



Initial Clinical Data for BEAM-302 in Alpha-1 Antitrypsin Deficiency (AATD)

March 10, 2025

Beam conference call participants



TOPIC	PARTICIPANT
Introduction	Holly Manning Vice President, Investor Relations & External Communications
Beam's Vision & Liver Genetic Disease Franchise	John Evans Chief Executive Officer
Alpha-1 Antitrypsin Deficiency & BEAM-302 Overview	Giuseppe Ciaramella, Ph.D. President
Initial BEAM-302 Clinical Data	Amy Simon, M.D. Chief Medical Officer
Closing Remarks	Mr. Evans
Q&A	Mr. Evans, Dr. Simon, Dr. Ciaramella & Sravan Emany, Chief Financial Officer

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; the initiation, design and progress of clinical trials, including trials for BEAM-101, BEAM-103, 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; our cash, cash equivalents and marketable securities as of December 31, 2024 and our expectations related thereto; 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," "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 or continue 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, 2024, 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

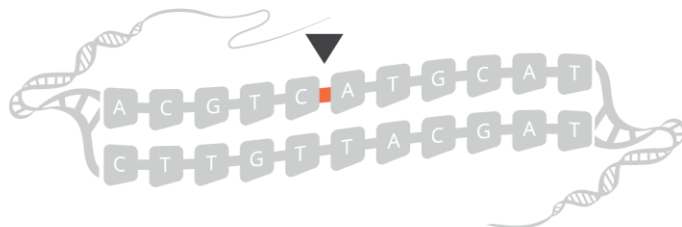


PLATFORM FOR
rapidly programmable
precision medicines

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



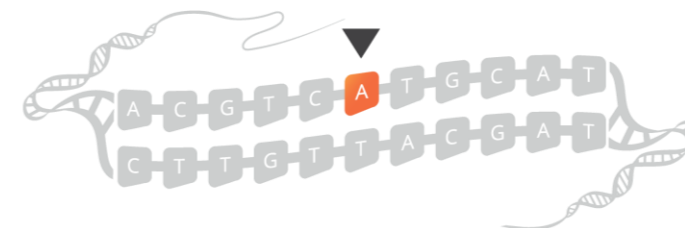
Lack of control of
gene sequence
outcomes

...ACG --- GCAT...
...ACGTC **GCTT** ATGCAT...
...A --- TGCAT...
...ACGTC **T** ATGCAT...
...AC --- AT...
...ACGTC **AAC** --- GCAT...
Etc.

----- Deletions
A G C T Insertions

BASE EDITING BEAM THERAPEUTICS

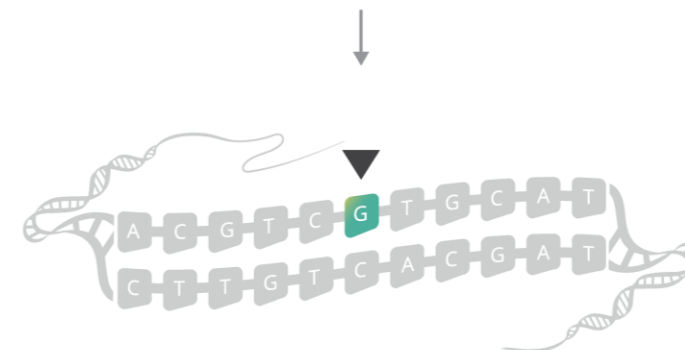
Precision
targeting
with CRISPR



Enzymatic base
conversion



Highly efficient,
with predictable
gene sequence
outcomes



Key elements of Beam's leadership position in gene editing



BASE EDITING PLATFORM

Clinical Validation,
Fully Integrated
Manufacturing



**HIGH VALUE
FRANCHISES**
with Best-in-Class
Potential



**RAPID
EXECUTION**
for Clinical
Programs



**MULTIPLE
CATALYSTS**
Expected
in 2025

With proceeds from today's \$500M financing, along with \$850.7M in cash, cash equivalents and marketable securities as of December 31, 2024, our anticipated cash runway extends into 2028

Strategic focus areas with potential for significant value creation and patient impact



**HIGH VALUE
FRANCHISES**
with Best-in-Class
Potential

Hematology

- Best-in-class potential for BEAM-101 in sickle cell disease (SCD) → Initial data at ASH 2024
- Well established FDA path to BLA
- Lifecycle strategy with ESCAPE and *in vivo* editing
- Platform for future hematology pipeline

Liver Genetic Diseases

- Best-in-class potential for BEAM-302 in alpha-1 antitrypsin deficiency (AATD) → Initial data today
- Potential one-time treatment for AATD lung and liver manifestations under normal gene regulation
- Platform for future liver-targeted pipeline

BEAM-302 initial clinical data provide proof-of-concept as a potential treatment for AATD and for *in vivo* base editing broadly



**HIGH VALUE
FRANCHISES**
with Best-in-Class
Potential

LIVER GENETIC DISEASES

BEAM-302

- Well tolerated at all dose levels
- Increased total AAT above therapeutic threshold at third dose level
- Significantly increased circulating corrected M-AAT and decreased mutant Z-AAT in dose dependent manner
- Newly produced AAT in circulation (canonical M and M-variant) functional at neutrophil elastase inhibition

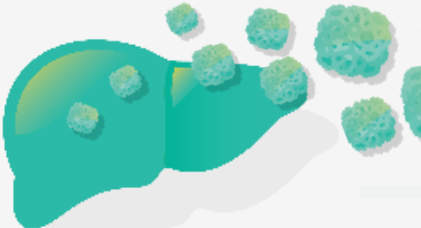
FRANCHISE

- First proof-of-concept for *in vivo* gene correction with base editing
- First Beam *in vivo* data in liver
- Demonstration of Beam's state-of-the-art lipid nanoparticle (LNP) and in-house manufacturing capabilities
- Foundation for platform for future liver-targeted pipeline

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

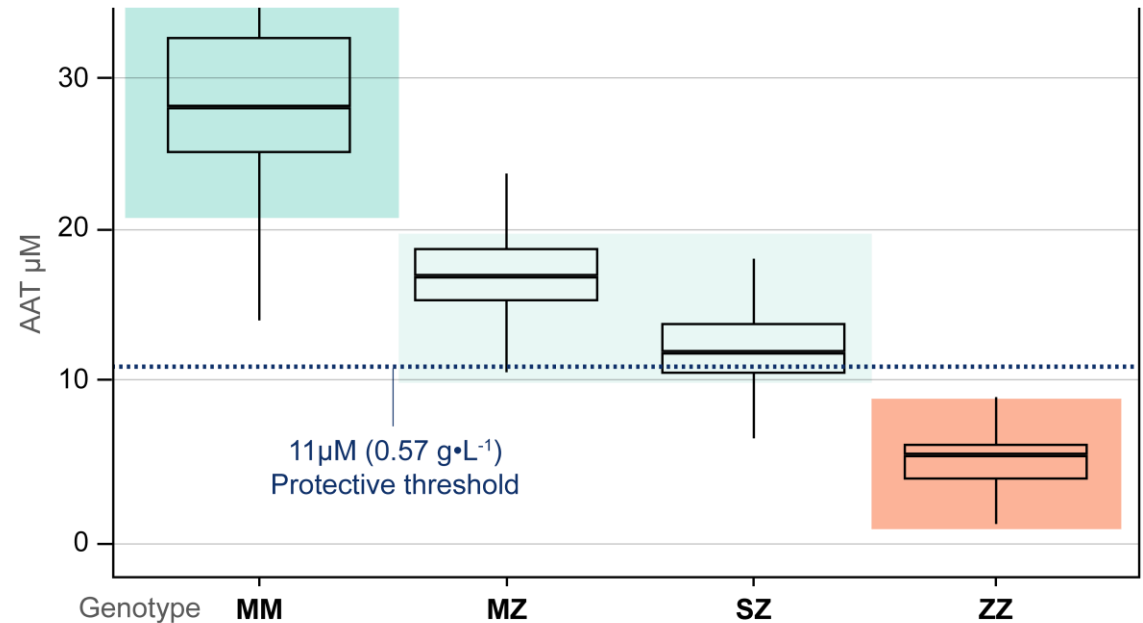
Alpha-1 antitrypsin deficiency (AATD) is a genetic disorder that leads to lung and liver disease



