Beam THERAPEUTICS

PRECISION GENETIC MEDICINES THROUGH BASE EDITING

DECEMBER 2024 NASDAQ: BEAM

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 initiation, timing, progress and results of preclinical studies and research and development programs, including the initiation, design and progress of clinical trials, including trials for BEAM-101, BEAM-201, BEAM-301 and BEAM-302; the advancement of our pipeline and additional liver programs in multiple preclinical studies; our current expectations and anticipated results of operations, including our expected use of capital; the potential activities and benefits under license and collaboration agreements and the formation of new collaborations; our potential presentations at the ASH annual meeting; 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," “strategy,” “possibility,” “promise,” "believe," "intend," "project," "forecast," "estimates," "targets," "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; 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; the uncertainty that our product candidates will receive regulatory approval necessary to initiate human clinical trials, 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, 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**

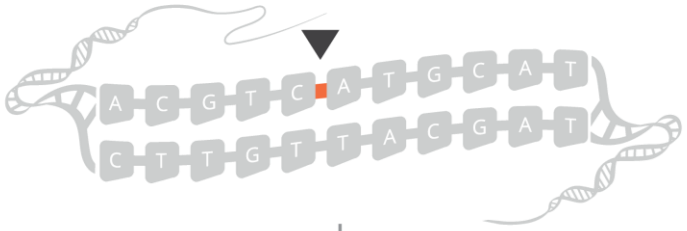
PLATFORM FOR **rapidly-programmable precision medicines**

Beam THERAPEUTICS

Base editing is an efficient, predictable and potentially best-in-class gene editing technology

NUCLEASE CRISPR, ZFN, TALENs

Precision targeting with CRISPR



Double-stranded breaks

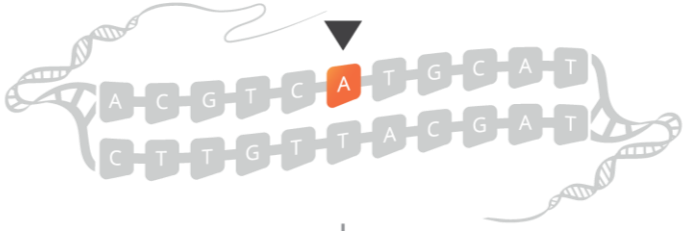
Lack of control of gene sequence outcomes

…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

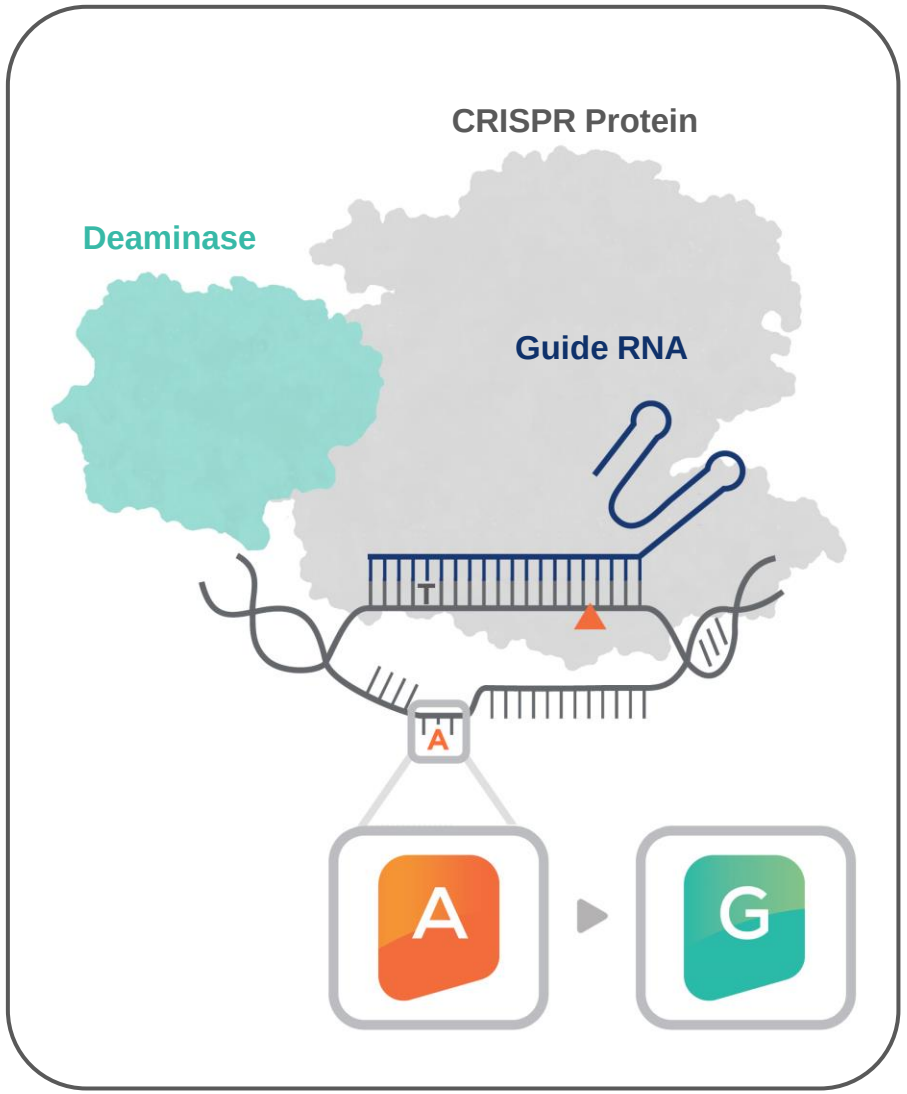
Precision targeting with CRISPR



Enzymatic base conversion

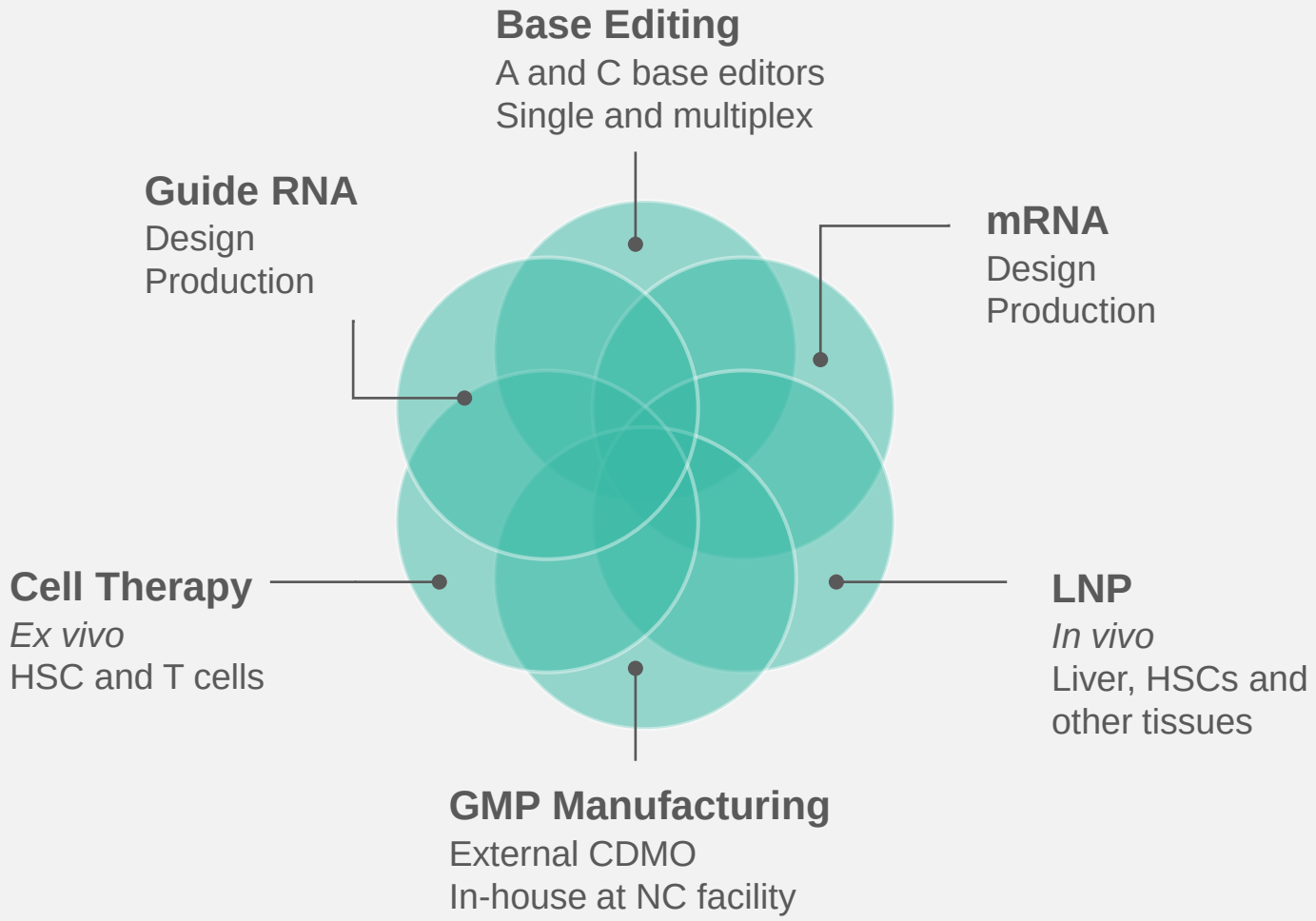
Highly efficient with predictable gene sequence outcomes

Base editing technology has multiple, highly versatile applications



		PROGRAMS
Correct mutations	Repairs the most common type of gene mutation, single base changes	BEAM-302, BEAM-301
Silence proteins	Turns off gene with disease-causing activity	Multiple at Beam and partners
Activate expression	Turns on genes to restore or increase function	BEAM-101
Modify proteins	Changes how proteins bind or signal without disrupting their function	ESCAPE
Multiplex edits	Targets multiple pathways simultaneously with high efficiency	BEAM-201, ESCAPE

We have built a comprehensive, fully-integrated platform for precision genetic medicines



FULLY INTEGRATED TECHNOLOGY AND CAPABILITIES

MODULAR PLATFORM FOR RAPID DEVELOPMENT OF NEW BASE EDITING PROGRAMS

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
- Validated FDA regulatory pathway
- **ESCAPE has potential to eliminate chemotherapy from transplant**, expanding reach of base editing to more patients
- Platform for future hematology pipeline

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

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

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

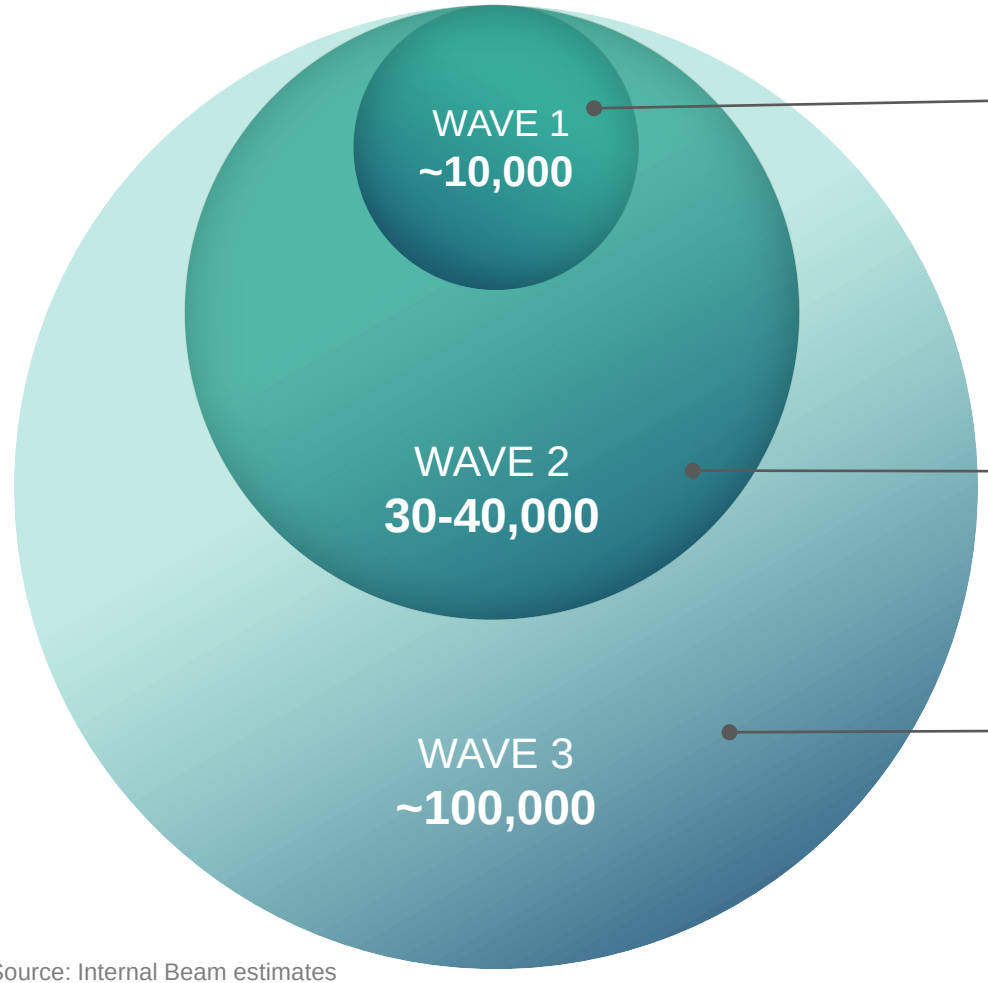
What if we could develop better one-time therapies for patients with SCD?

