BEACON Clinical Study of BEAM-101 in Sickle Cell Disease

Sunday, Dec. 8, 10 a.m. PT
Abstract #513

ORAL

Preclinical Data for ESCAPE in a Rhesus Autologous Transplantation Model

Sunday, Dec. 8, 10:45 a.m. PT
Abstract #516

POSTER

Impact of BEAM-101 Treatment on Red Blood Cell Hemoglobin Expression, Rheology and Sickling Properties

Monday, Dec. 9, 6-8 p.m. PT
Abstract #4957

POSTER

Initial Data from the Phase 1/2 Study of BEAM-201, Multiplex Base-Edited Allogeneic Anti CD7 CAR-T-Cells

Monday, Dec. 9, 6-8 p.m. PT
Abstract #4838

Available for download on the Publications page of beamtx.com

On display at San Diego Convention Center, Halls G-H and available for download on beamtx.com tomorrow at 6p.m.

Significant progress on Beam's vision and base editing platform

HEMATOLOGY

- BEAM-101 showing potential for clinical differentiation in SCD
- Significant momentum in BEACON trial
- Opportunity to remove chemotherapy from transplant and expand SCD market with ESCAPE

GENETIC DISEASE

- BEAM-302 potential to be a one-time treatment addressing both lung and liver disease in AATD
- Near-term clinical catalyst for BEAM-302 expected in 1H 2025

BASE EDITING

- More precise, efficient, predictable and versatile than nucleases
- Clinically validated
- Strong translation from preclinical to clinical

Beam THERAPEUTICS

Q&A