	Genetics	Liver	Lung
Normal AAT Function	 Wild type SERPINA1 gene (PiM or “M” allele)	 M-AAT protein is secreted from liver	 M-AAT protein protects lungs from inflammatory mediators (i.e., elastases)
AAT Deficiency	 E342K mutation (PiZ or “Z” mutation)	 Z-AAT aggregates and causes liver damage	 Decreased AAT secretion plus circulating Z-AAT aggregates lead to lung damage
PiZZ genotype is >95% of severe AATD population >100,000 PiZZ individuals in the U.S.; ~10% are diagnosed		~30% patients have liver disease, including fibrosis and cirrhosis	~80% patients have lung disease, including early onset emphysema, chronic cough, shortness of breath

Increasing total AAT levels above protective threshold reduces patients' lifetime risks for lung and/or liver disease

AAT Levels and Disease Manifestations Across Genotypes



	No Disease	No Disease Unless Other Risk Factor Present		Disease
Genotype	MM	MZ	SZ	ZZ
AAT < 11 μM	0%	0%	~40%	100%
Emphysema risk	No	Very Low	Low	High
Liver disease risk	No	Possibly	Possibly	High

Critical Attributes for an AATD Therapeutic

- **Increase circulating total AAT above 11 μM “protective threshold”**
 - No severely deficient individuals (PiZZ) have AAT > 11 μM
 - Clinically accepted level for augmentation approval, which demonstrated some clinical benefit
 - Development of lung or liver disease in individuals with ≥ 1 abnormal AAT alleles requires exposure to additional risk factors (e.g., smoking, obesity)
- **Reduce Z-AAT levels** in the liver and blood to prevent ongoing organ damage
- **Restore physiologic control of AAT** during periods of inflammation to minimize lung damage

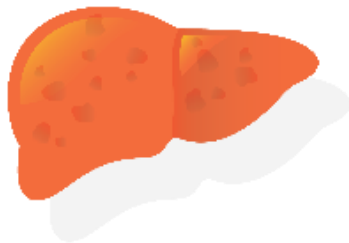
AATD current management and unmet needs

Lung disease treatment



- Routine emphysema care: bronchodilators, inhaled steroids, oxygen and antibiotics, as needed
- Only approved therapy: plasma-derived AAT (augmentation therapy) given intravenously weekly
 - Does not reduce mutant Z-AAT protein in the liver
 - Unable to increase AAT levels during inflammation
 - Slows progression of lung disease, but does not prevent ongoing lung damage and destruction

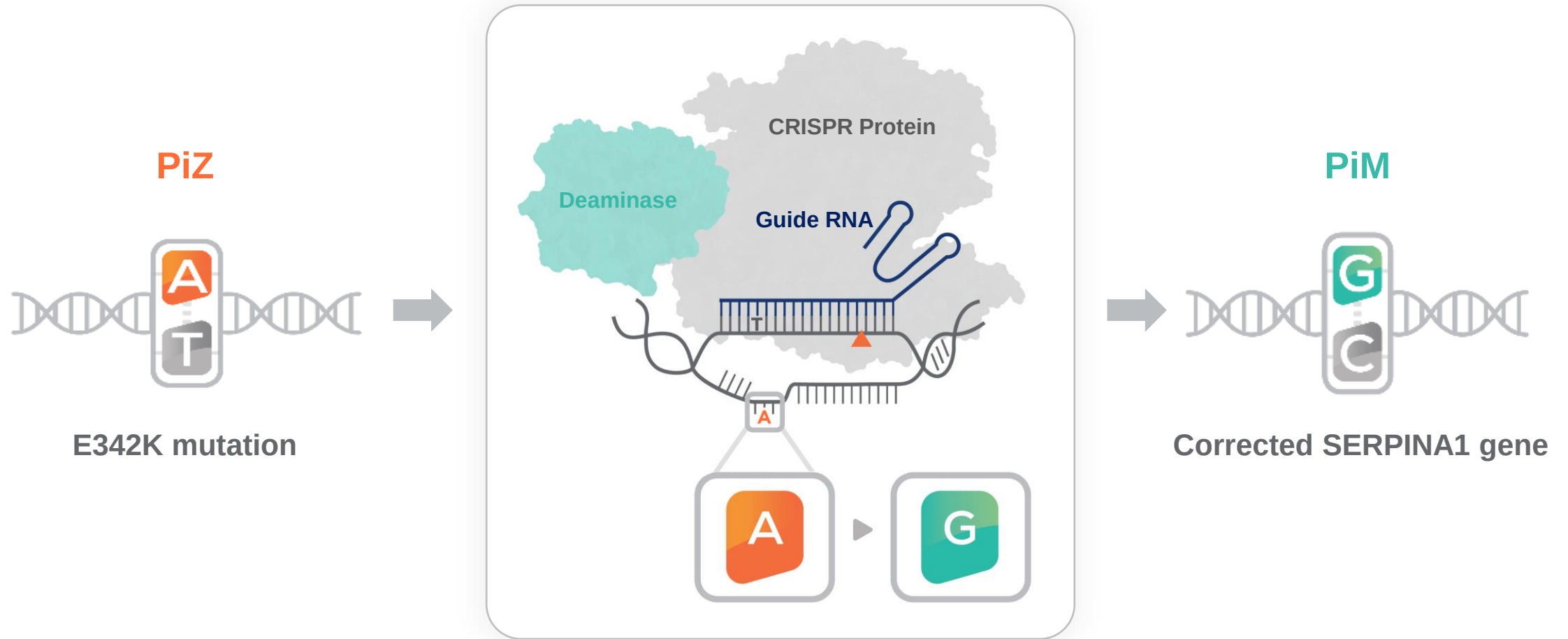
Liver disease treatment



- No approved therapies for liver disease currently
- Supportive care
- Liver transplantation for late-stage liver disease
- RNAi therapies in late-stage development, but do not treat lung manifestations

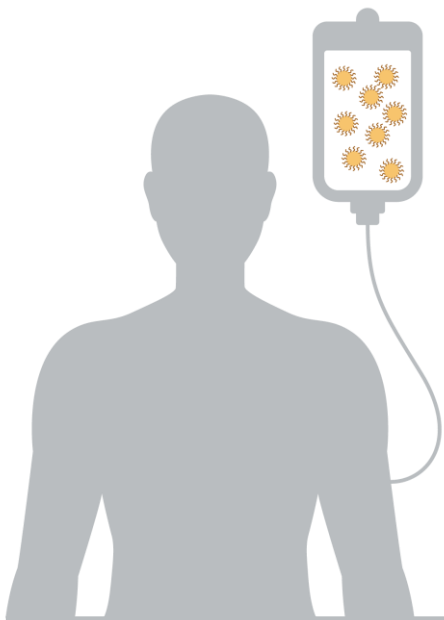
BEAM-302 is a potential one-time therapy that uses base editing to directly correct the E342K mutation causing AATD

BEAM-302 BASE EDITOR

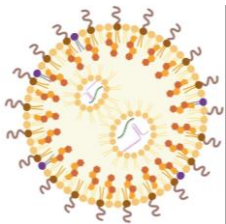


Beam has also established leading LNP capabilities for *in vivo* treatment of liver-targeted genetic diseases

Advantages of LNP delivery



- ✓ Outpatient dosing via simple IV infusion
- ✓ Titratable and redosable
- ✓ Synthetic and highly scalable manufacturing process
- ✓ Once optimized, potential for predictable and reproducible platform
- ✓ Low cost of goods