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:

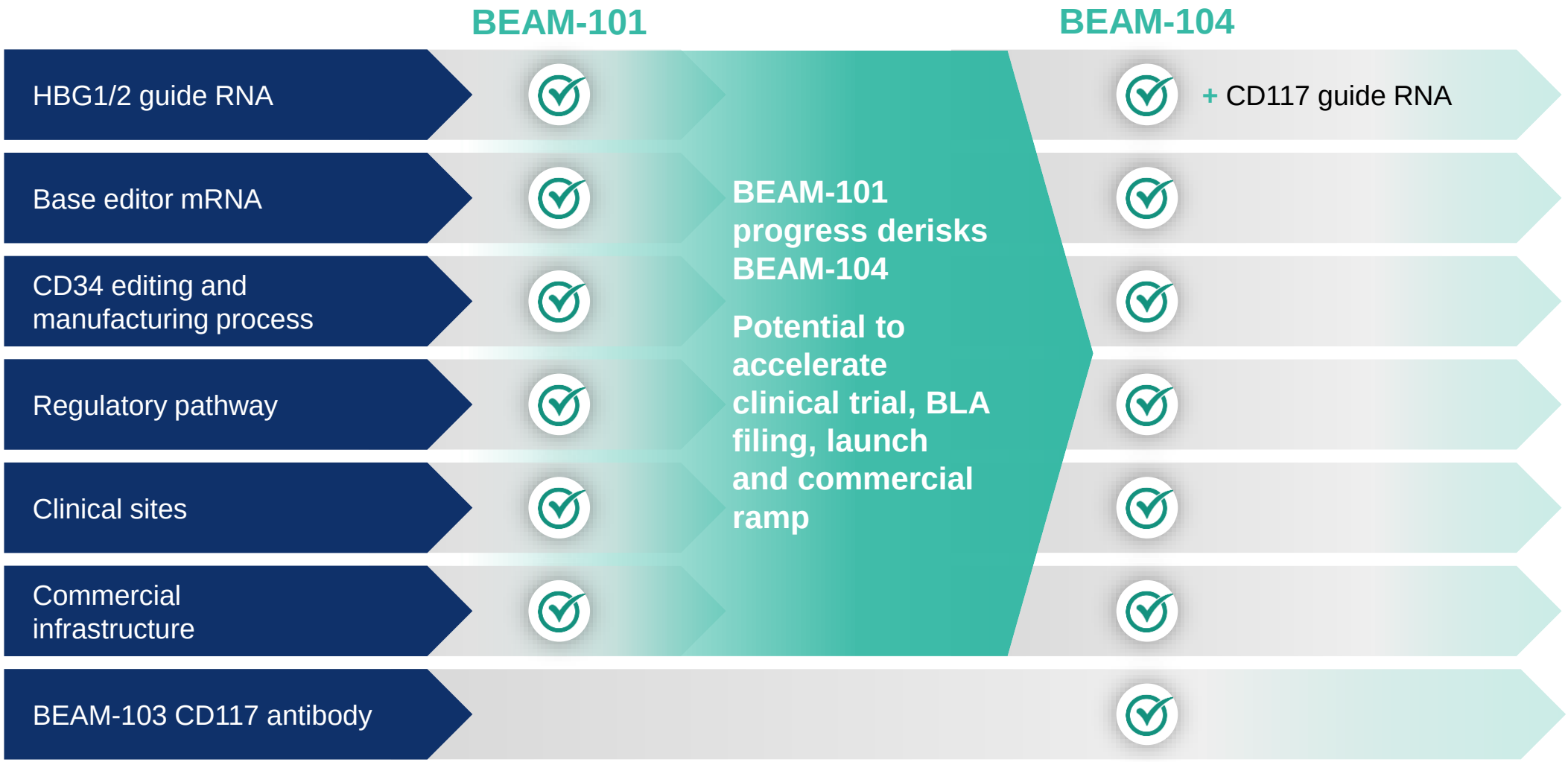
- Broader range of disease severity
- Broader age range
- Increased willingness-to-treat

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

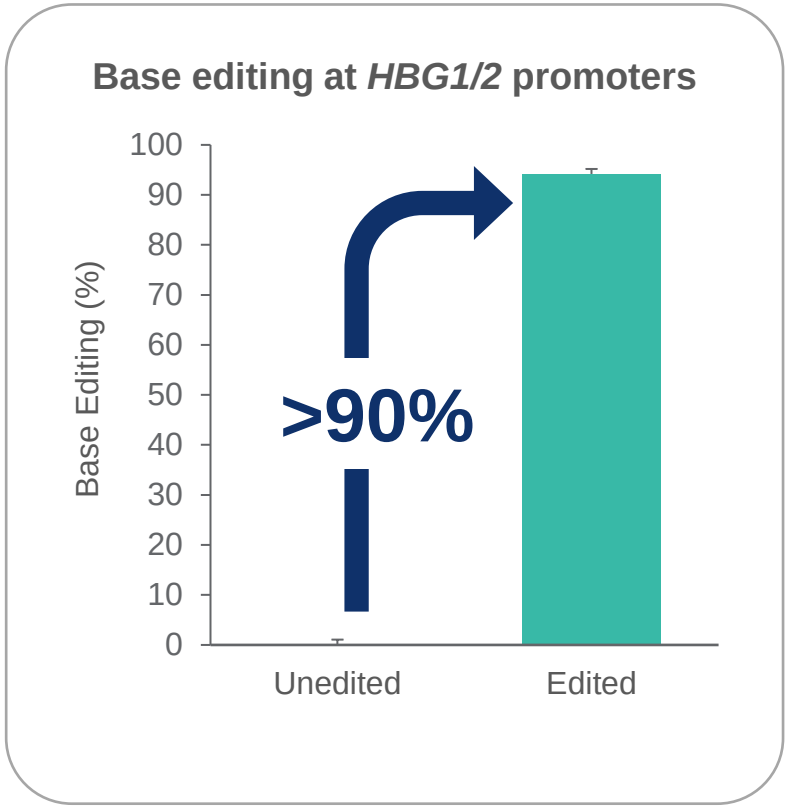
Base editing

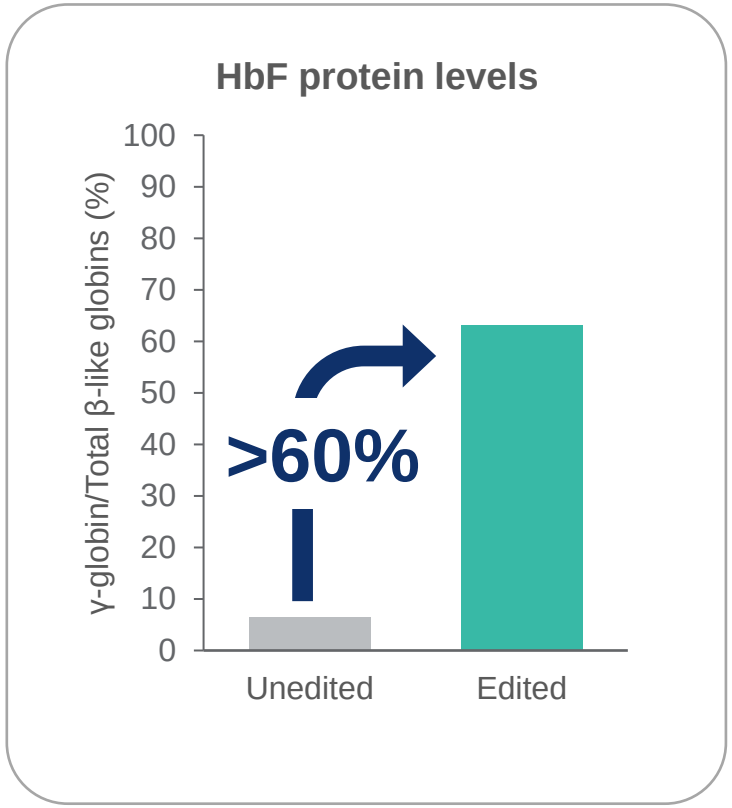
>60% HbF (anti-sickling)

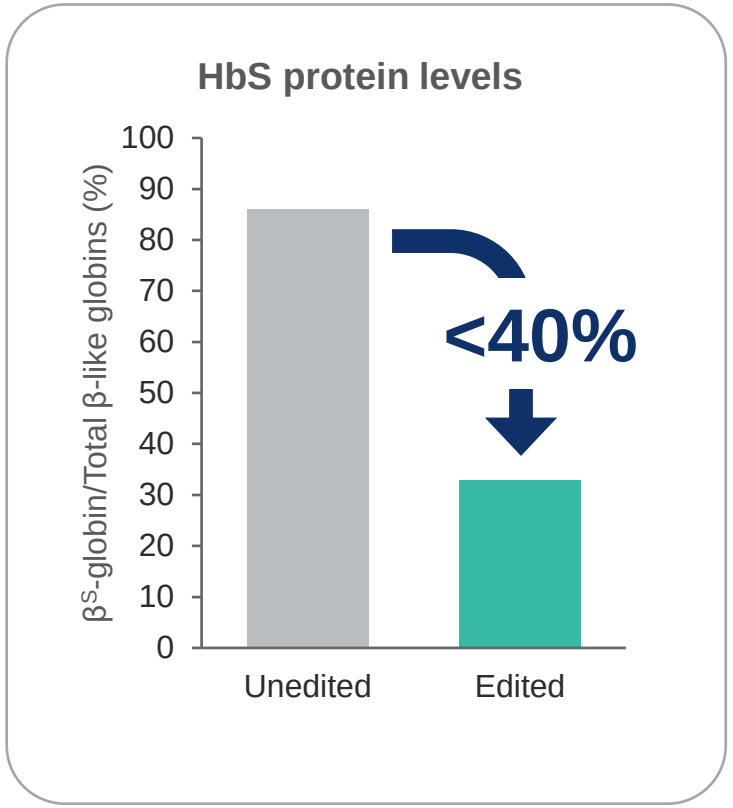
<40% HbS

Minimize cells expressing only HbS

Preclinical data suggest BEAM-101 has potential for highest HbF induction and lowest residual HbS levels vs. other approaches







Preclinical data presented at ASGCT 2020

Precise, single-base editing without need for double-stranded breaks or viral insertion results in highest editing efficiency in preclinical models

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

BEAM-101 Phase 1/2 Clinical Data

2024 ASH ANNUAL MEETING – ORAL PRESENTATION

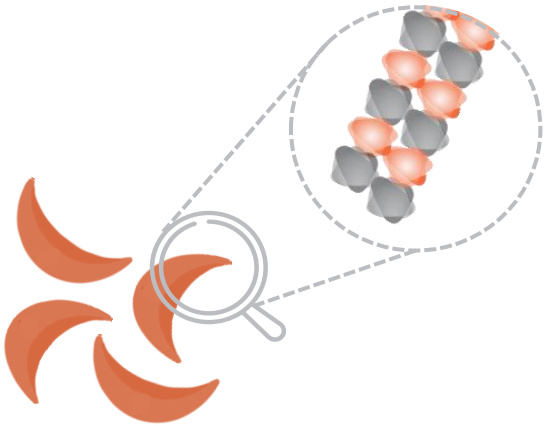
Beam THERAPEUTICS

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

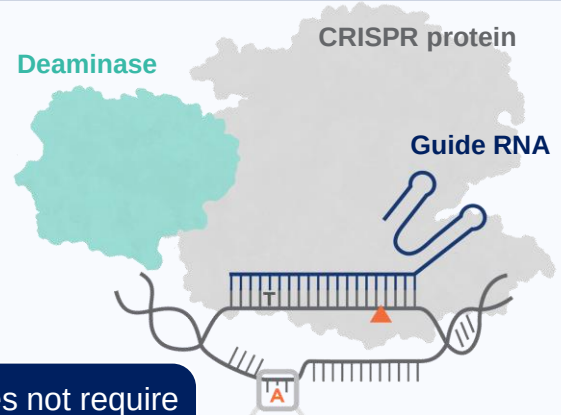
Sickle cell disease[1,2]

HbS ↓ ↑ HbF

Increased HbS leading to sickled cells

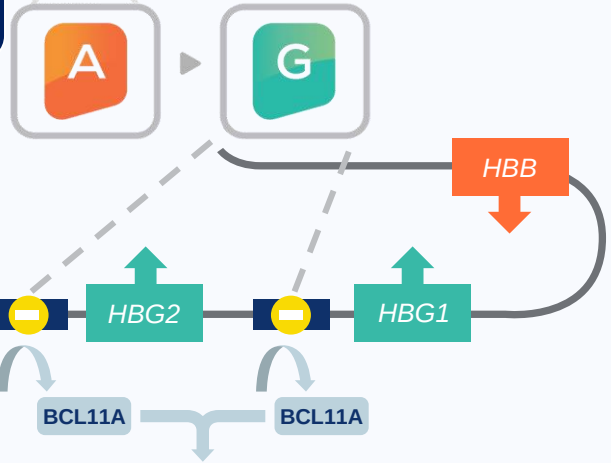


Base editing with BEAM-101[3,4]



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

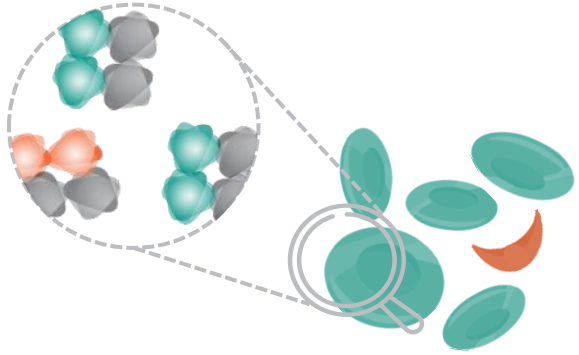
Does not require double-stranded breaks



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

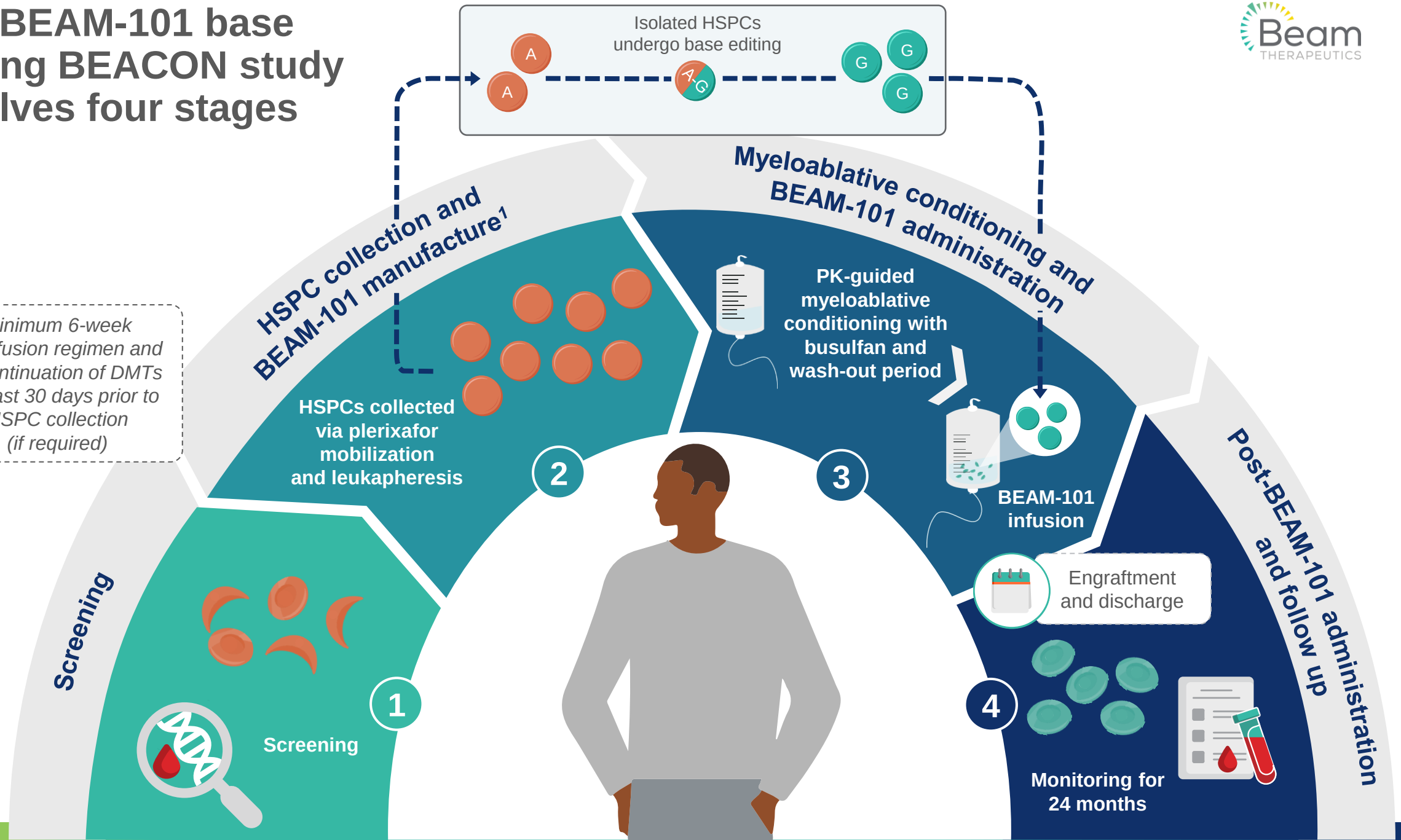
- Proportion of patients with successful neutrophil engraftment
- Time to neutrophil engraftment
- Time to platelet engraftment

