
SPUR THERAPEUTICS
Toward More™
February 2025

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Imagine a world where a single dose of genetic medicine could truly alter the course of a disease—and the course of people’s lives.

This is the vision that spurs us forward. That drives us on our mission to redefine what gene therapy can do, so we can bring its transformative impact to more people.

Moving toward life-changing therapies, and brighter futures.

Toward more.

Toward tailored gene therapies

Where many first-generation therapies fall short

- Safety
- No improvement on standard of care
- Commercial uptake

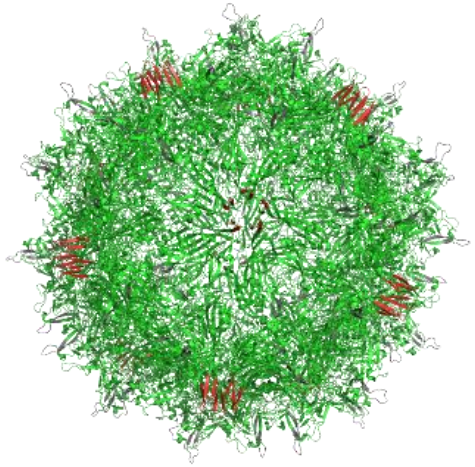
Tailored gene therapies offer more

- Optimized for specific diseases to drive higher efficacy at lower doses
- Improved outcomes, including changing the course of the disease
- Potential to impact more prevalent conditions

Optimizing every component of our product candidates to realize outsized clinical results at lower doses

Selective capsids

Improved tissue targeting, more efficient transfers of genetic material, and reduced immunogenicity



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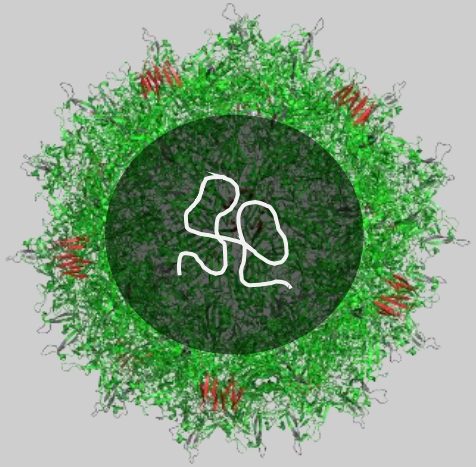
Optimized genomes

Promoter design and codon optimization improve tissue selectivity and advance protein synthesis