PEG
Lipid



Ionizable
Lipid



Structural
Lipid



Sterol



Base
Editor
mRNA



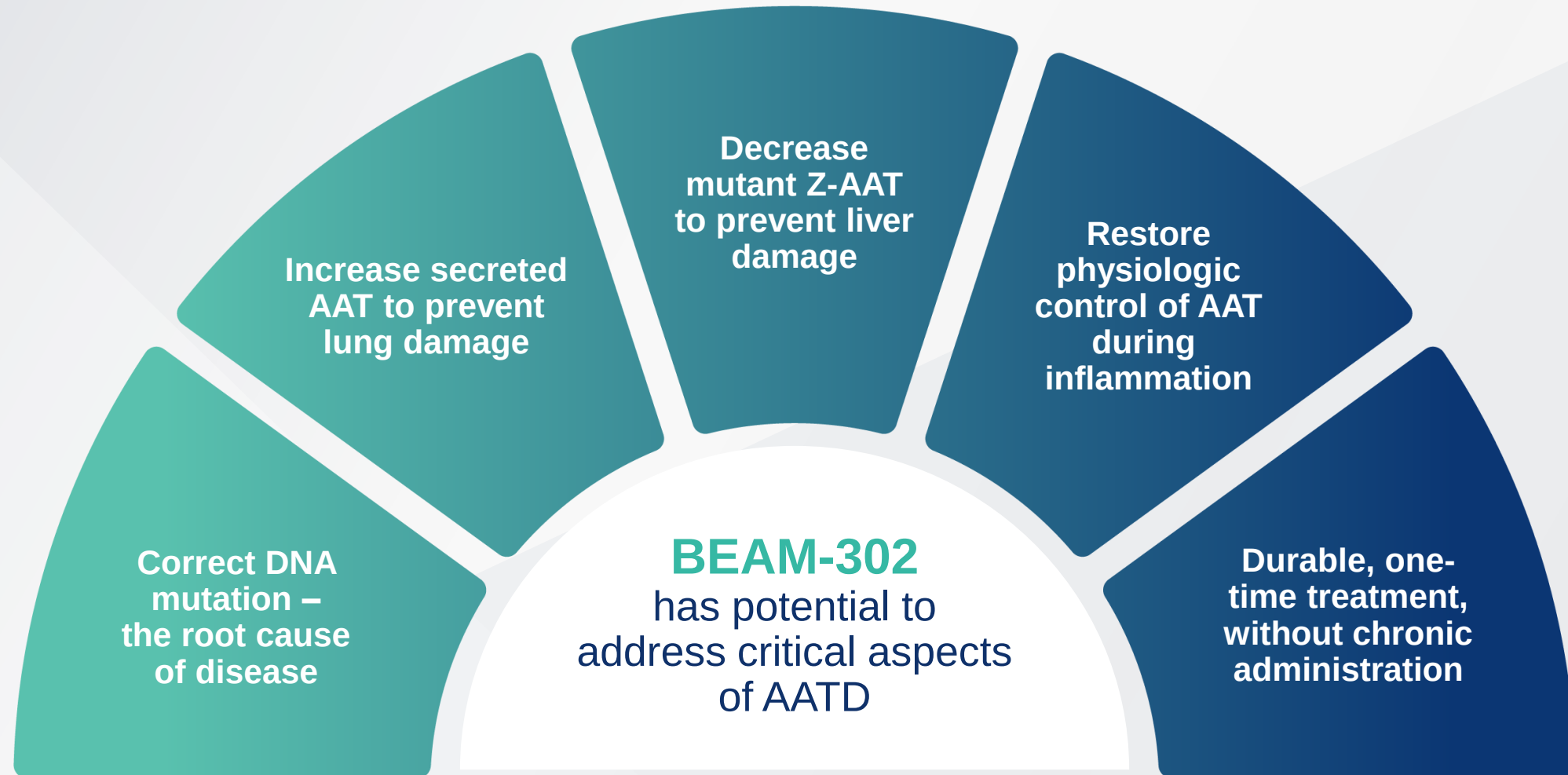
Guide
RNA



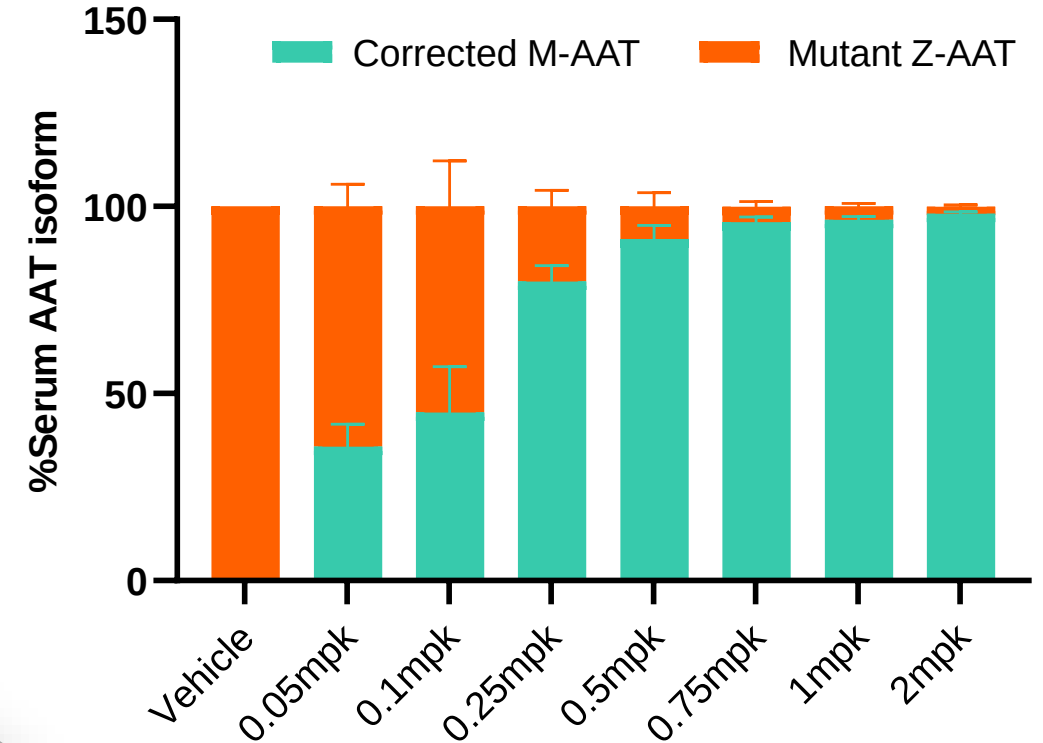
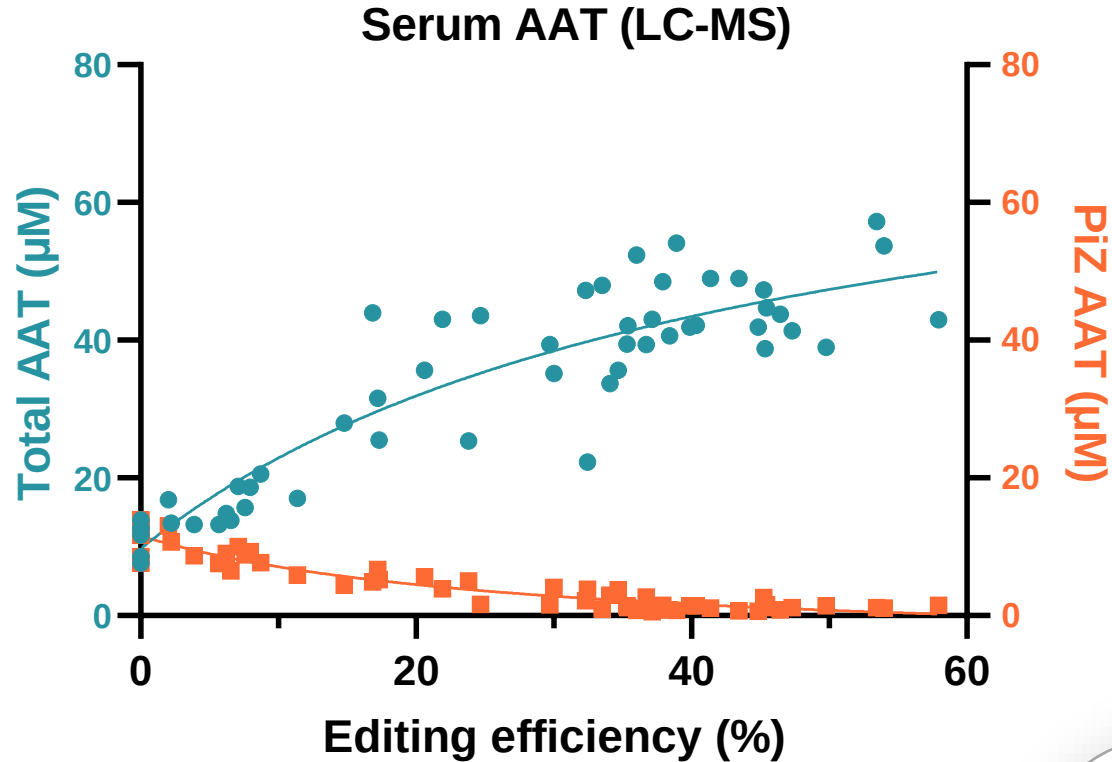
Beam's LNP Leadership Position

- Significant investment and expertise in LNP optimization and process development
- Internal and externally sourced ionizable lipids
- Internal GMP capabilities in NC facility to manufacture at scale
- Beam LNPs have shown high levels of tolerability and potency in preclinical studies
- Re-usable platform for future liver programs – changing base editor target not expected to change LNP tolerability or efficacy
- Actively exploring potential to retarget LNPs to other tissues (e.g., HSCs)