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

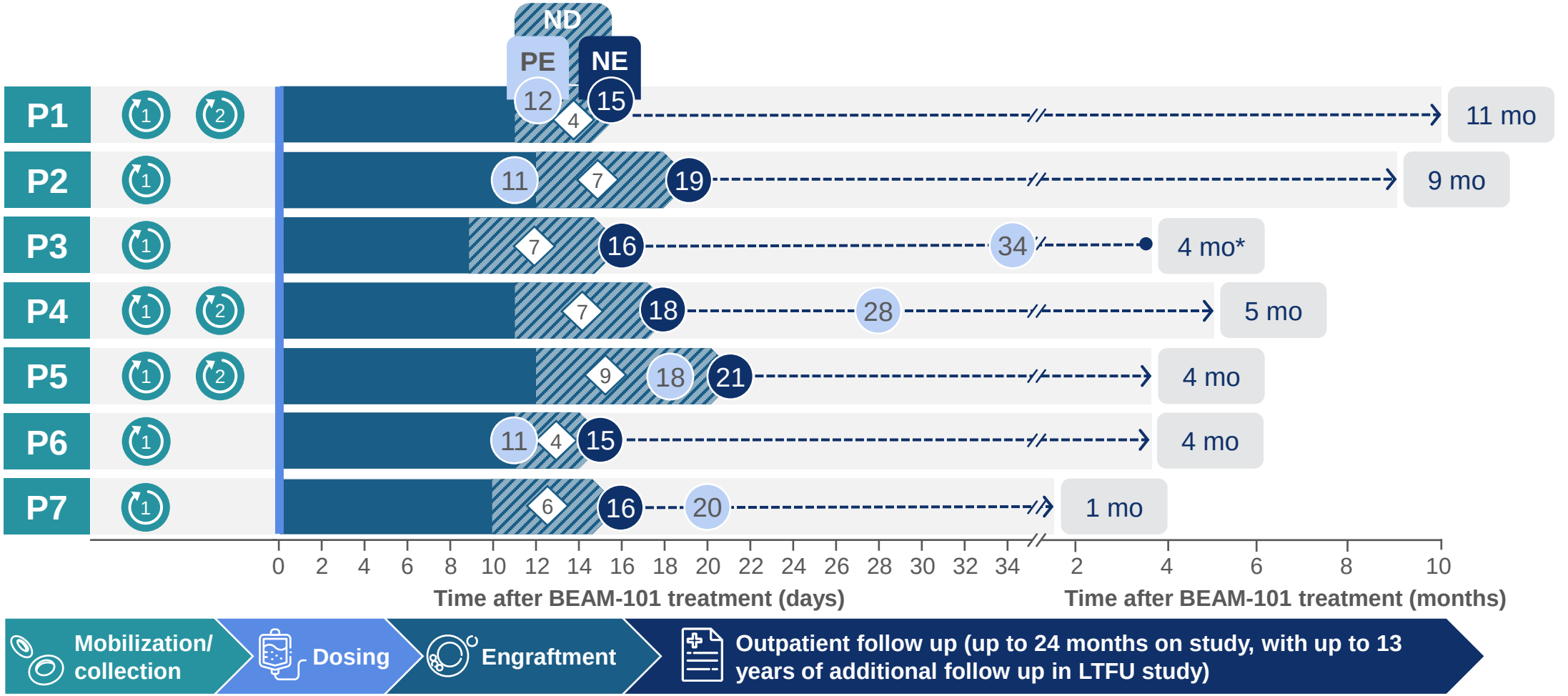
BEAM-101 treatment and engraftment characteristics

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 ($\times 10^6$ 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*)
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

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

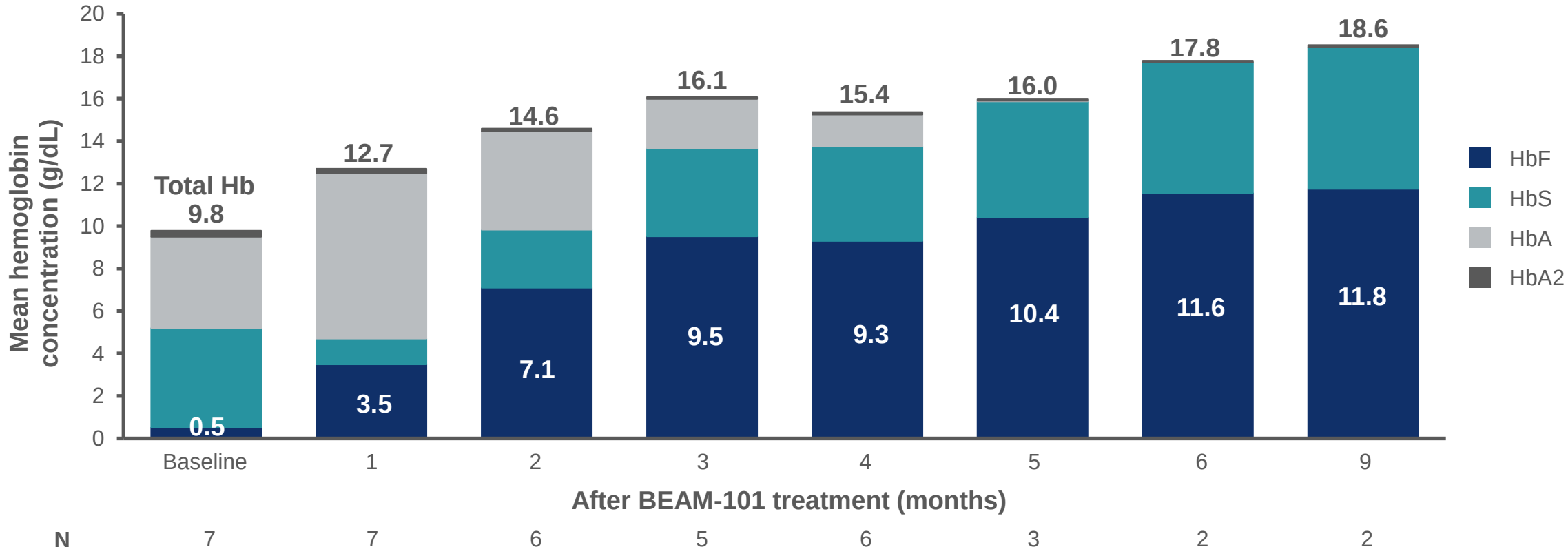
P3 medical history	• Female / 21 yrs / β^S/β^S with history of SCD with ACS, severe VOCs, obstructive sleep apnea, and e-cigarette use
Conditioning and dosing	• Conditioned with busulfan dose of 0.8 mg/kg Q6H x 4 days, cumulative AUC of 74.2 µg•h/mL • Busulfan dose and AUC within protocol target • Cell 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



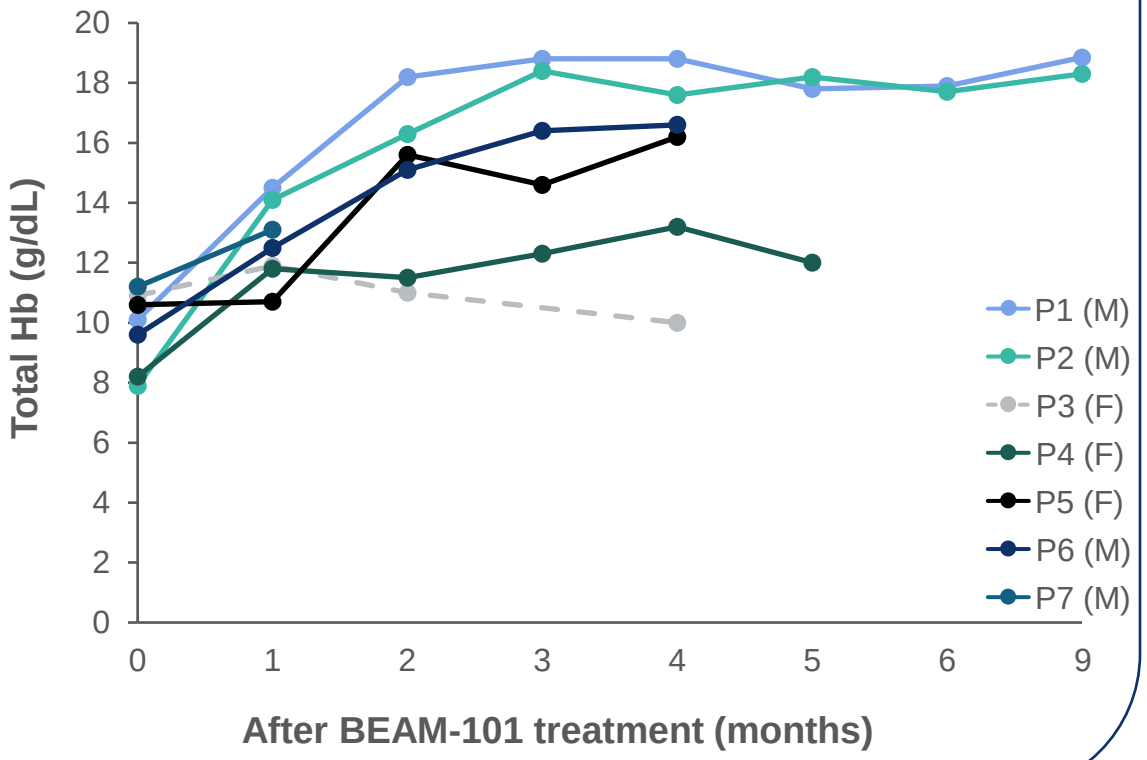
N	7	7	6	5	6	3	2	2
%HbF (HbF/HbF+HbS)	10%	74%	72%	70%	67%	65%	65%	64%

Data cutoff Oct 28, 2024

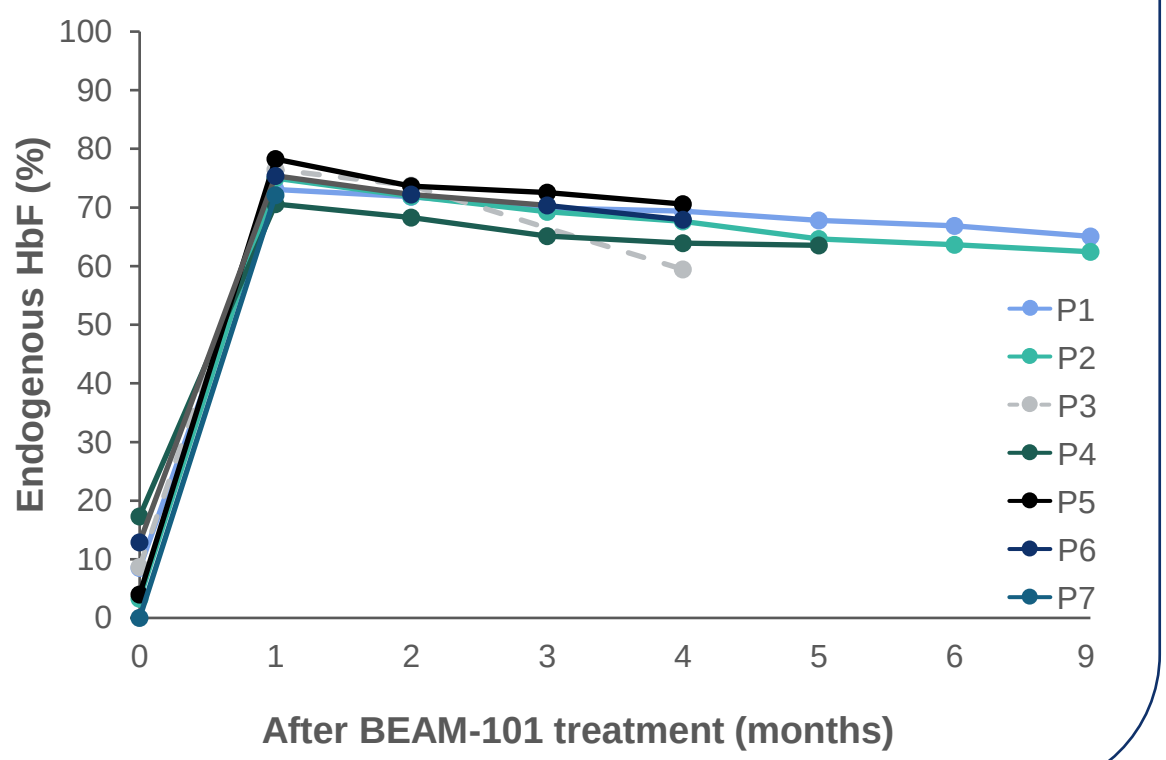
Female total Hb LLN-ULN: 11.5-15 g/dL; Male LLN-ULN: 13-17 g/dL. Hb, hemoglobin; HbA, adult hemoglobin; HbF, fetal hemoglobin; HbS, sickle hemoglobin; LLN, lower limit of normal; ULN, upper limit of normal