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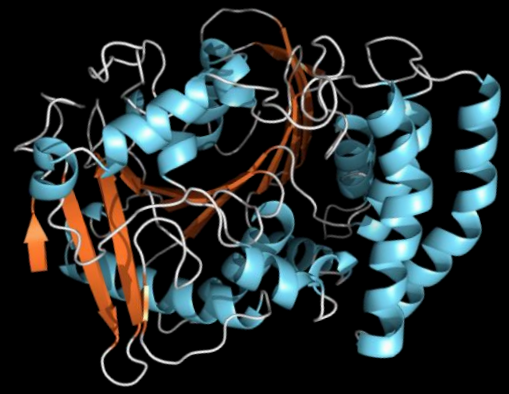
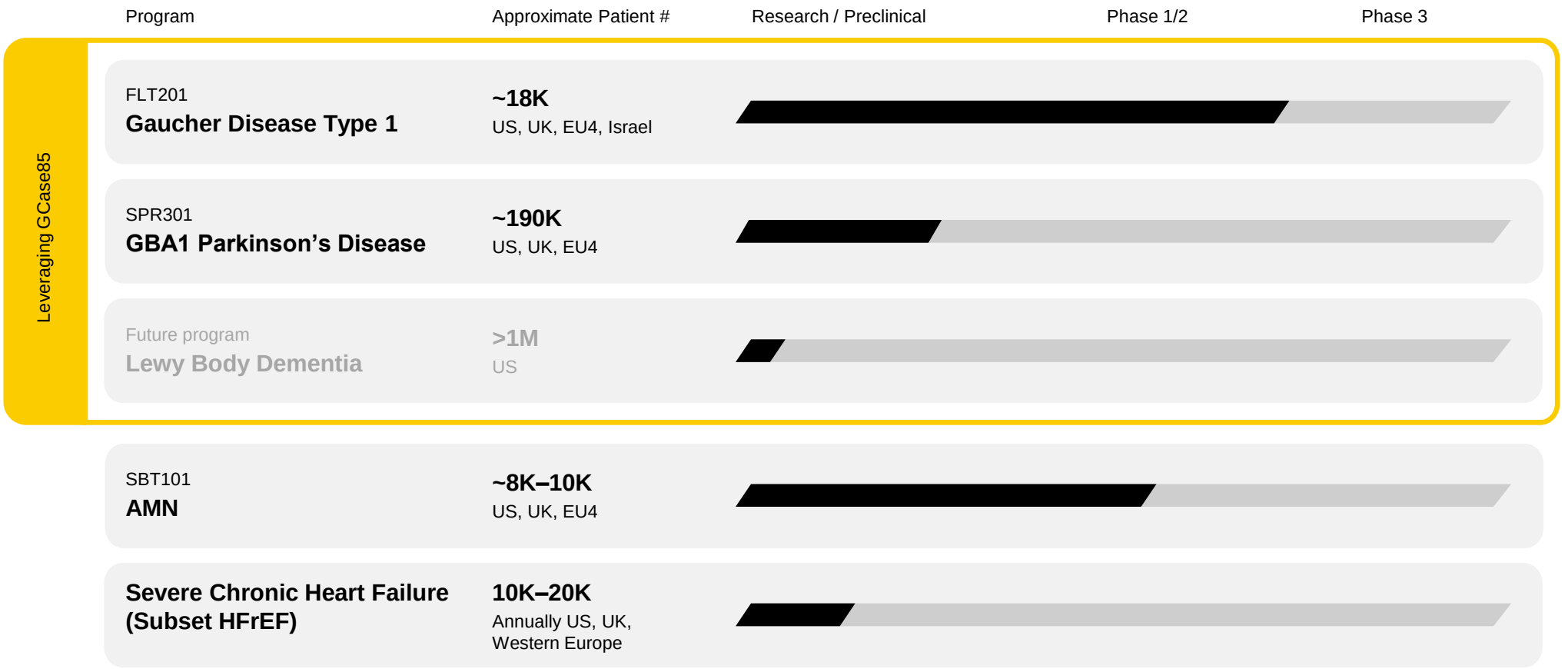
Engineered therapeutic gene

Increased half-life, stability, and activity, and more precise targeting of the therapeutic protein



Come together to create our product candidates

Moving from rare to more prevalent conditions

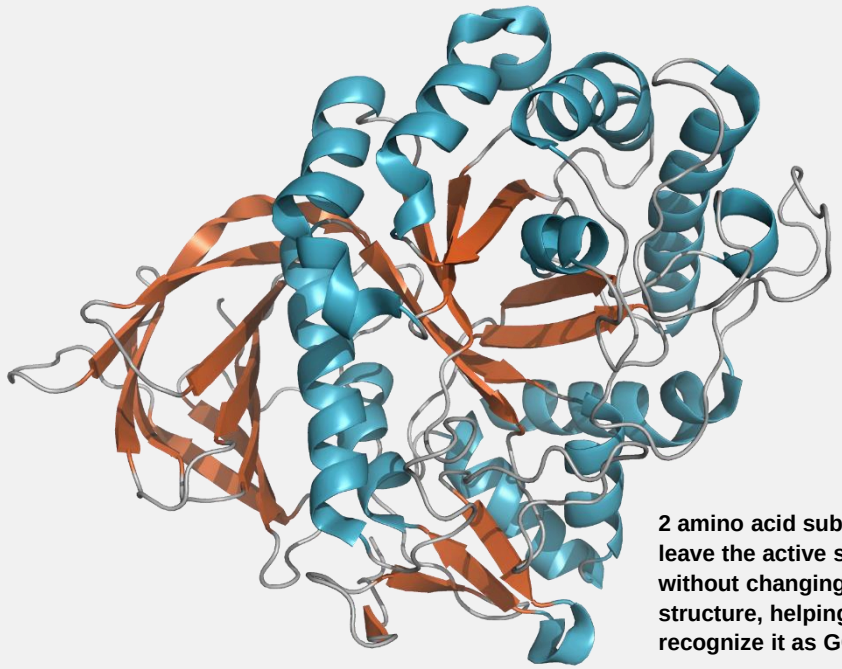


HFrEF = heart failure with reduced ejection fraction

Estimated patient numbers for Gaucher disease type 1 represent the total theoretical genetic prevalence of the indication. The seroprevalence of antibodies against the AAVS3 capsid renders some patients ineligible for AAVS3 gene therapy. Estimated GBA1-PD population is based on 5%-15% of diagnosed PD patients, representing the approximate number of patients with *GBA1* mutations. Lewy body dementia patient number from the Lewy Body Dementia Association. Estimated adrenomyeloneuropathy (AMN) population from Turk et al. *Int J Dev Neurosci.* 2020: 80:52-72. Estimated annual incidence of HFrEF based on company analysis.