BEAM-302 has the potential to be the only one-time treatment for both lung and liver manifestations of AATD



In preclinical *in vivo* studies, BEAM-302 resulted in both increased serum total & corrected M-AAT and decreased mutant Z-AAT



NSG-PiZ
Mouse

Initial BEAM-302 Clinical Data

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

Part A: AATD-associated Lung Disease

Dose Exploration

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

Dose Expansion

Part B: AATD-associated Liver Disease with or without Lung Disease

Dose Exploration

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

Dose Expansion

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

- First ever clinical proof-of-concept of *in vivo* base editing leading to correction of a disease-causing mutation
- CTA clearances achieved in four countries
- Global site activation and enrollment ongoing

Initial clinical data includes nine patients across first three dose cohorts

Part A: AATD-associated Lung Disease

Dose Exploration

Dose Expansion

DOSING COMPLETE in first 3 cohorts of Part A



Cohort 1
15 mg
N = 3



Cohort 2
30 mg
N = 3



Cohort 3
60 mg
N = 3



Cohort 4

Part B: AATD-associated Liver Disease with or without Lung Disease

Dose Exploration

Dose Expansion

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

PART A: KEY ELIGIBILITY CRITERIA

- 18-70 years of age
- Homozygous for PiZZ mutation
- Blood total AAT level < 11 μ M
- FEV1 > 40% predicted; FEV/FVC < 70%
- Confirmed diagnosis of emphysema
- No evidence of liver disease

PART A: KEY OBJECTIVES & ENDPOINTS

- **Phase 1:** Safety and efficacy (AAT, corrected M-AAT, functional AAT, Z-AAT) of BEAM-302
- **Phase 2:** Efficacy and Safety of BEAM-302; confirm optimal biologic dose

Patient demographics



PATIENT DEMOGRAPHICS		15 mg (N=3)	30 mg (N=3)	60 mg (N=3)
Gender, n	Male	2	2	3
	Female	1	1	0
Age in years, median (min, max)		49 (37, 53)	58 (53, 61)	48 (38, 57)
Weight (kg), median (min, max)		92.4 (76.0, 93.1)	72.2 (71.7, 83.0)	88.1 (76.5, 98.5)
Baseline FEV1 % predicted, mean (SE)		57.7 (6.96)	61.2 (4.31)	58.7 (11.09)
Baseline total AAT levels (µM), mean (SE)		4.4 (0.22)	5.3 (0.25)	4.4 (0.30)
Years since AATD diagnosis [1], median (min, max)		3.0 (2.4, 14.4)	10.1 (1.5, 17.6)	3.9 (1.7, 4.4)

[1] Calculated as (date of informed consent signed – date of AATD diagnosis +1)/365.25. Partial diagnosis dates are imputed as 01 of the Month if the Day is missing or 01 January of the year if both Month and Day are missing.

For total AAT, baseline for each patient is defined as the average of all assessments conducted within the 84-day screening period prior to BEAM-302 infusion. For other variables, baseline is defined as the last available assessment prior to BEAM-302 infusion.

Preliminary data support the safety of BEAM-302 at doses up to 60 mg

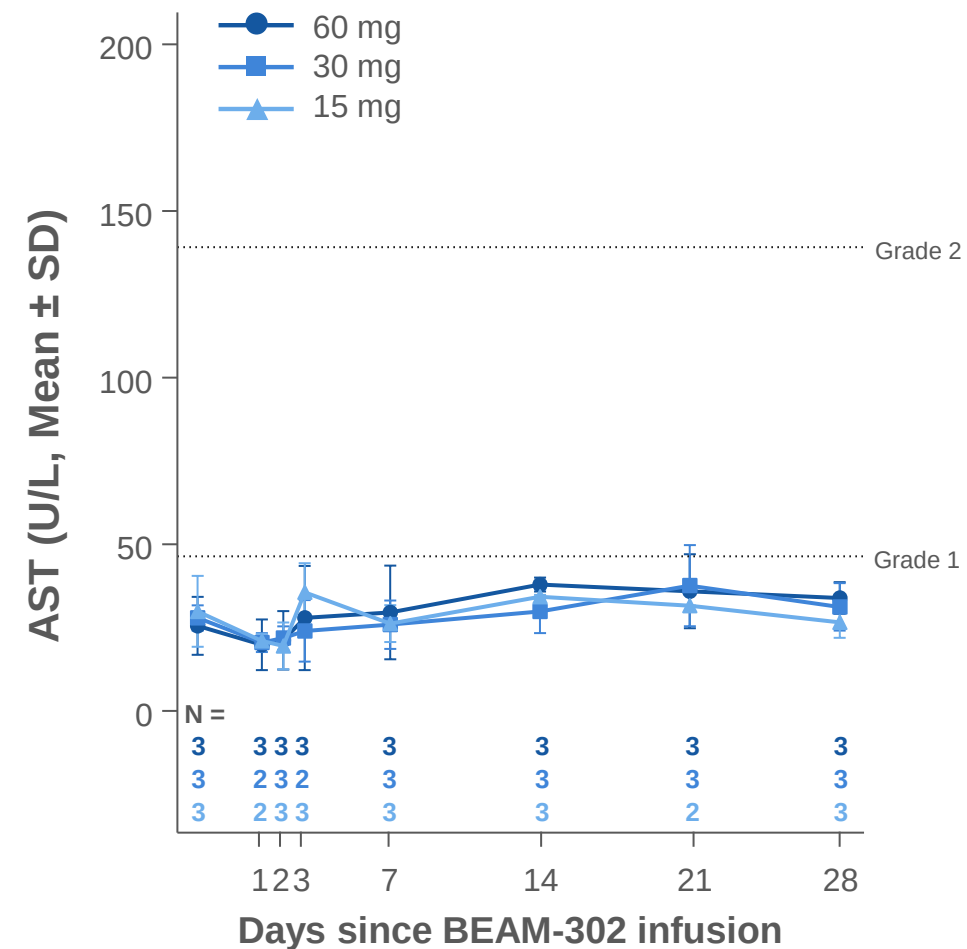
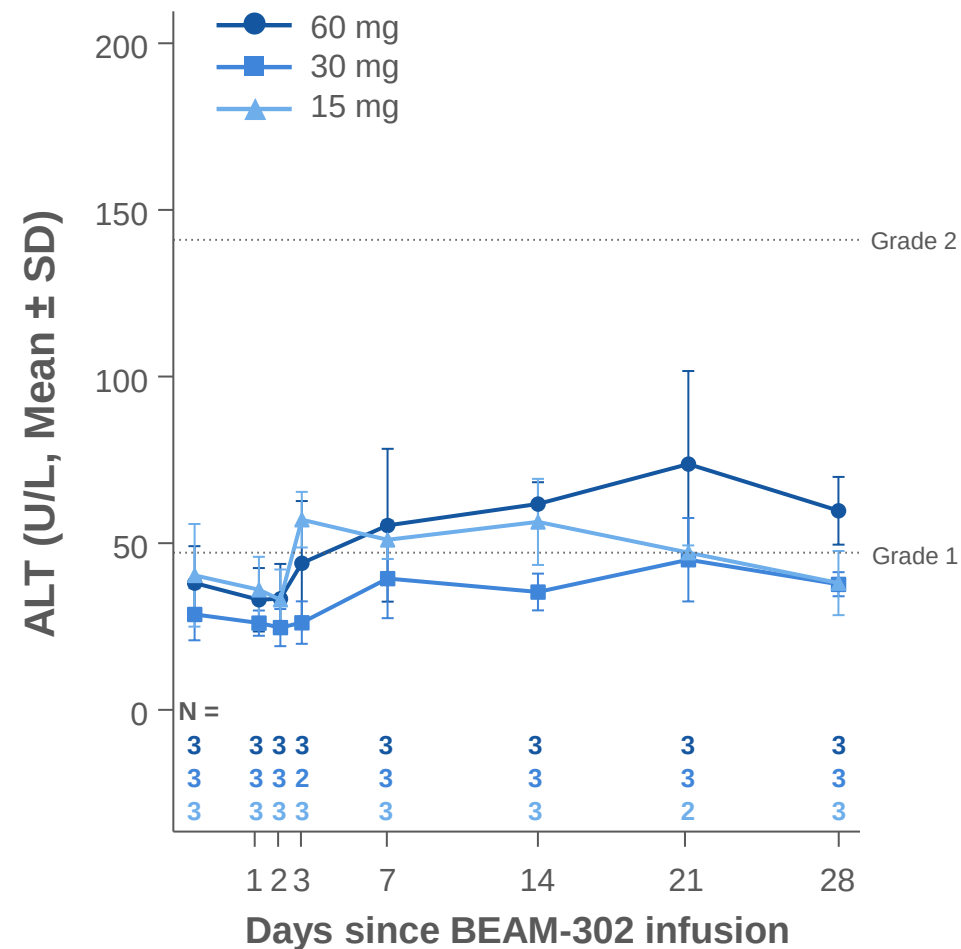