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



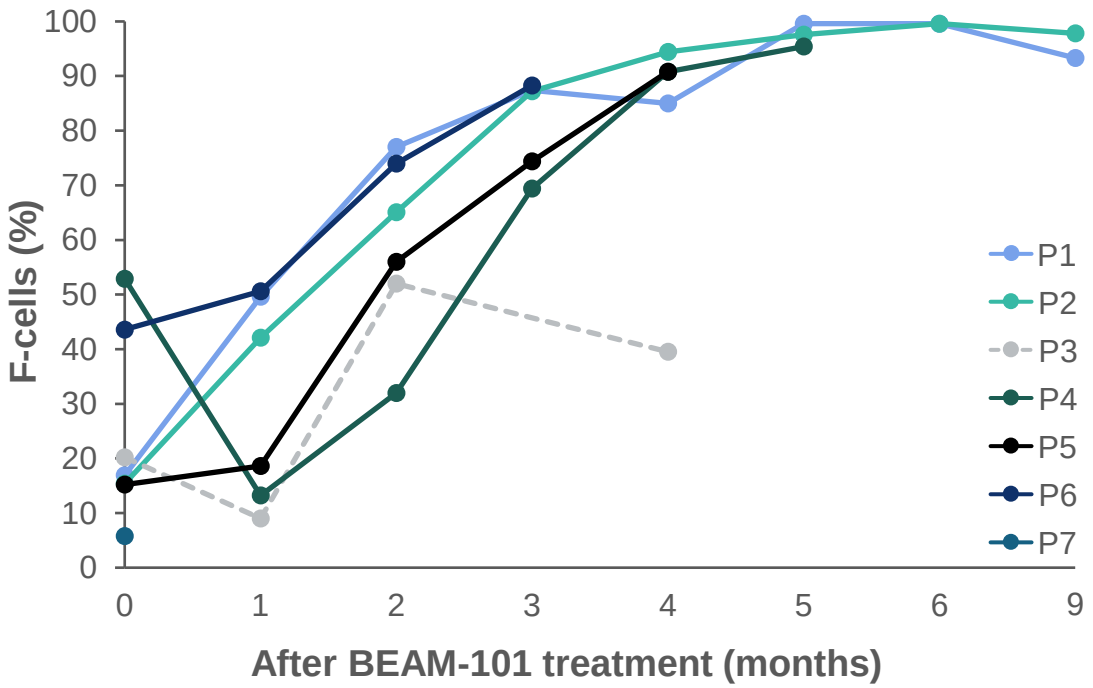
Rapid and robust increase in % endogenous HbF that remained >60% through follow up



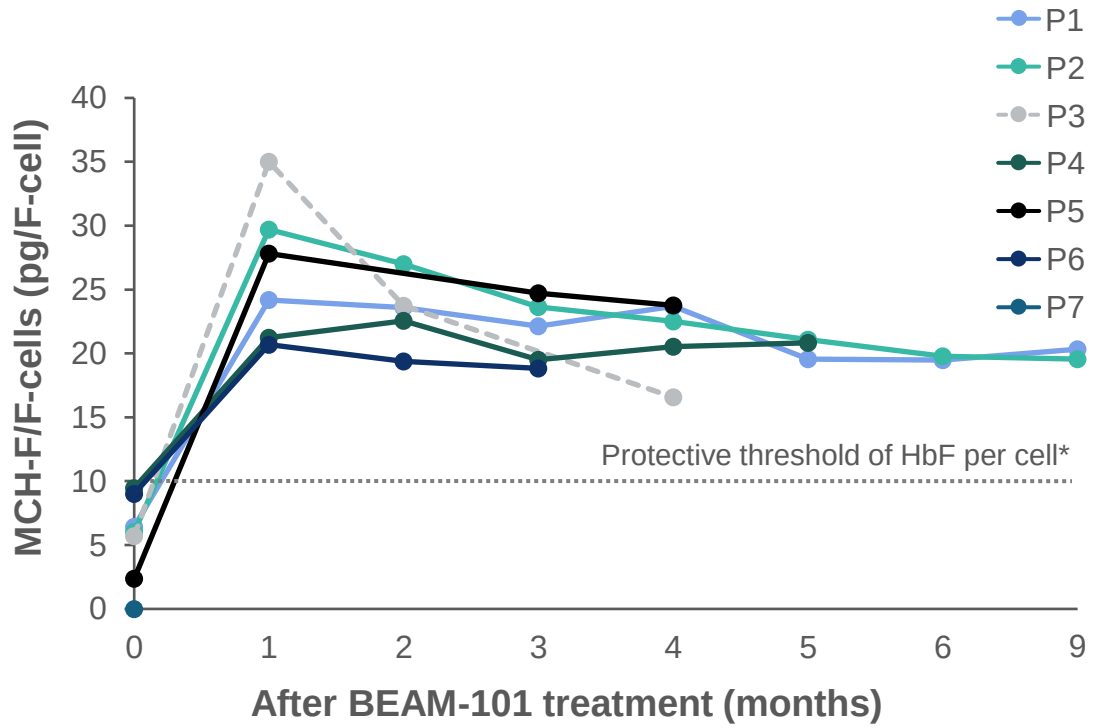
Data cutoff Oct 28, 2024
Female total Hb LLN-ULN: 11.5-15 g/dL; Male LLN-ULN: 13-17 g/dL
Hb, hemoglobin; HbF, fetal hemoglobin; F, female; M, male

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



Data cutoff Oct 28, 2024

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

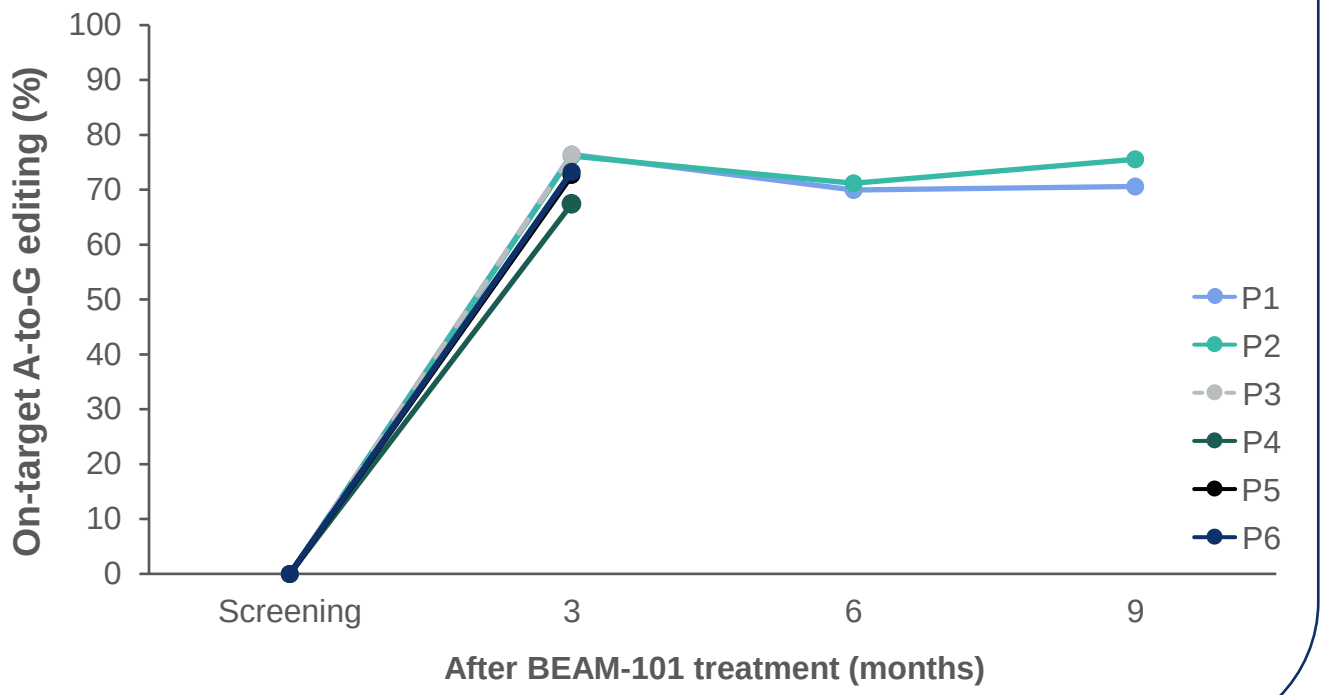
F-cell, HbF-containing cell; HbF, fetal hemoglobin; HbS, sickle hemoglobin; M, month; MCH, mean corpuscular hemoglobin; P, patient

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

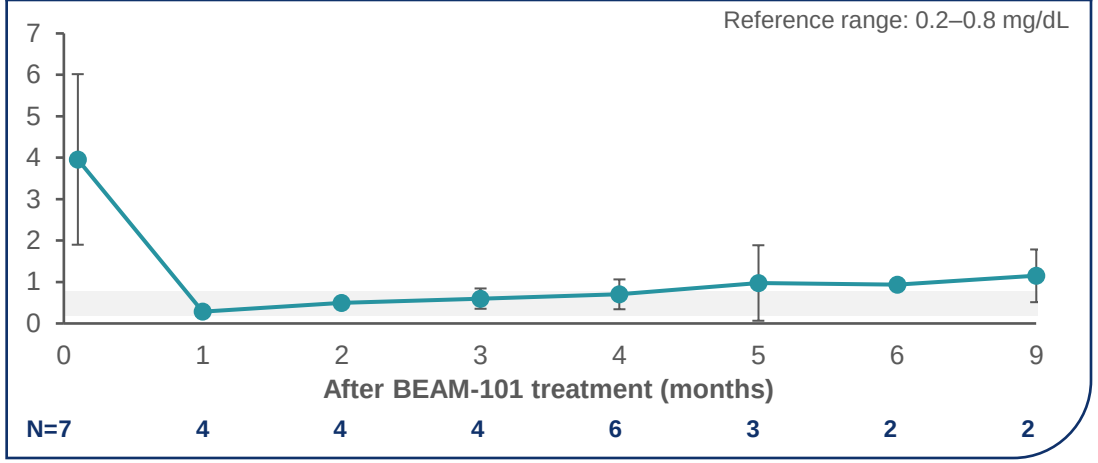
Early data show consistent high levels of persistent editing in peripheral blood after BEAM-101 treatment



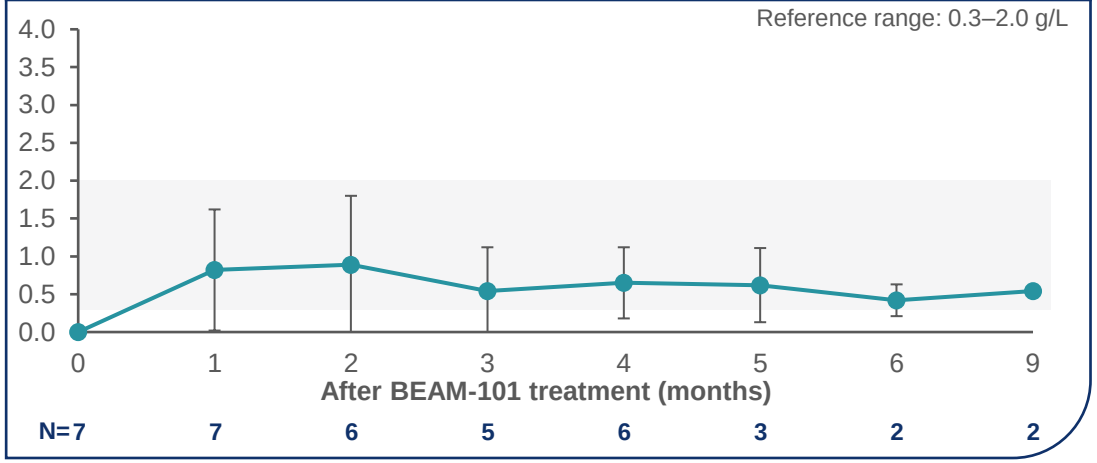
Data cutoff Oct 28, 2024
Percent of target bases that undergo A-to-G edit; Percent of editing from the drug product release is measured at day 14 of in vitro erythroid differentiation by NGS
NGS, next-generation sequencing; P, patient

Hemolysis markers normalized or improved following BEAM-101 treatment

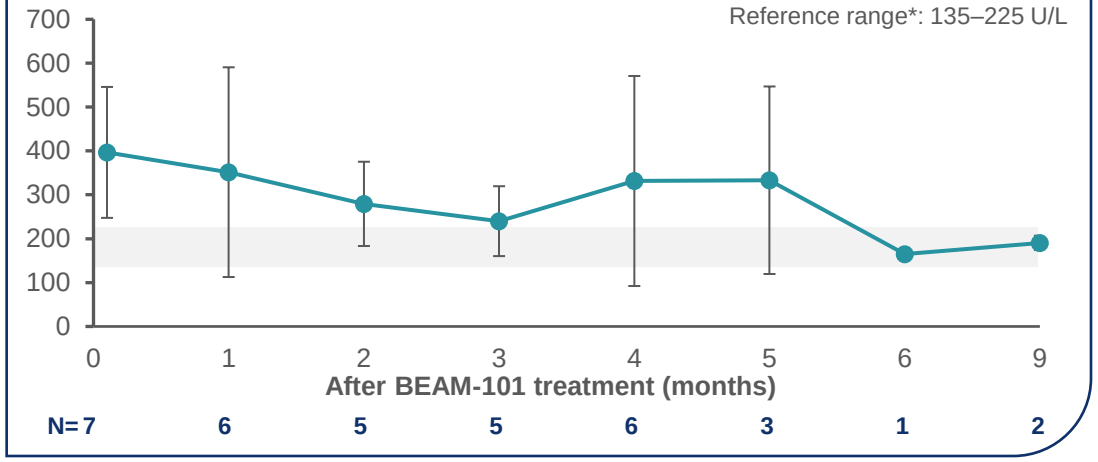
Indirect bilirubin (mg/dL ± SD)



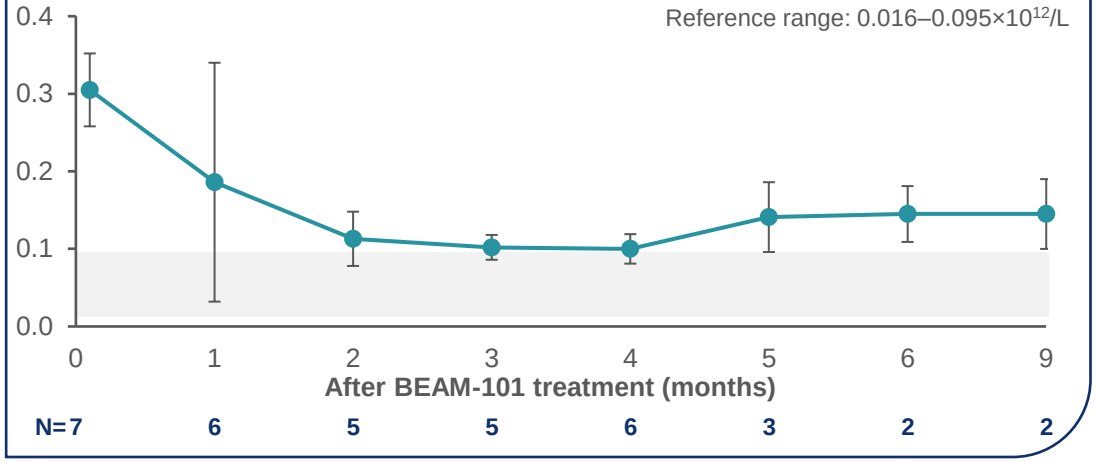
Haptoglobin (g/L ± SD)