GCase85: An enzyme with transformative potential

Our rationally engineered GCase85 offers a longer half-life and increased stability, supporting greater activity levels at lower doses.



2 amino acid substitutions leave the active site clear without changing the outside structure, helping the body recognize it as GCase

6X

longer half-life in serum than the wildtype

21X

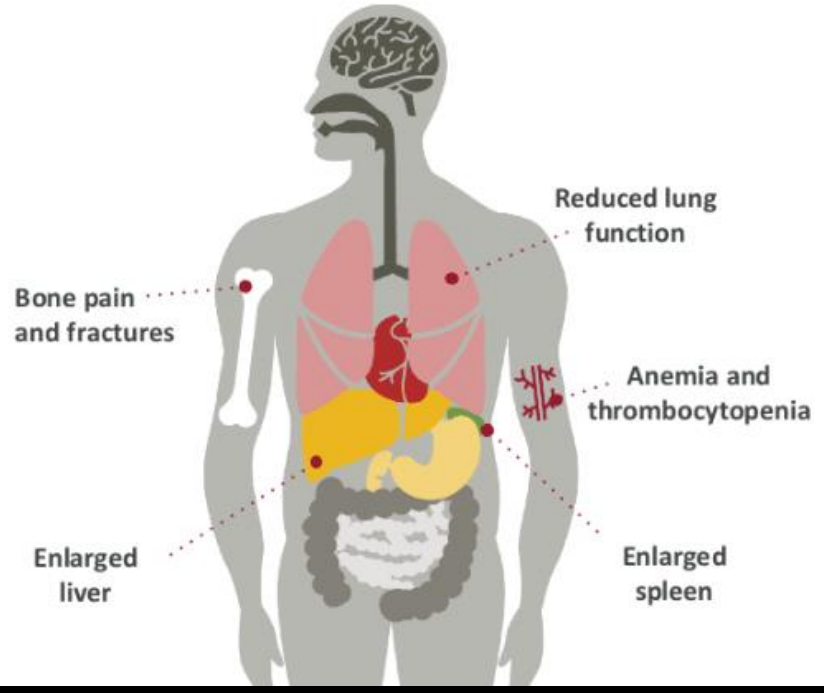
longer half-life in lysosomal pH— **6 days** instead of 6 hours

Gaucher disease can be debilitating, even with current treatments.

Our new therapy candidate could change that—and change lives.

Targeting a chronic, progressive, and life-altering condition

Gaucher disease type 1
GCase deficiency leads to a buildup of toxic substrates, Gb-1 and lyso-Gb1, impacting multiple organ systems.



Many people experience debilitating symptoms despite lifelong treatment on ERT (current standard of care).

95% of people with Gaucher disease have type 1[1]

~18K patients
in US, UK, EU4 & Israel

[1]Charrow 2000

A need for a new treatment

The enzyme used in ERT has a short half-life, leaving patients without enzyme coverage between doses and with lingering symptoms.

Up to

60%

of people with Gaucher still experience symptoms after 10+ years on ERT[1]

[1] Weinreb et al. 2013

80%

of people with severe bone marrow burden showed no meaningful improvement after 8 years on ERT[2]

[2] De Fost 2006; low ERT dose cohort

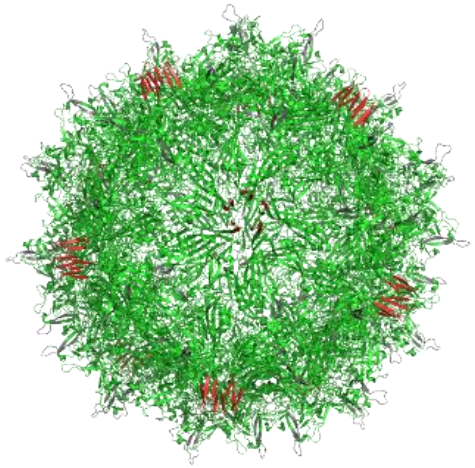
65%

report fatigue despite treatment with ERT[3]