Patients with	15 mg N=3 n (%)	30 mg N=3 n (%)	60 mg N=3 n (%)
Any TEAEs	3 (100)	3 (100)	2 (66.7)
Related to BEAM-302	2 (66.7)	0	1 (33.3)
Any TEAEs ≥Grade 3	0	0	0
Dose-limiting toxicities	0	0	0
Serious TEAEs	0	0	0
Death	0	0	0

- No serious AEs, DLTs or ≥Grade 3 AEs observed
- All treatment-emergent AEs (TEAEs) were mild-to-moderate
- Grade 1 asymptomatic elevations in ALT (+/- AST) were observed within the first 28 days after dosing in all cohorts
- 3 patients had mild infusion-related reactions (IRR) that resolved without intervention or interruption (2 at 15 mg; 1 at 60 mg)
- Most common AEs occurring in ≥ 2 patients included: upper respiratory tract infection, back pain, IRR and infective exacerbation of chronic obstructive airways disease

Data cutoff February 26, 2025
 Data are based on follow-up exposure data between approximately 28 days and 8 months
 Related events include events where investigator has assessed relationship as possibly or definitely related to BEAM-302
 Related events include 2 patients at the 15mg dose each with 1 IRR (mild); 1 patient at the 60mg dose with IRR (mild) and back pain (moderate)

Asymptomatic, Grade 1 liver transaminase elevations were observed in some patients following BEAM-302 treatment



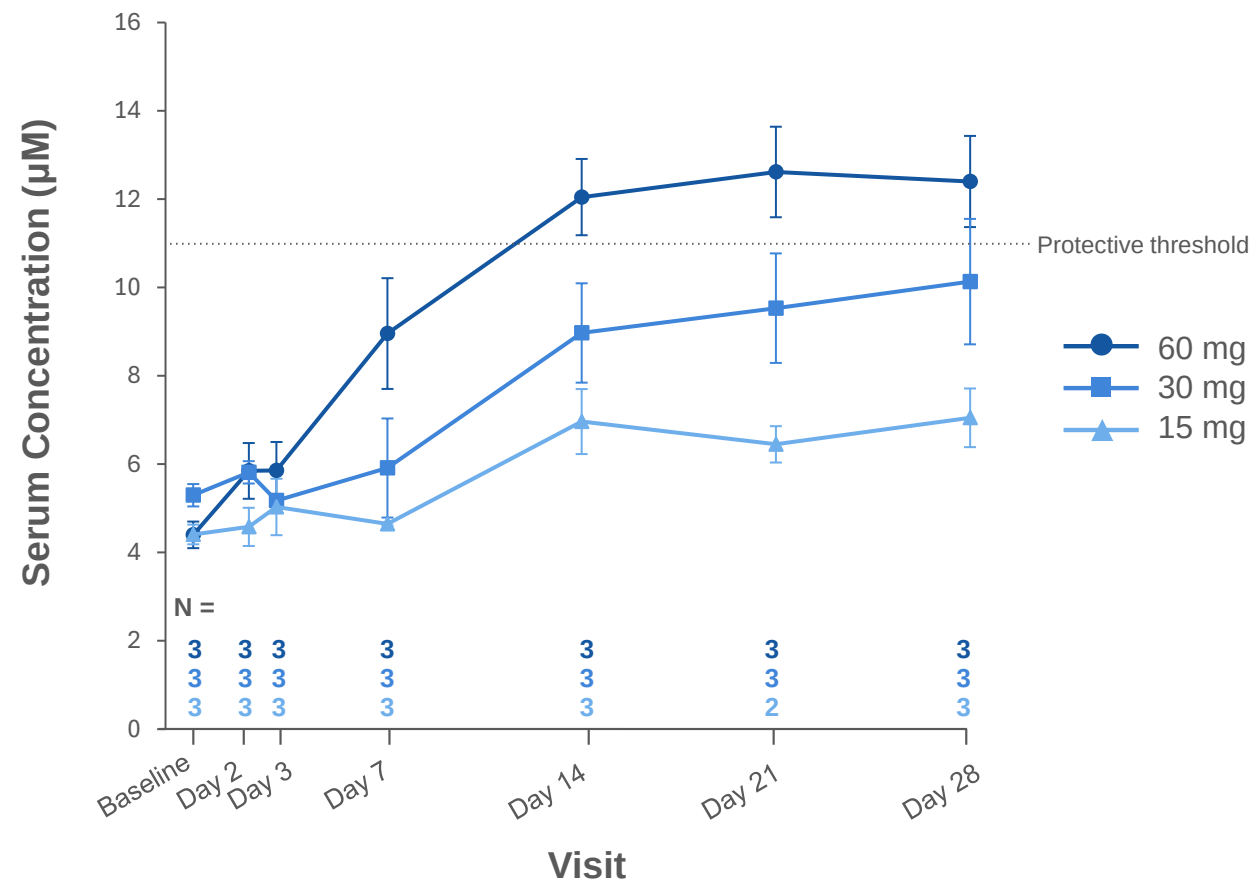
Data cutoff February 26, 2025
Grade 1 is defined as: > upper limit of normal (ULN) - 3.0 x ULN if baseline was normal; 1.5 - 3.0 x baseline if baseline was abnormal; ULN is calculated using a weighted average of male and female reference values, based on the proportion of each gender in the study. One patient in the 15 mg cohort could not attend their Day 21 visit due to a COVID infection.

Bilirubin levels remained within the normal range or at baseline across all dose cohorts

BEAM-302 treatment led to a rapid, dose-responsive increase of total AAT above the 11µM protective threshold



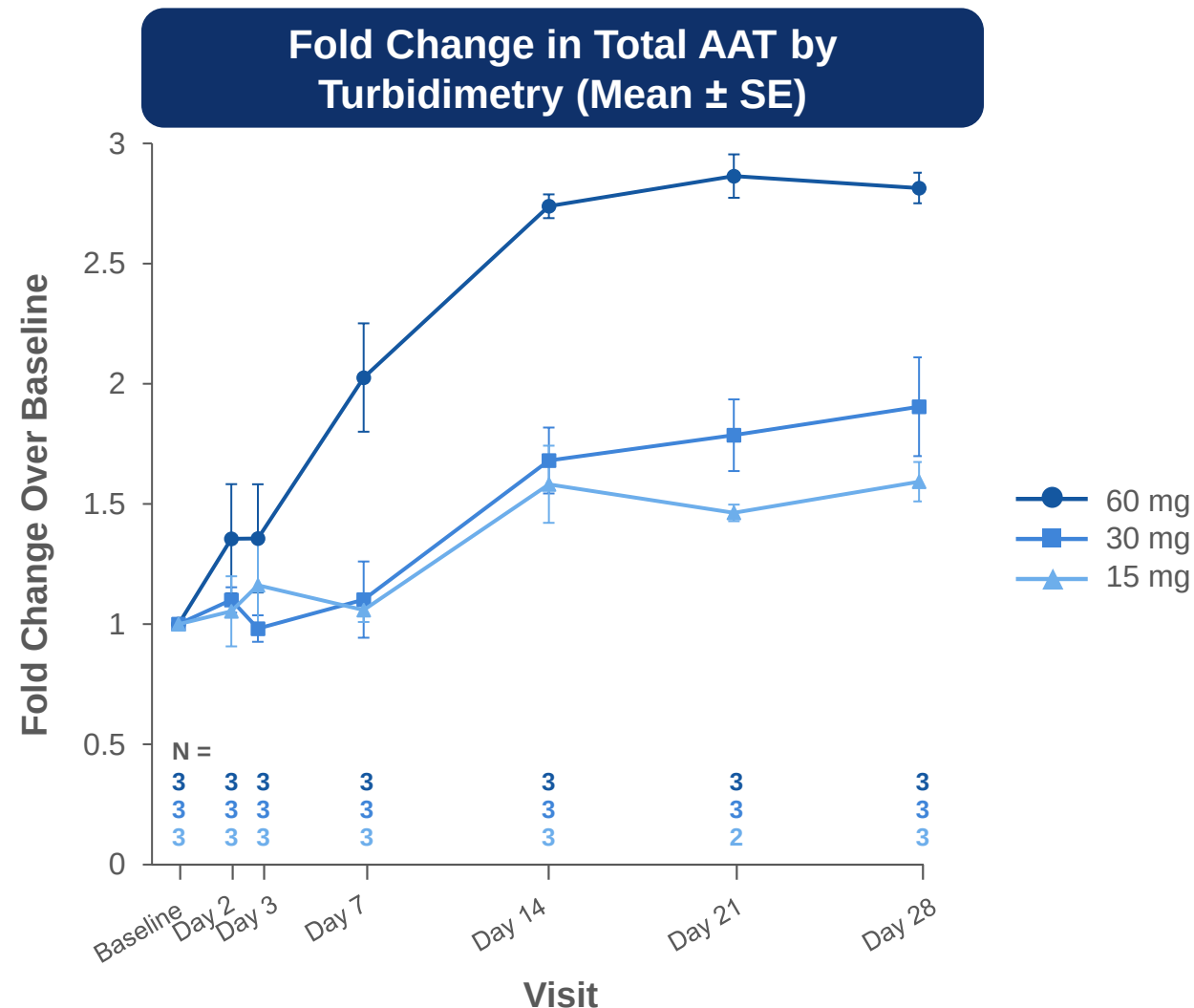
Total AAT by Turbidimetry (Mean ± SE)