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

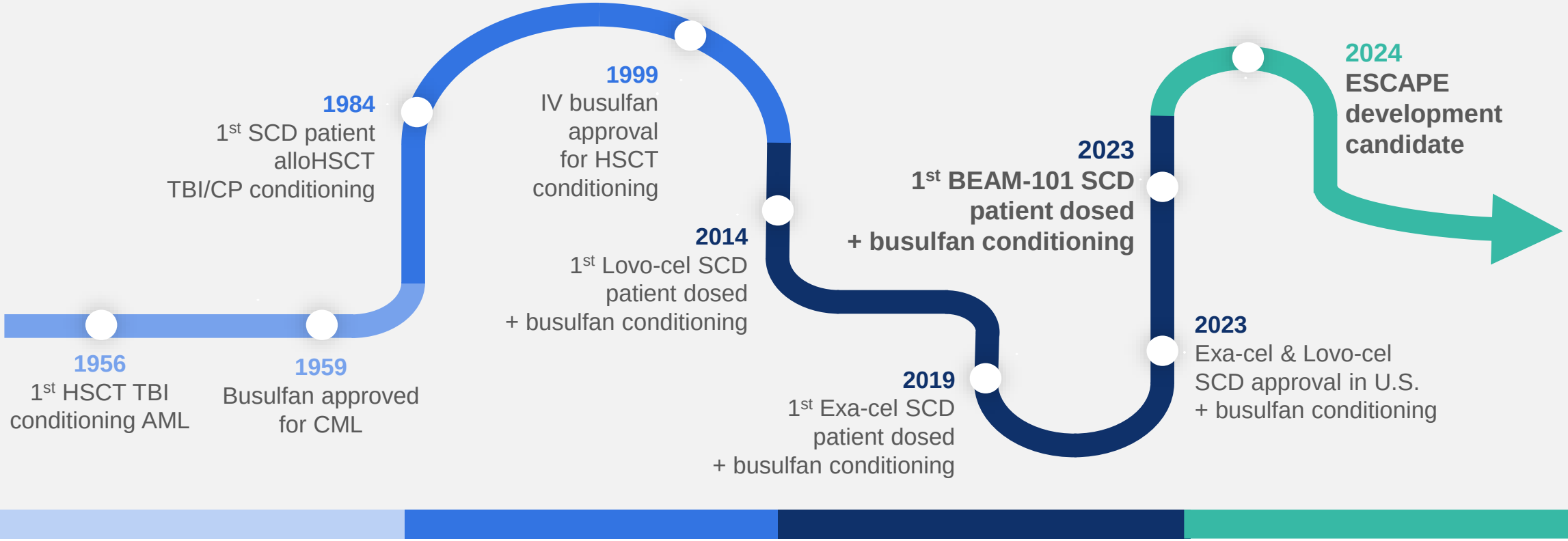
HbF, fetal hemoglobin; HbS, sickle hemoglobin; HSCT, hematopoietic stem-cell transplantation; SCD, sickle cell disease; VOC, vaso-occlusive crisis

ESCAPE Program

2024 ASH ANNUAL MEETING – ORAL PRESENTATION

Beam THERAPEUTICS

ESCAPE technology designed to bring a paradigm shift to 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

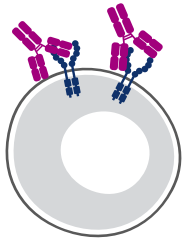
- Prevent acute and chronic toxicities
- Preserve fertility
- Potential to be outpatient

ESCAPE technology designed for selective depletion of diseased cells to enable non-genotoxic conditioning

ESCAPE technology for hemoglobinopathies is comprised of two components:

BEAM-103

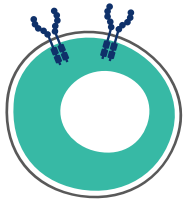
Anti-CD117 conditioning monoclonal antibody (mAb), which binds to the specific epitope edited by ESCAPE



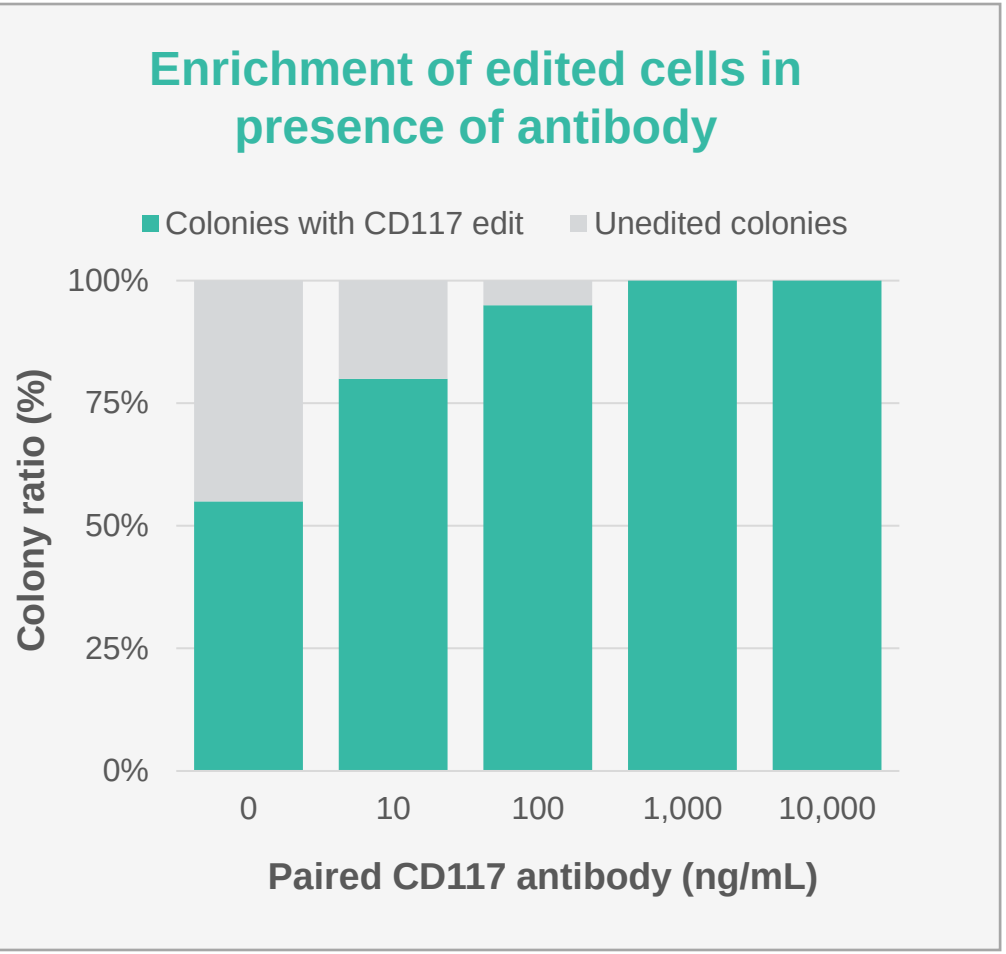
Old diseased cells are suppressed and eliminated by BEAM-103, creating space for the graft

BEAM-104

Engineered CD34 cell product with a therapeutic edit (the same as in BEAM-101) plus an edit to CD117, which prevents binding of BEAM-103



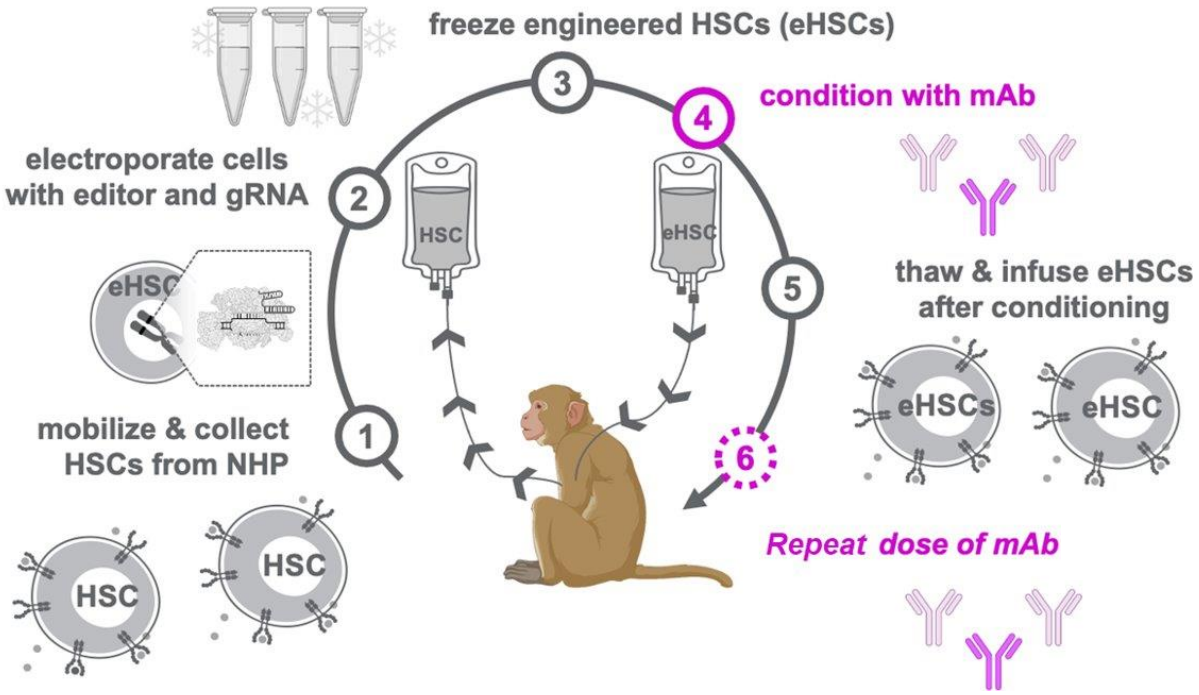
New edited cells “escape” binding by BEAM-103 and expand, leading to engraftment



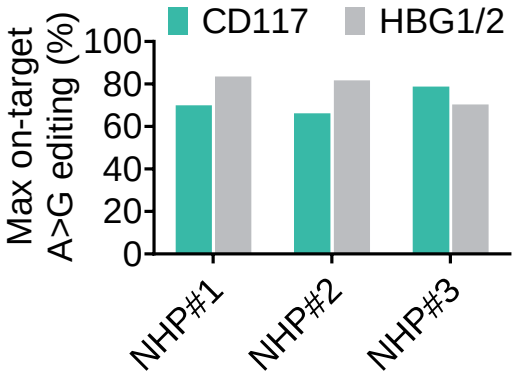
Data presented at FASEB 2022

NHP autologous transplant model for our ESCAPE conditioning approach

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

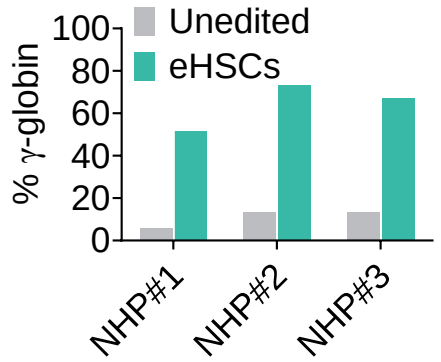


Multiplex editing in Rhesus HSPCs



Next generation sequencing

Potential for therapeutic levels of HBF upon multiplex editing



In vitro erythroid differentiation

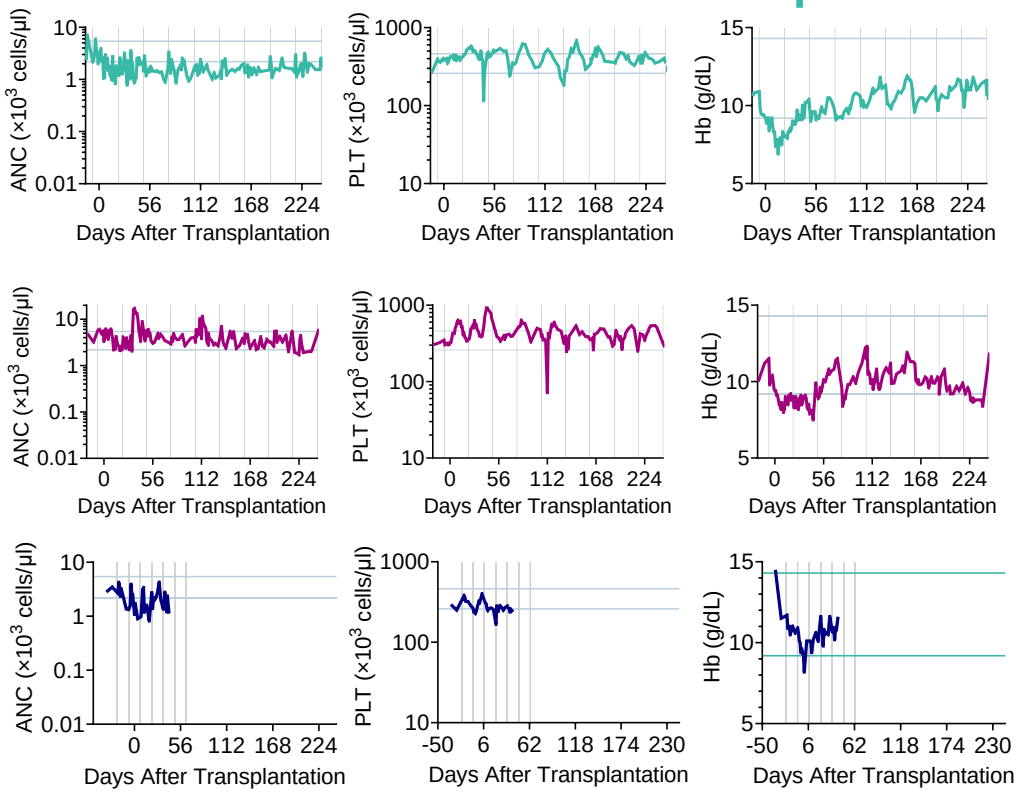
Infusion product was manufactured with priority for maximizing total CD34+ cell dose for transplant