[3] Wagner 2018

FLT201: A first-in-class gene therapy candidate for Gaucher disease

AAVS3 capsid has much higher transduction efficiency than other AAVs



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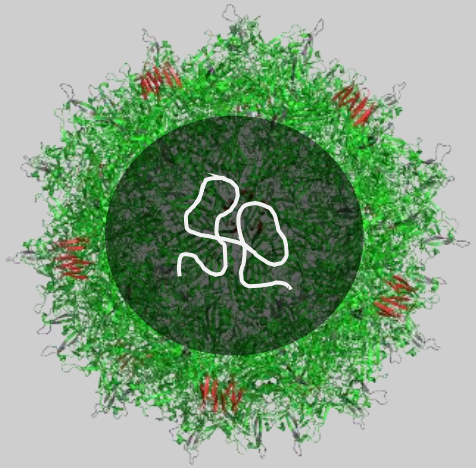
Optimized genome focuses expression in the liver



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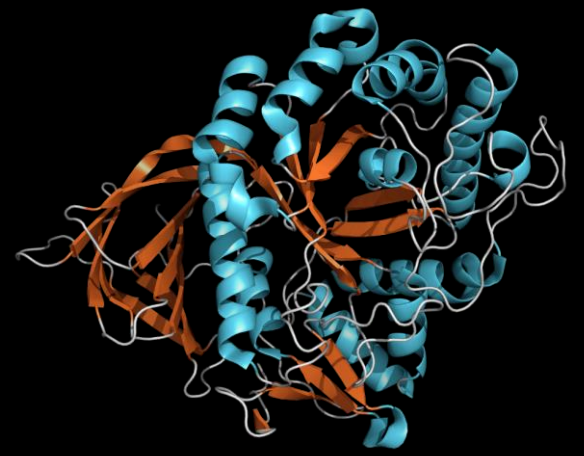
Engineered GBA transgene encodes more stable GCase85



Demonstrating compelling efficacy and safety profile

Data from ongoing Phase 1/2 trial

GALILEO-1 trial results:

Demonstrated safety and efficacy

Data support selection of low dose of 4.5e11 vg/kg for planned Phase 3 trial

Clean safety

Favorable safety and tolerability in **all** dosed patients

Compelling efficacy[1]

Dramatic improvements in **lyso-Gb1** in patients with persistently high levels despite prior therapy

Maintenance or improvement in **hemoglobin, platelets, bone disease** and **organ volume**

Significant reduction in **pain** and **fatigue** in the one patient who entered trial with debilitating pain and fatigue

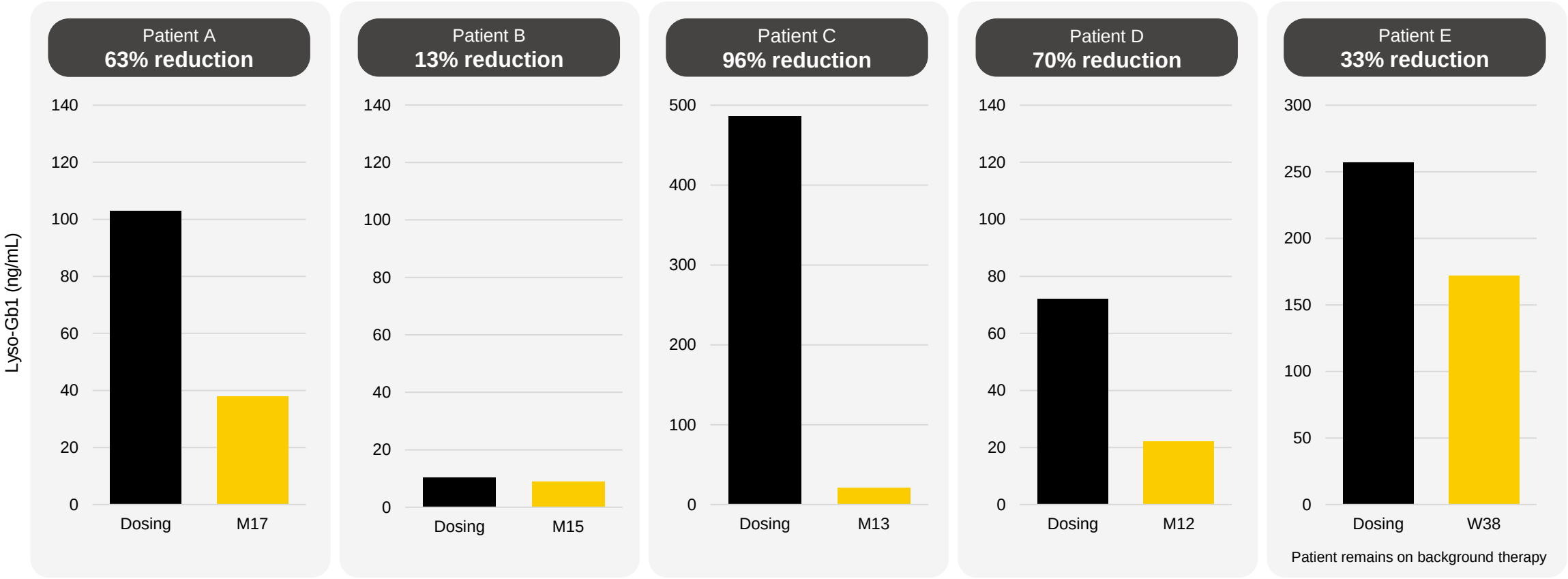
~**50% of Gaucher disease type 1 patients** are AAVS3 NAb-negative and available for treatment with FLT201