Dose	Baseline, mean	Total AAT at Day 28, mean
15 mg	4.4µM	7.0µM
30 mg	5.3µM	10.1µM
60 mg	4.4µM	12.4µM

Data cutoff February 26, 2025
Baseline for each patient is defined as the average of all assessments conducted within the 84-day screening period prior to BEAM-302 infusion.
One patient in the 15 mg cohort could not attend their Day 21 visit due to a COVID infection.

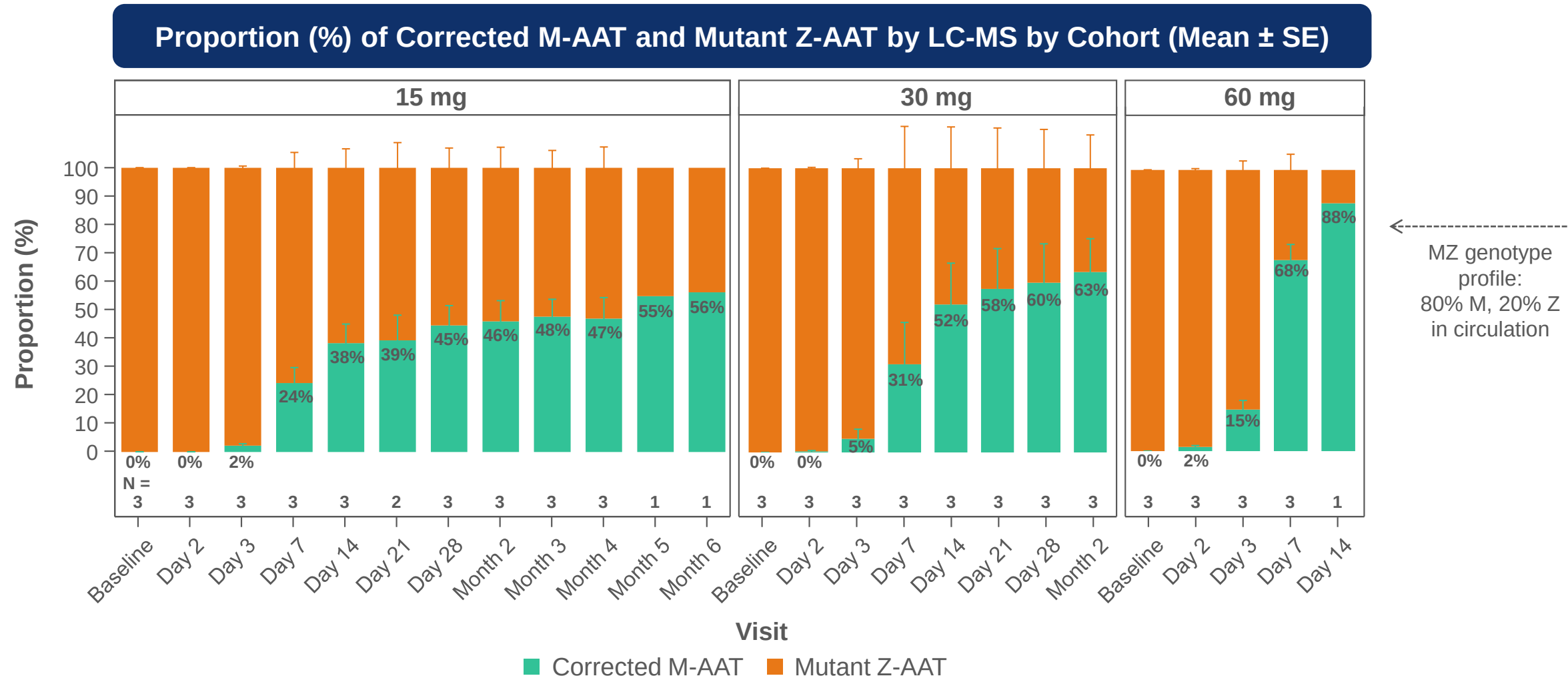
Dose-dependent increase in fold change in total AAT observed following treatment with BEAM-302



Dose	Baseline, mean	Fold Change in Total AAT at Day 28, mean
15 mg	4.4µM	1.6x
30 mg	5.3µM	1.9x
60 mg	4.4µM	2.8x

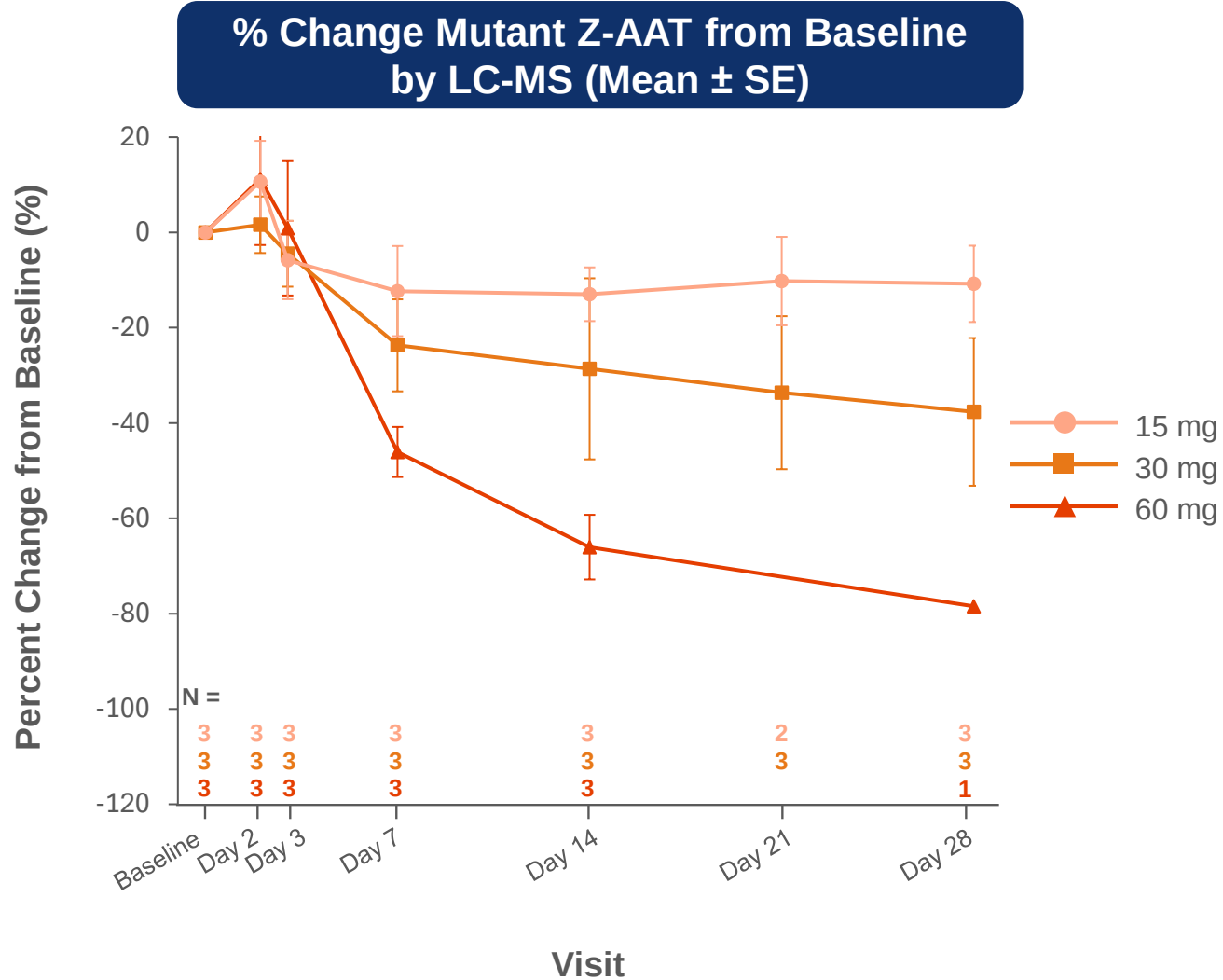
Data cutoff February 26, 2025
Baseline for each patient is defined as the average of all assessments conducted within the 84-day screening period prior to BEAM-302 infusion.
One patient in the 15 mg cohort could not attend their Day 21 visit due to a COVID infection.