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

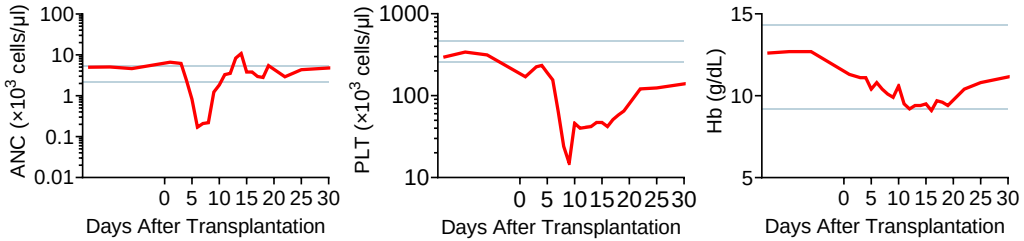
- In contrast with busulfan conditioning, NHPs dosed with mAb demonstrated only minor dips in neutrophil counts
- Although platelet counts dropped after each mAb dose, levels recovered quickly
- Minor drops in hemoglobin upon mAb dosing recovered post-transplant
- **The ESCAPE transplant strategy presented 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

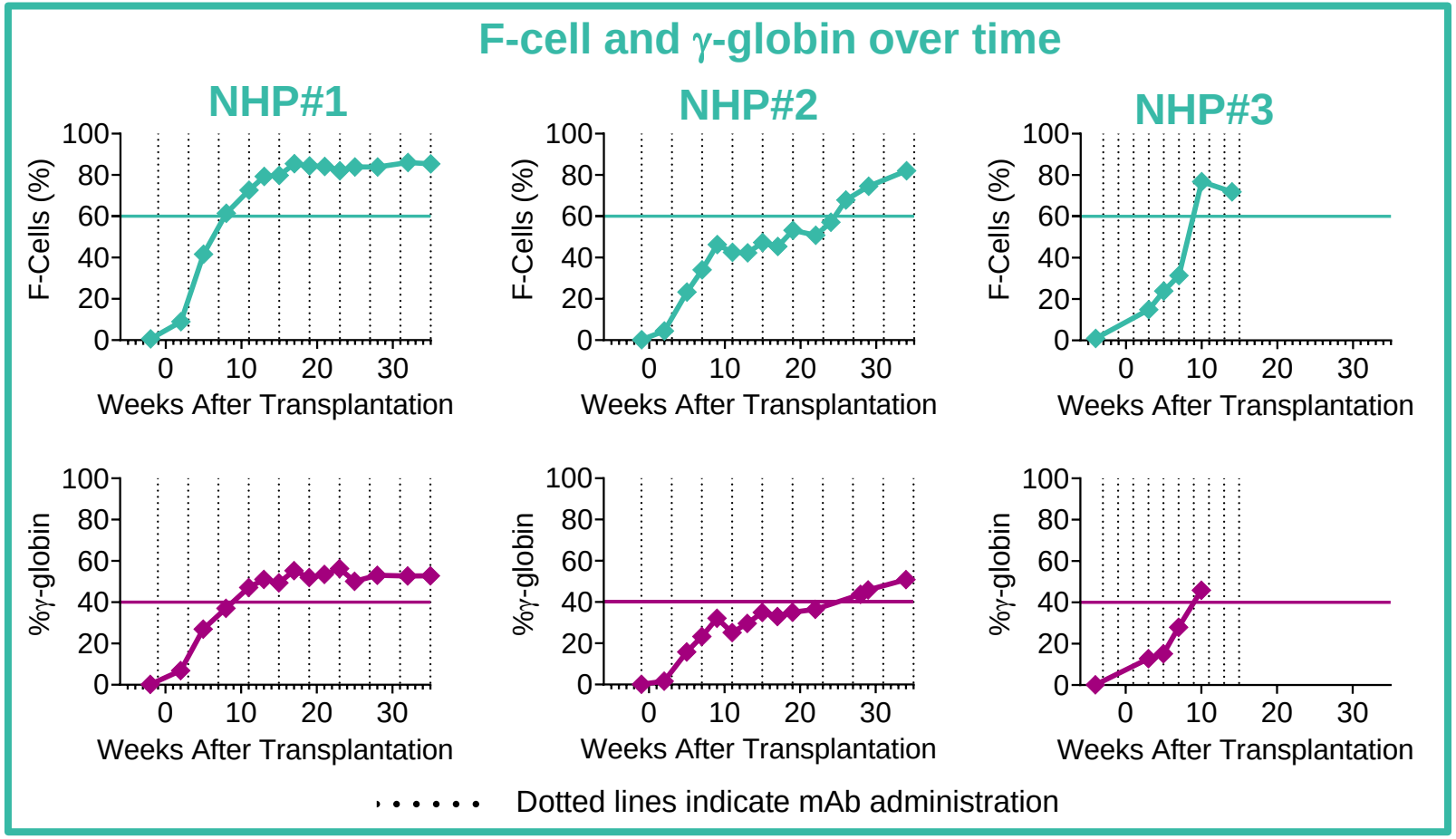
BEAM-103 conditioned transplants



Historical busulfan conditioned transplant



NHPs dosed with mAb demonstrated rapid turnover of unedited erythroid cells and early induction of therapeutic g-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% g-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

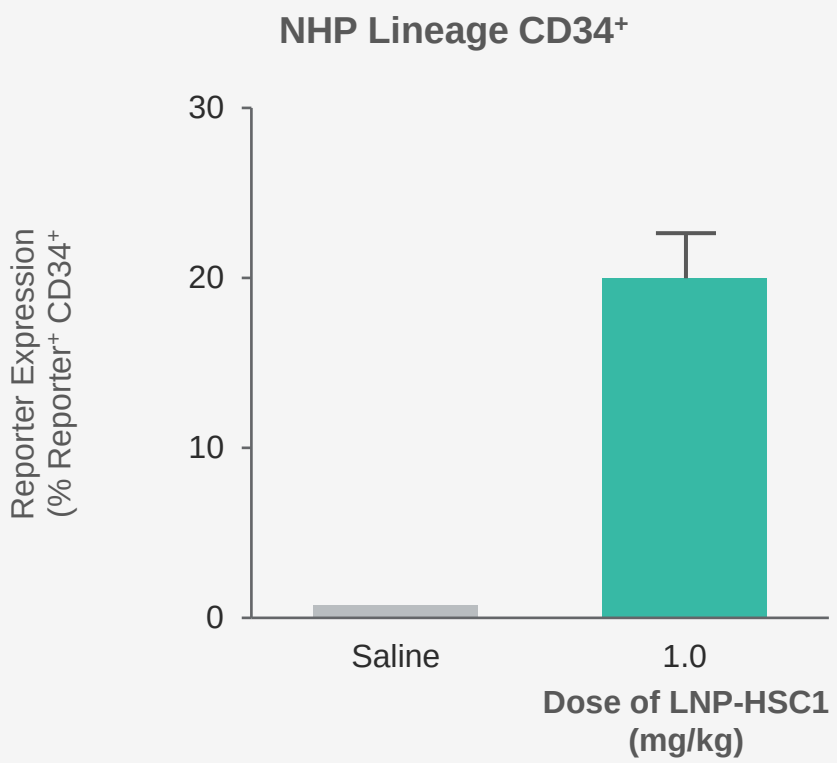
4

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

Wave 3 *in vivo*: Developing LNPs for delivery of base editors to blood stem cells

- In preclinical studies, Beam LNP technology allowed targeting of blood stem cells for delivery of mRNA payloads at clinically relevant doses
- Research to adapt system to base editing payloads is ongoing
- Ultimate goal: deliver curative base editing machinery directly to HSCs with an intravenous transfusion

Expression of mRNA payload in NHP HSCs at clinically relevant doses



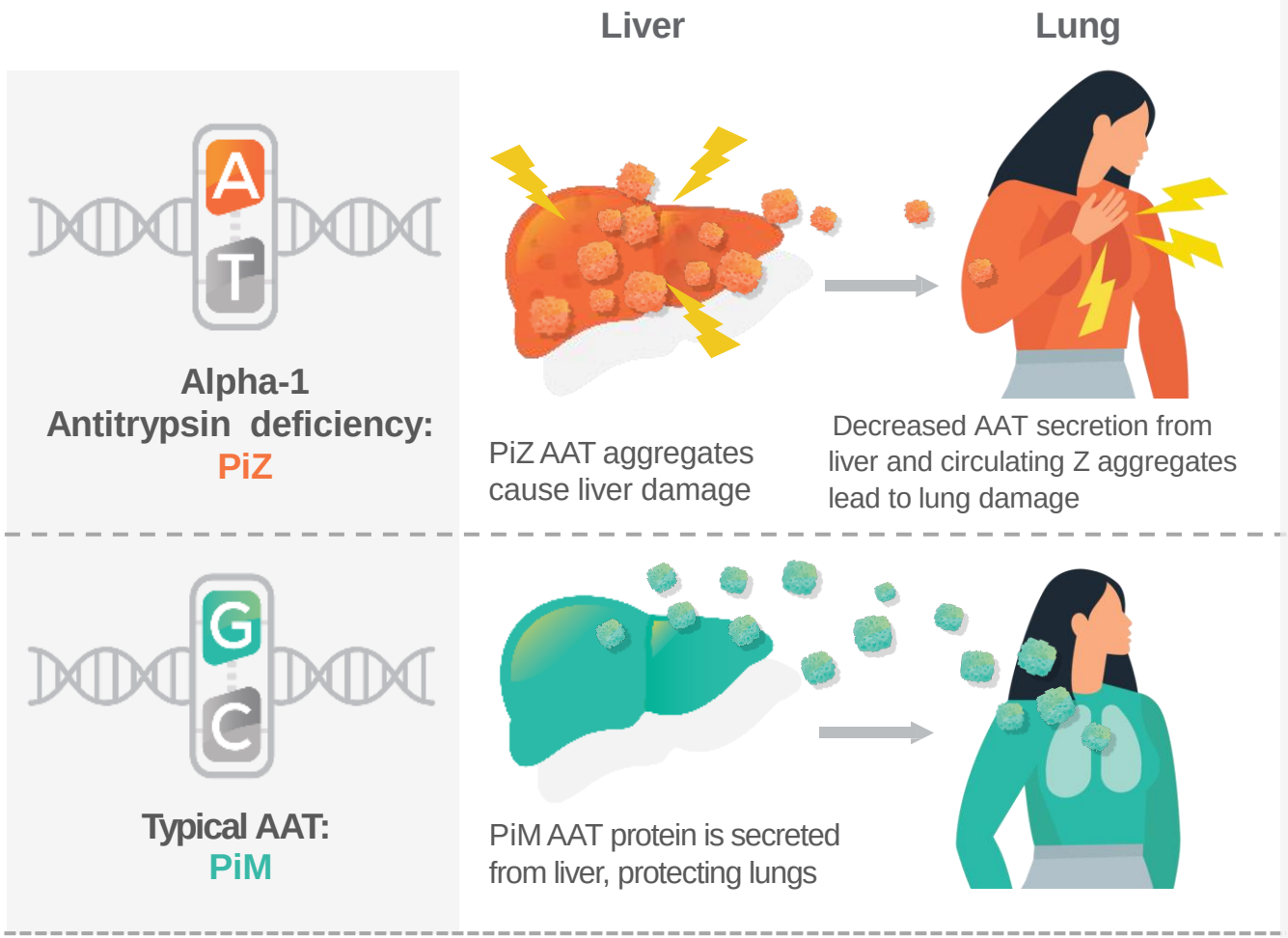
Presented at ASH 2021

What if we could use base editing to correct disease-causing mutations *in vivo?*

GENETIC DISEASES

Beam THERAPEUTICS

BEAM-302: Aims to restore expression of functional AAT to address Alpha-1-related lung and liver disease



Alpha-1 Cause

- PiZ is caused by a single G > A point mutation in the *SERPINA1* gene
- PiZ AAT is poorly secreted by the liver into circulation and has decreased function

Alpha-1 Unmet Need

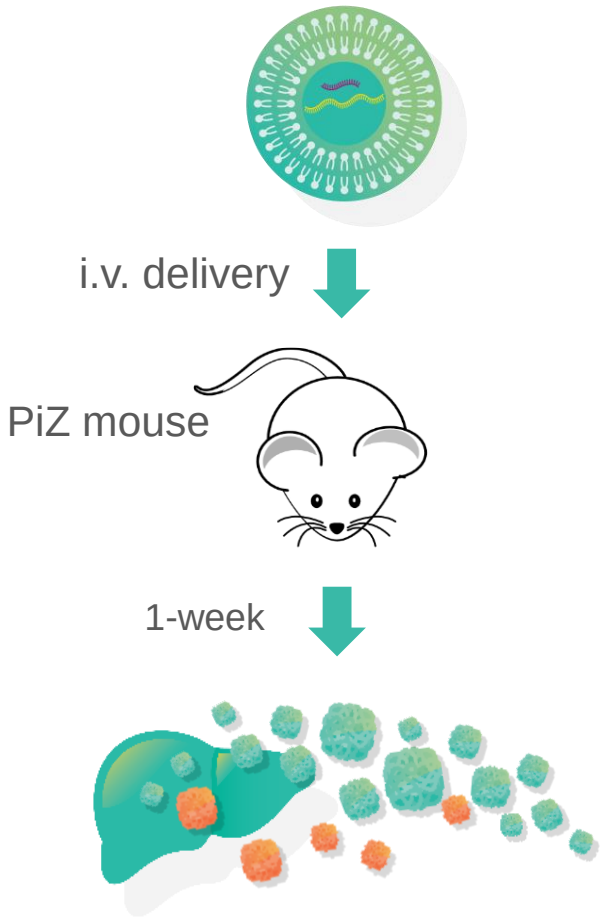
- PiZZ genotype is >95% of severe AATD population that typically develop progressive lung and/or liver disease
- 100,000 PiZZ individuals in U.S.; ~10% diagnosed