[1]One patient with detectable neutralizing antibodies (NAbs) to the AAVS3 capsid below protocol cut-off excluded from efficacy analysis. Only patients with no detectable NAbs will be eligible for Phase 3 trial.

GALILEO-1 trial results:

Dramatic and sustained reductions in lyso-Gb1 levels

One of the best predictors of disease severity and clinical response, lyso-Gb1 is a potential endpoint for 6-month approval pathway

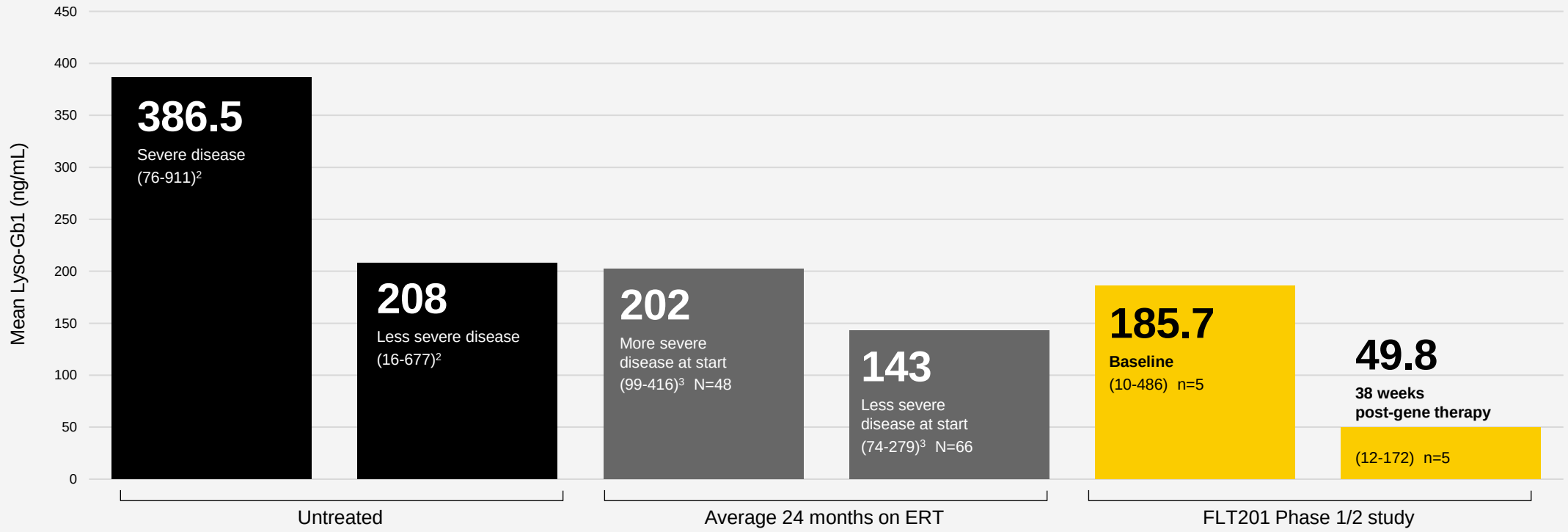


Dried blood spot lyso-Gb1 concentration over time.
Patients A-D have been off their background therapies for ~10.5-15 months
Data cut off Dec. 6, 2024