Corrected M-AAT was detected in the circulation of patients for the first time within 3 days after BEAM-302 treatment



Data cutoff February 26, 2025
Baseline for each patient is defined as the average of all assessments conducted within the 84-day screening period prior to BEAM-302 infusion.
One patient in the 15 mg cohort could not attend their Day 21 visit due to a COVID infection.
Donato et al. Respiratory Research (2015) 16:96

BEAM-302 treatment also led to rapid, dose-dependent reductions in circulating mutant Z-AAT



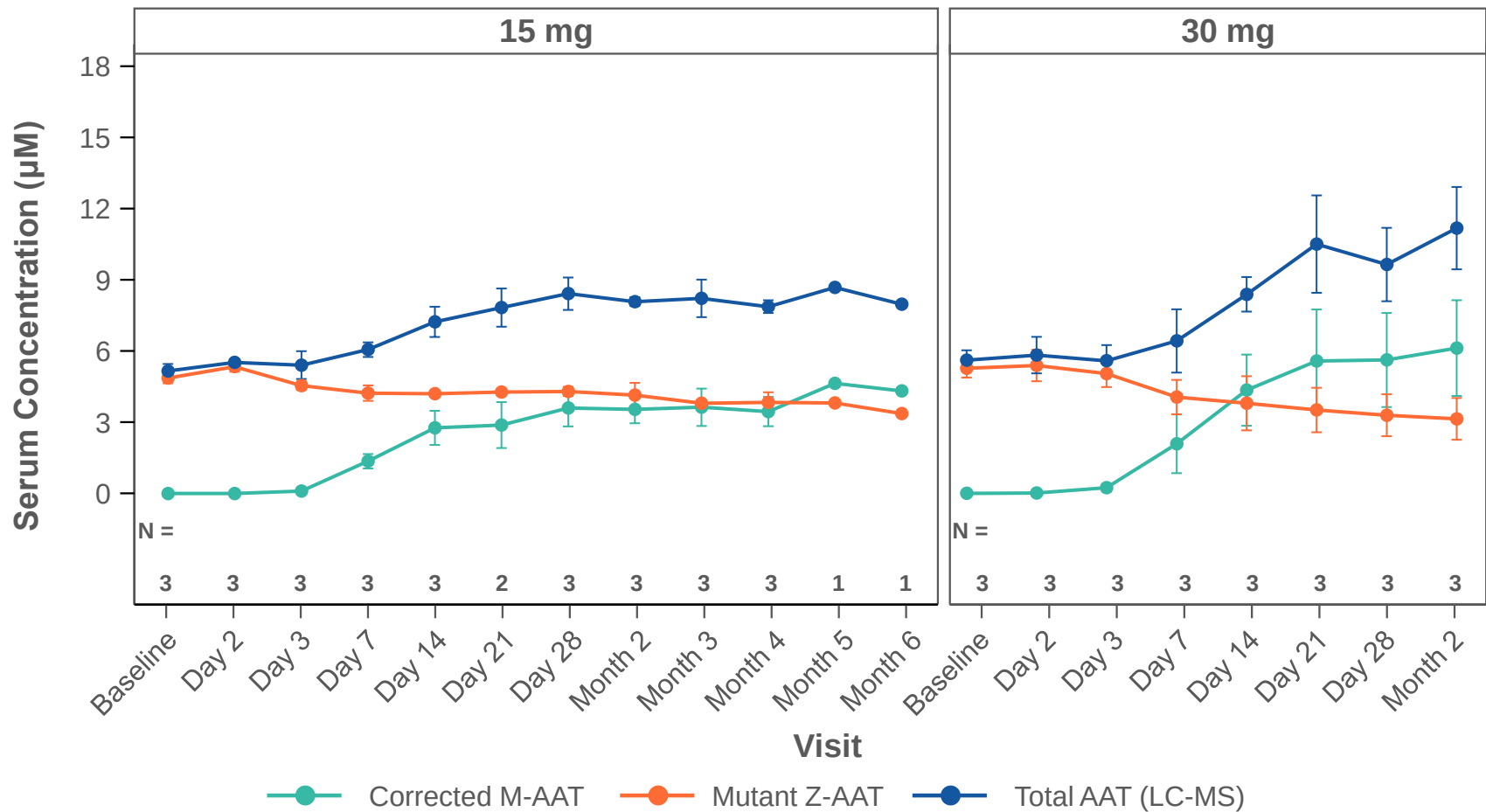
Dose	% change in Z-AAT at Day 28, mean
15 mg	-11%
30 mg	-38%
60 mg	-78%

Data cutoff February 26, 2025
Baseline for each patient is defined as the average of all assessments conducted within the 84-day screening period prior to BEAM-302 infusion.
One patient in the 15 mg cohort could not attend their Day 21 visit due to a COVID infection.

AAT correction was durable, with up to 6 months of follow-up, after a single dose of BEAM-302

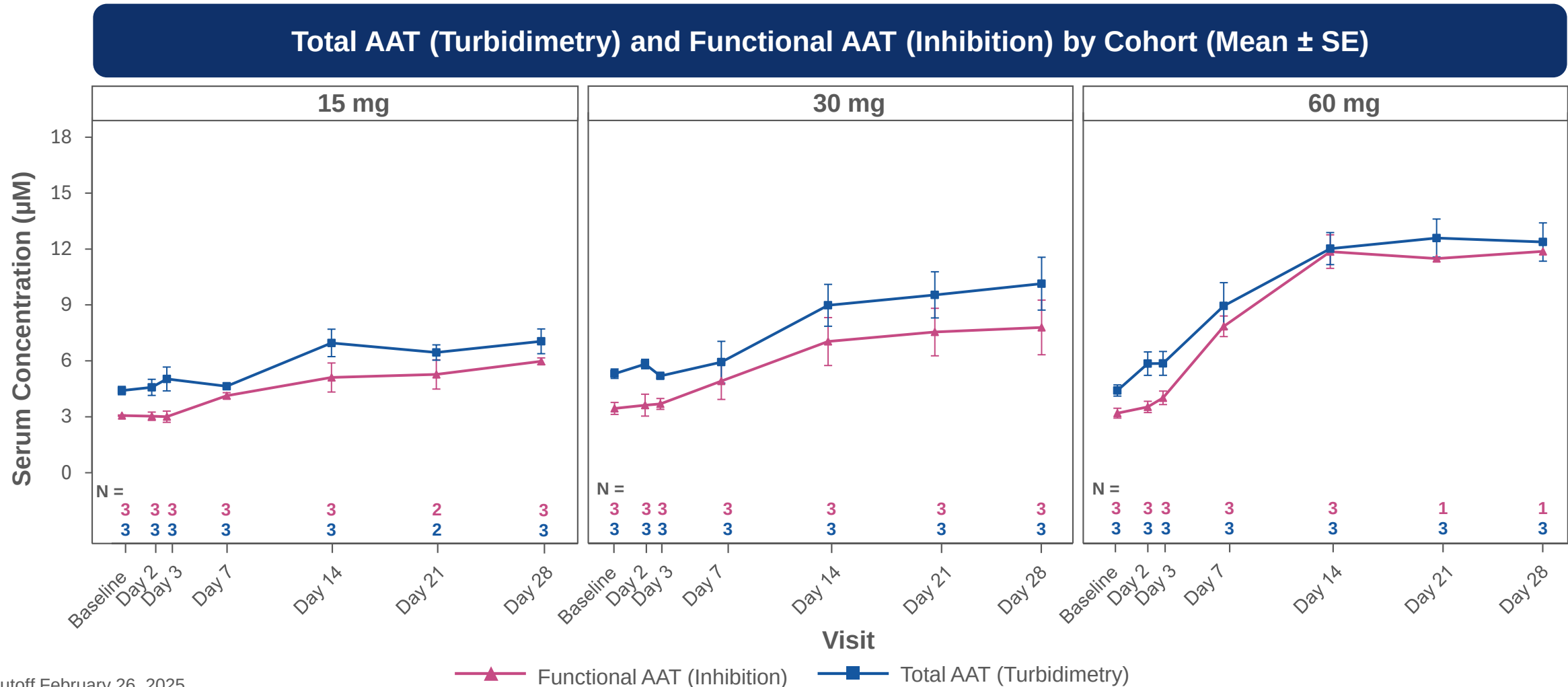


Durability of Total AAT, Corrected M-AAT and Mutant Z-AAT by LC-MS Beyond Month 1 (Mean $\pm$ SE)