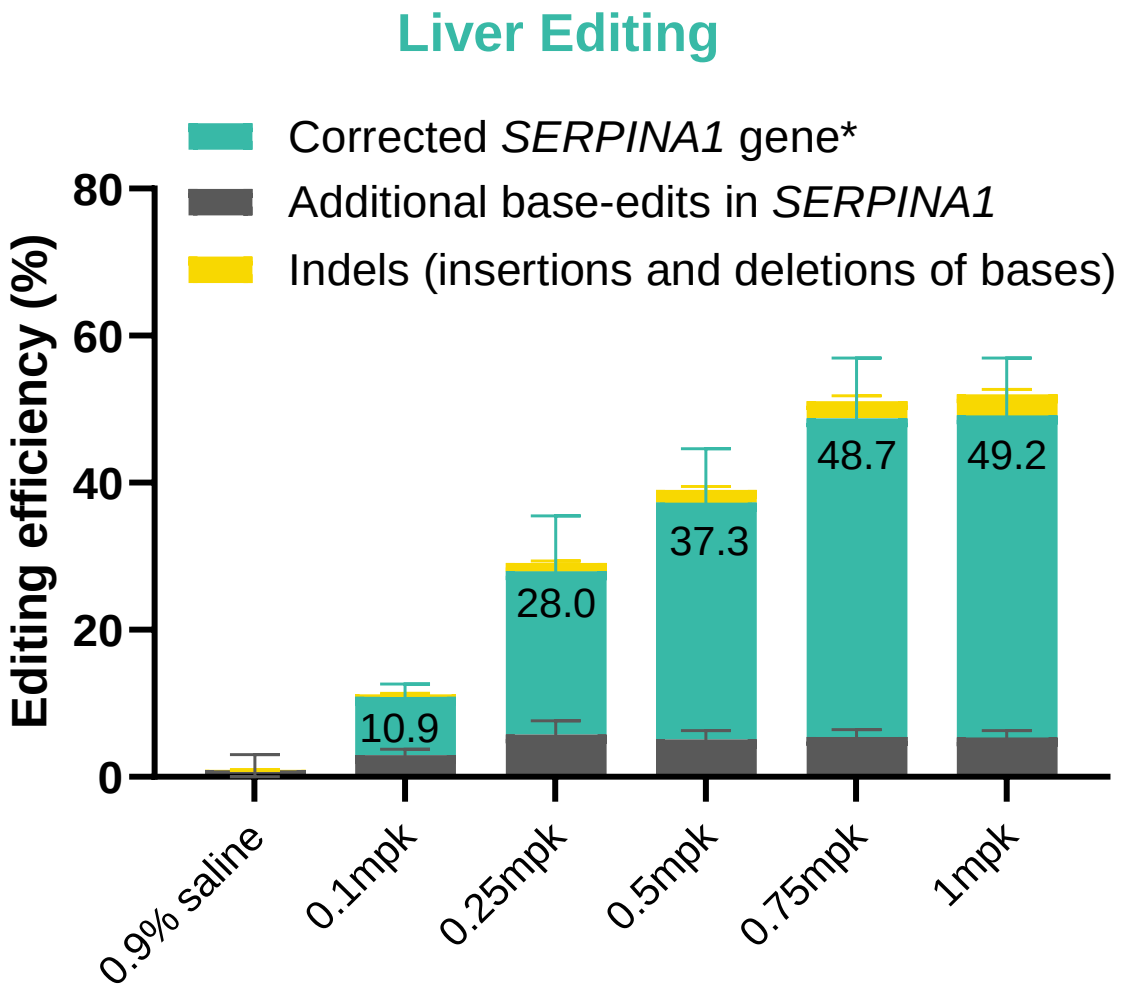
BEAM-302 Potential

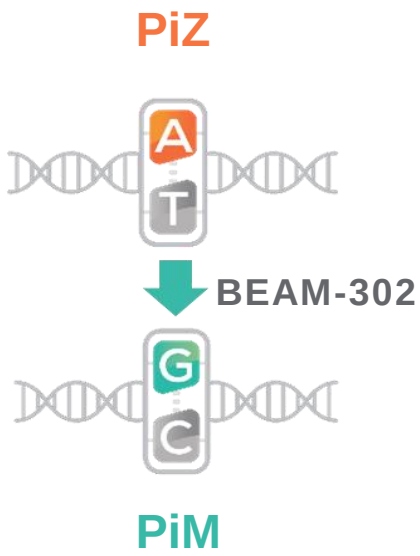
- One-time therapy that addresses both lung and liver disease, with corrected gene under normal regulation
- Reduction of PiZ AAT in liver and bloodstream, and restored circulating functional AAT

American Thoracic Society/European Respiratory Society statement: standards for the diagnosis and management of individuals with alpha-1 antitrypsin deficiency Am J Respir Crit Care Med, 2003

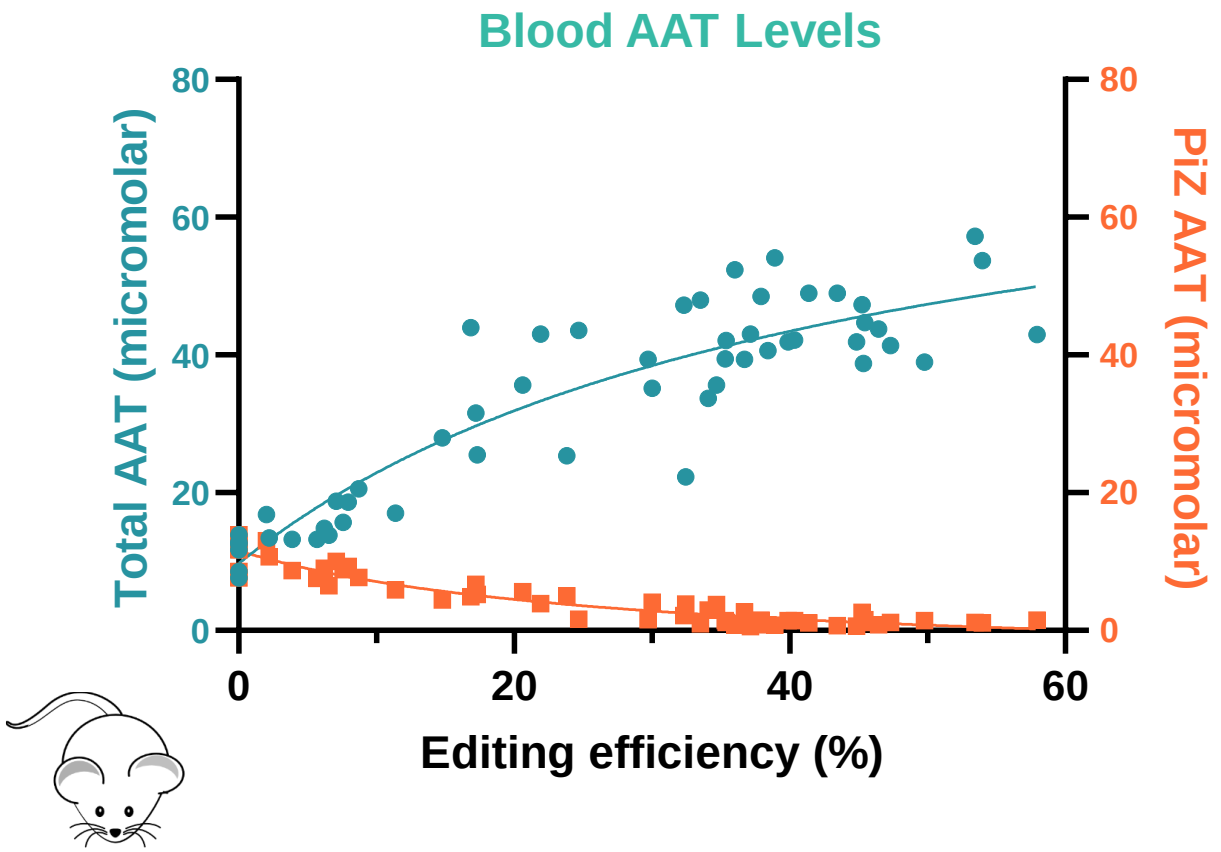
BEAM-302: BEAM-302 corrected the PiZ variant to PiM in a dose dependent manner in an Alpha-1 mouse model

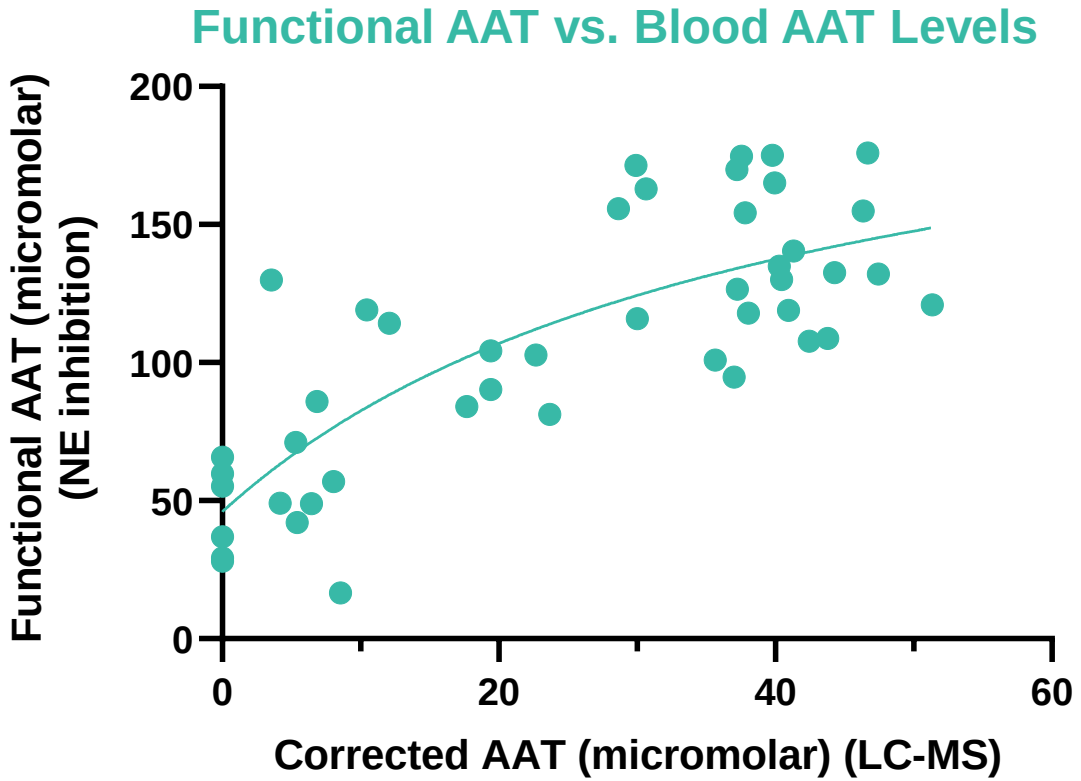




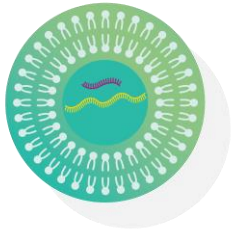


BEAM-302: Editing decreased Z-AAT and increased total blood AAT protein, which correlated to increased functional AAT





BEAM-302: BEAM-302 correction of the PiZ variant also addressed liver disease in an Alpha-1 mouse model



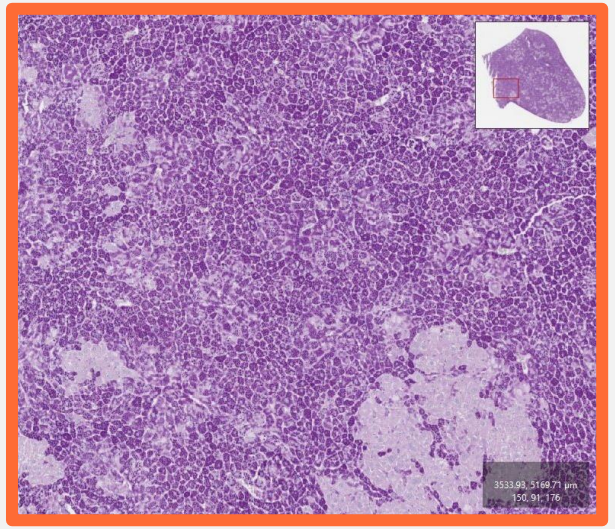
i.v. delivery

PiZ Mouse

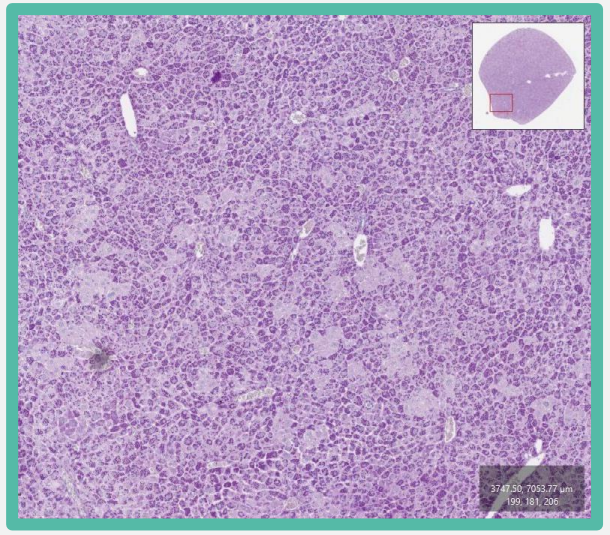
1-week

Stain for abnormal Z aggregates

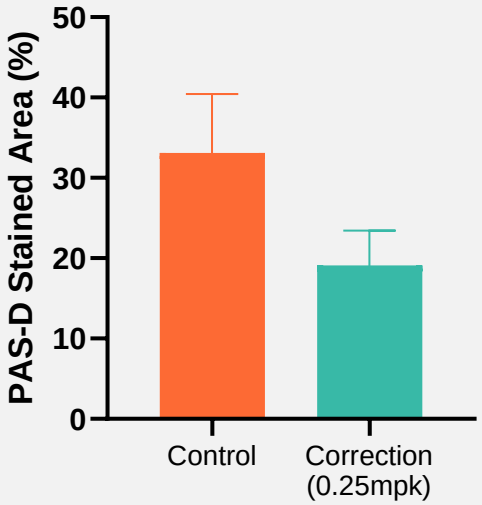
Day 7
No Beam-302
("Control")



Day 7
BEAM-302
("Correction")