GALILEO-1 trial results:

FLT201 reduces lyso-Gb1 to near-normal levels

FLT201 drives lyso-Gb1 lower relative to ERT

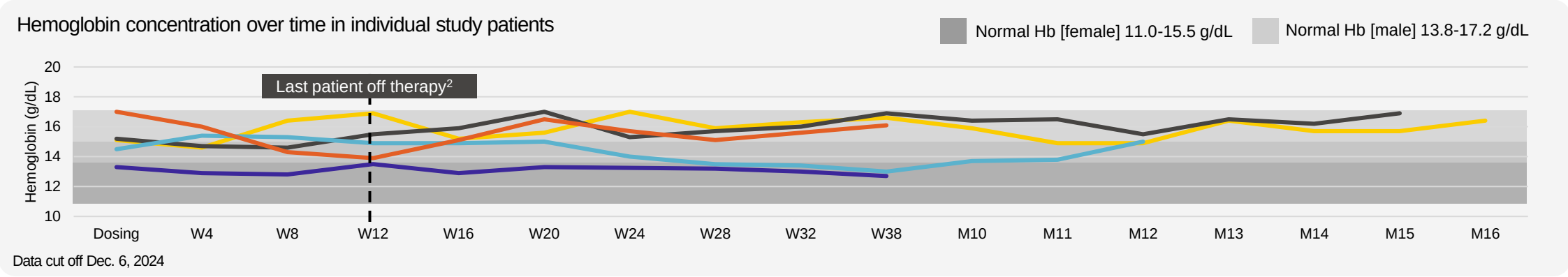


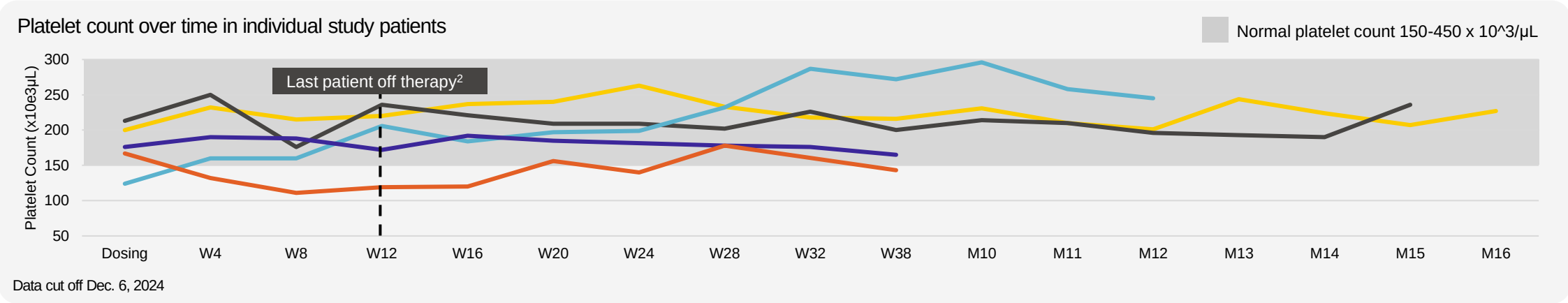
Mean DBS lyso-Gb1 concentration (range); mean concentration in healthy population is 5.4 (1.5-16) ng/mL; measured in different populations at different timepoints.
[1]Median value and range (Dinur 2022); [2]Curado 2023; [3]Dinur 2021
Data cut off Dec. 6, 2024

GALILEO-1 trial results:

Sustained improvement or maintenance of hemoglobin and platelets observed after withdrawal of ERT or SRT

Reductions are seen quickly in heme and platelets when patients come off ERT/SRT[1]