Data cutoff February 26, 2025
Patient baseline defined as the average of all assessments conducted within the 84-day screening period prior to BEAM-302 infusion.

Increased total AAT in circulation was functional in neutrophil elastase inhibition assay



Data cutoff February 26, 2025
Baseline for each patient is defined as the average of all assessments conducted within the 84-day screening period prior to BEAM-302 infusion.

Increased total AAT in circulation also functional in neutrophil elastase binding assay

Established clinical proof of concept for BEAM-302 as a potential one-time, differentiated treatment for AATD



To date, BEAM-302 was well tolerated with an acceptable safety profile at 15, 30, 60 mg doses

- • All adverse events (AEs) were mild to moderate, with no serious AEs and no dose-limiting toxicities (DLTs)
- Asymptomatic Grade 1 ALT and AST elevations and transient Grade 1 infusion-related reactions were observed in some patients and have not required treatment

Single dose of BEAM-302 led to durable, dose-dependent correction of the PiZ mutation

- • Demonstrated by increases in total AAT, production of corrected M-AAT, and decreased mutant Z-AAT in circulation

Total AAT increased to a mean of 12.4µM for patients treated with the 60 mg dose (N=3)

- • Above the protective threshold of 11µM

Mutant Z-AAT reduced up to 78% in circulation in a dose-dependent manner

- • M-AAT to Z-AAT ratio above 80% in circulation, similar to the MZ genotype

Increased total AAT is functional by both neutrophil elastase inhibition and neutrophil elastase binding assays

Anticipated next steps in development of BEAM-302 for AATD

Part A: AATD-associated Lung Disease

Dose Exploration

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

Dose Expansion

- Continue dose escalation to identify optimal biologic dose
- Expand country and site activation, including U.S.
- Present updated data in 2H 2025

Part B: AATD-associated Liver Disease with or without Lung Disease

Dose Exploration

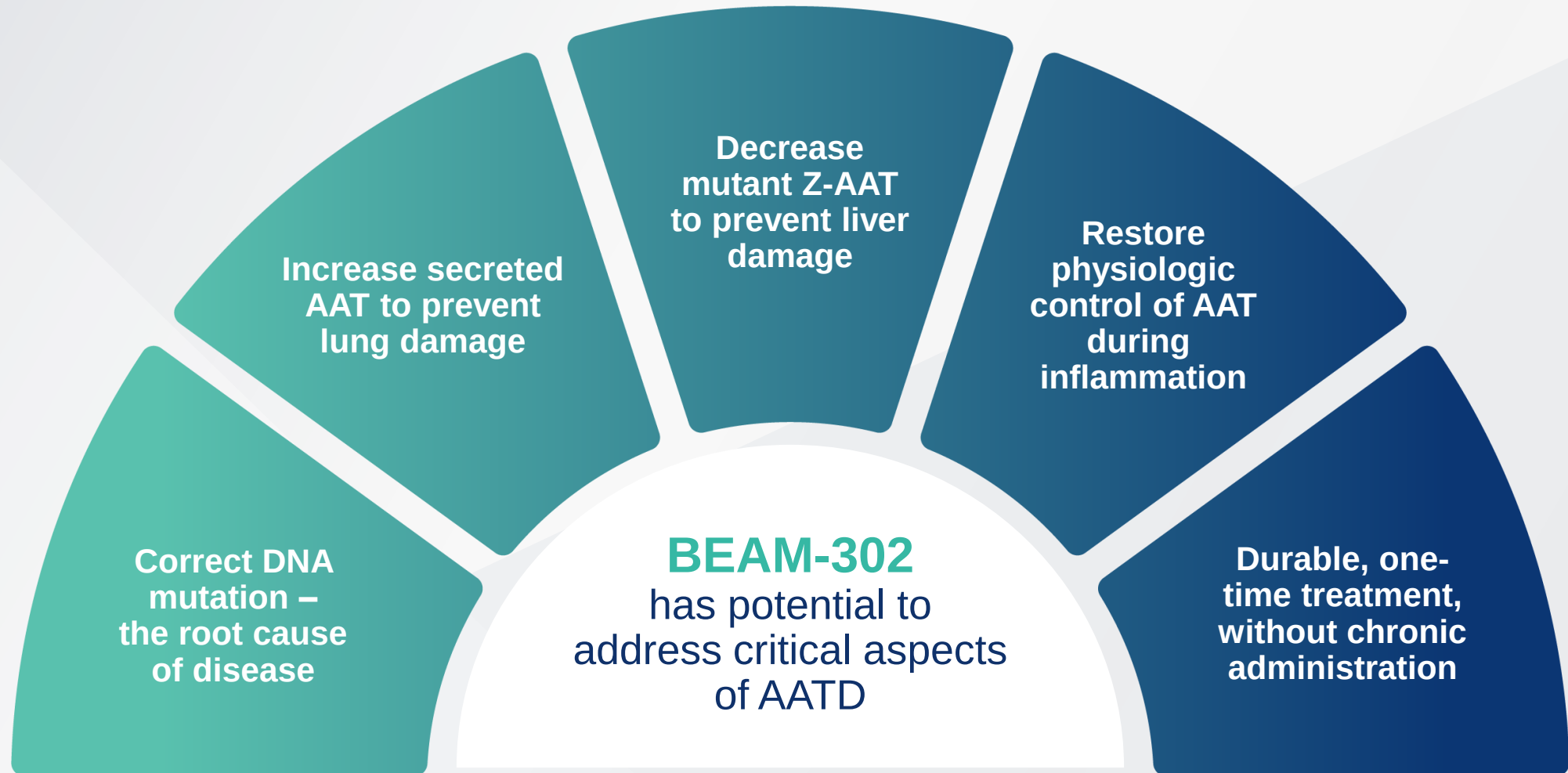
- Up to 4 dose cohorts
- Patients included with mild to moderate liver disease

Dose Expansion

- Initiate dose exploration in 2H 2025

Wrap up

BEAM-302 has the potential to be the only one-time treatment for both lung and liver manifestations of AATD



Broader implications of BEAM-302 dataset

Milestone event in genetic medicine

Base editing delivers first ever genetic correction of a disease-causing mutation in DNA

Validation of Beam *in vivo* LNP capabilities

Proprietary, well-tolerated LNP creates a strategic platform for future liver programs

Beam track record of clinical translation

3 of 3 Beam base editing programs have delivered clinical proof of concept in line with preclinical studies

Significant potential catalysts on the horizon



**MULTIPLE
CATALYSTS**
Expected
in 2025

BEAM-101

SCD (BEACON TRIAL)

- Dose 30 patients by mid-2025
- Dose and continue to enroll adolescent patients
- Present updated data in mid-2025

BEAM-302

AATD

- ✓ Present initial data from multiple cohorts in 1H 2025
- Complete Part A dose escalation and initiate Part B dose escalation
- Present updated data in 2H25

ESCAPE

SCD & BETA-THALASSEMIA

- Initiate Phase 1 healthy volunteer trial of BEAM-103 antibody by YE

BEAM-301

GSD1a

- Dose first patient in Phase 1/2 trial in early 2025

Patients are at the heart of our vision



Kyle
SICKLE CELL DISEASE



Dan and Kathi
ALPHA-1 ANTITRYPSIN
DEFICIENCY



Alyssa and Gayle
GLYCOGEN STORAGE
DISEASE 1A