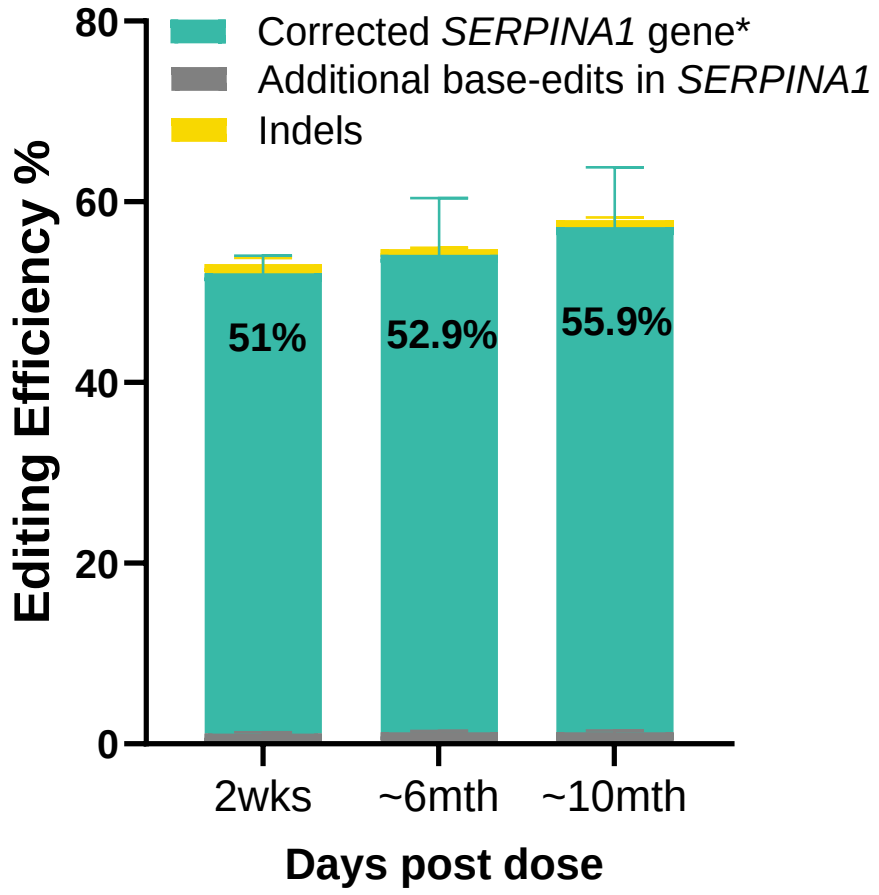


Reduction in toxic liver aggregates



BEAM-302: Single dose of BEAM-302 led to durable correction of the PiZ variant in AATD mouse model

Liver editing



***SERPINA1* gene editing and AAT levels were either stable or increasing after a single dose**

- **Gene editing and AAT levels remained stable** in rats as of 10 months
- **Gene editing remained stable** in mice as of 8 months
- **Gene editing increased** in mice as of 3 months, suggesting potential improved survival of corrected liver cells

Long term studies were performed with precursor research grade reagents (1.5mpk)

BEAM-302: Phase 1/2 trial designed to achieve clinical proof-of-concept in patients across the spectrum of AATD

Part A: AATD-associated Lung Disease

Dose Exploration → Dose Expansion

- Up to 4 dose cohorts
- Patients excluded with liver disease

Part B: AATD-associated Lung and/or Liver Disease

Dose Exploration → Dose Expansion

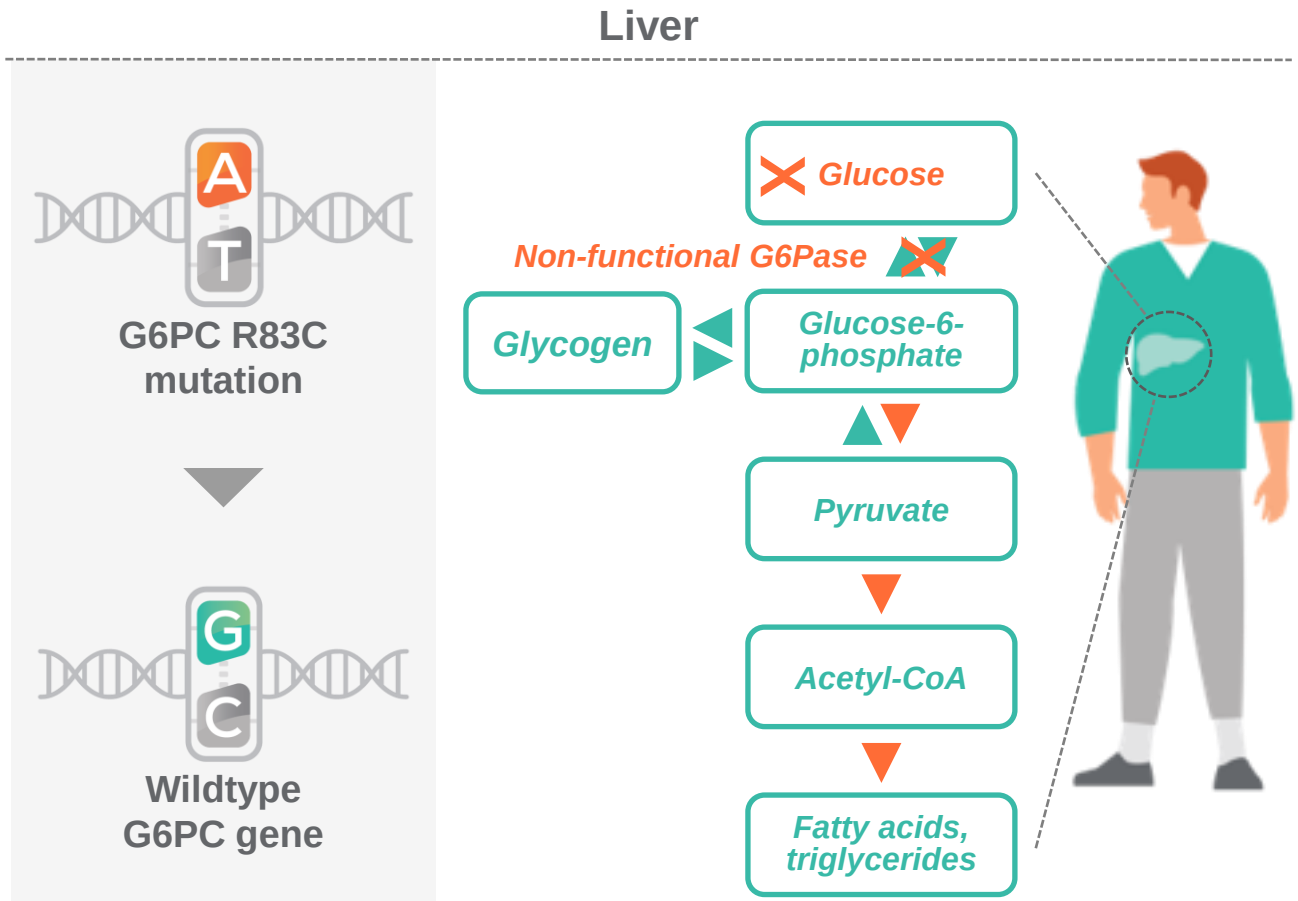
- Up to 4 dose cohorts
- Patients included with mild to moderate liver disease

Assess early safety and efficacy and identify optimal dose for pivotal study

- Opportunity to achieve first ever clinical proof-of-concept of *in vivo* base editing leading to correction of a disease-causal mutation
- Global site activation ongoing
- Dosing of first cohort complete

Anticipate reporting initial clinical data for multiple cohorts from Phase 1/2 trial in 1H2025

BEAM-301: Aims to normalize glycogen metabolism in patients with GSD1a to prevent hypoglycemia and other disease manifestations



Unmet Need in GSD1a Patients with Severe R83C Mutation:

- Inability to convert glycogen back to glucose to sustain blood sugar while fasting
- Patients at constant risk of hypoglycemia that can result in seizures, coma or death
- Estimated ~300 R83C patients in U.S. based on updated epidemiology

Current Standard of Care:

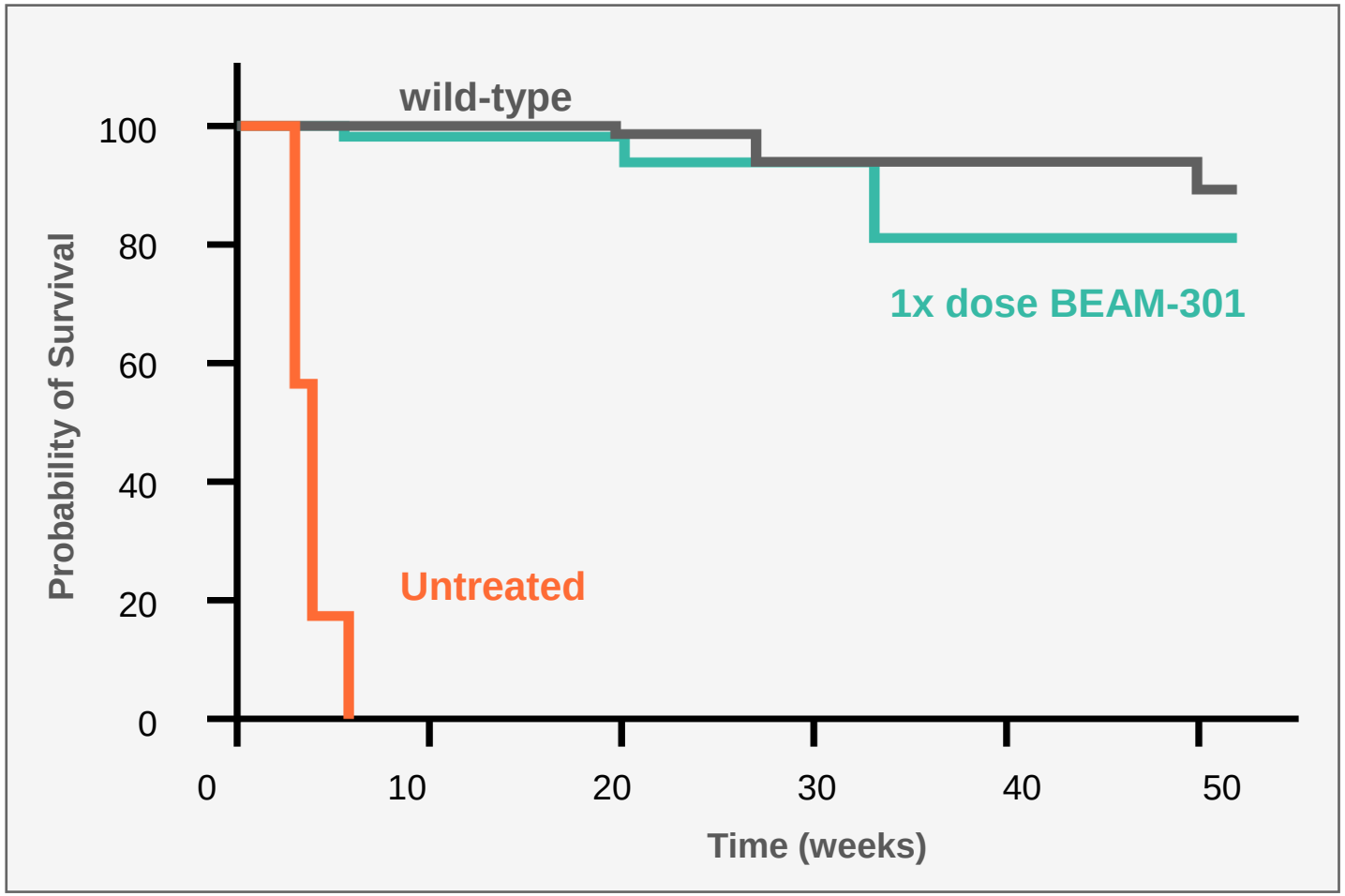
- Liquid cornstarch supplementation every 2-4 hours, even throughout the night

BEAM-301 Potential:

- Correct liver G6PC mutation to restore enzyme activity and enable normal glucose homeostasis, as well as eliminate chronic cornstarch supplementation
- Animal studies suggest ~11% enzyme activity sufficient for restoring fasting glucose and metabolic profile

Chou & Mansfield. 2007. Curr. Gen. Ther.; Internal Beam estimates

BEAM-301: Treatment with a single dose significantly improved long-term survival in GSD1a mouse model



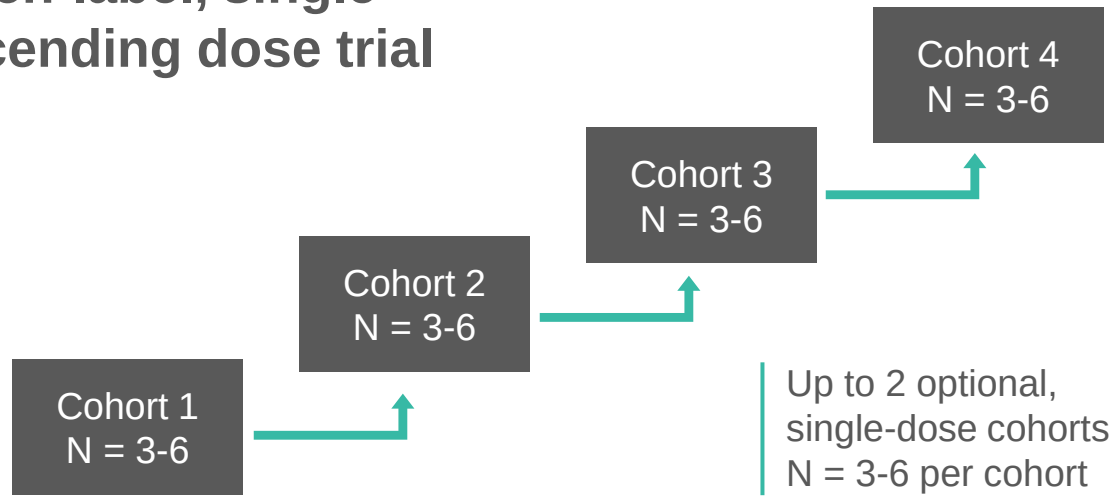
- Preclinical studies of BEAM-301 demonstrated a single dose **significantly improved long-term survival out to a year** in humanized R83C homozygous mice
- Untreated homozygous R83C mice die within weeks of birth

BEAM-301: Phase 1/2 trial in GSD1a patients with R83C mutation

- Given its rare nature and geographic distribution of patients, Beam will initially focus development of BEAM-301 in the U.S.
- U.S. IND application cleared in July 2024
- Beam initiating site activation activities for Phase 1/2 study

PHASE 1/2

Open-label, single-ascending dose trial



KEY ENDPOINTS

- Safety and tolerability
- Time to hypoglycemia during fasting
- Changes from baseline in starch supplementation

Patient dosing in the Phase 1/2 study expected to commence in early 2025

Creative pipeline and platform partnerships unlock additional value and broaden therapeutic impact

Strategic Deals

resulting in $675M upfront and more than $1B in potential milestones

Pfizer

- $300M upfront for 3 base editing targets
- Beam option at end of Phase 1/2 for 35% WW cost/profit split on 1 program

Verve Therapeutics / Lilly

- $250M in upfront/equity plus up to $350M in potential development-stage payments to acquire Beam's cost/profit split options in 3 Verve cardiovascular programs

Apellis

- $75M upfront for base editing for complement-mediated diseases
- Beam option at end of Phase 1 for 50% of U.S. rights on one program

Sana Biotechnology

- $50M upfront for non-exclusive license to Cas12b nuclease for certain engineered cell therapies

Innovator Deals

gaining rights to innovative and complementary technologies

prime medicine

- Prime editing (PE) technology is complementary to base editing
- Beam exclusive PE rights for all A-G and C-T edits plus any edit for SCD

Orbital Therapeutics

- Next-gen RNA and delivery technologies
- Beam equity stake in Orbital plus IP access in gene editing and other fields

Beam THERAPEUTICS

THANK YOU