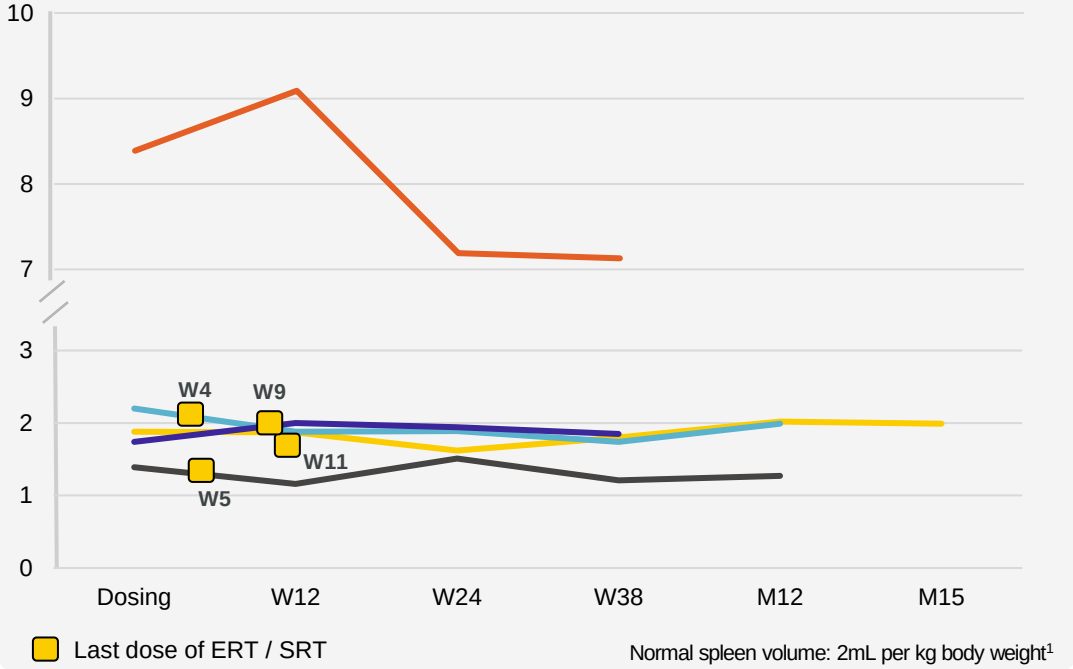
[1]Zimran 2011; [2]Patient E remains on background therapy

Patient A Patient B Patient C Patient D Patient E

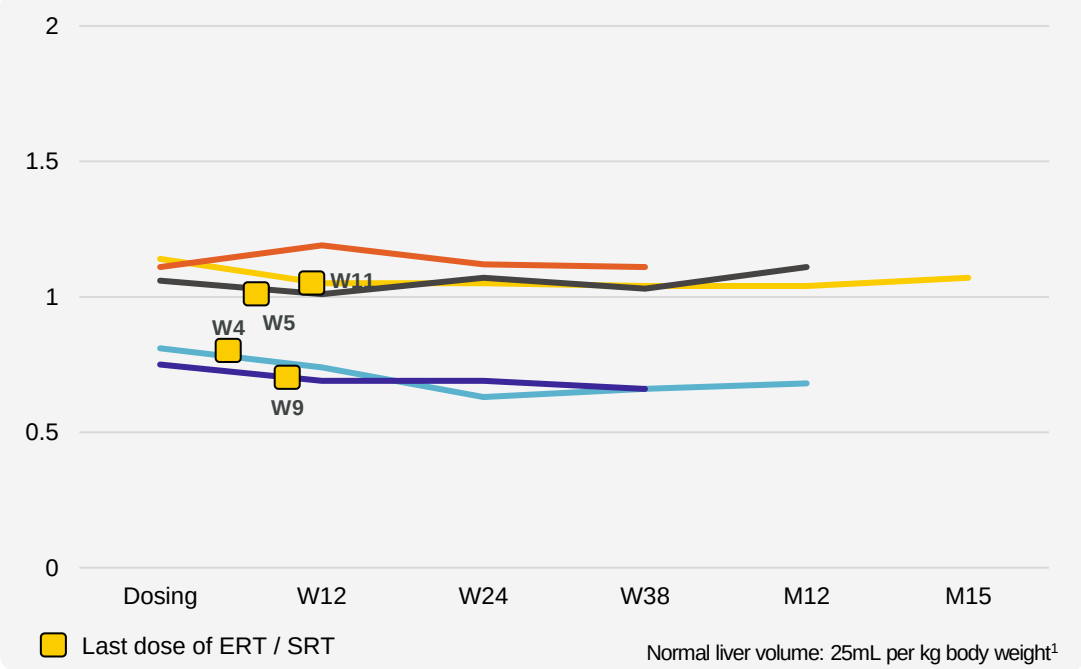
GALILEO-1 trial results:

Spleen and liver volume maintenance or improvement observed after withdrawal of ERT and SRT

Spleen volume by MRI as a multiple of normal in individual study patients



Liver volume by MRI as a multiple of normal in individual study patients



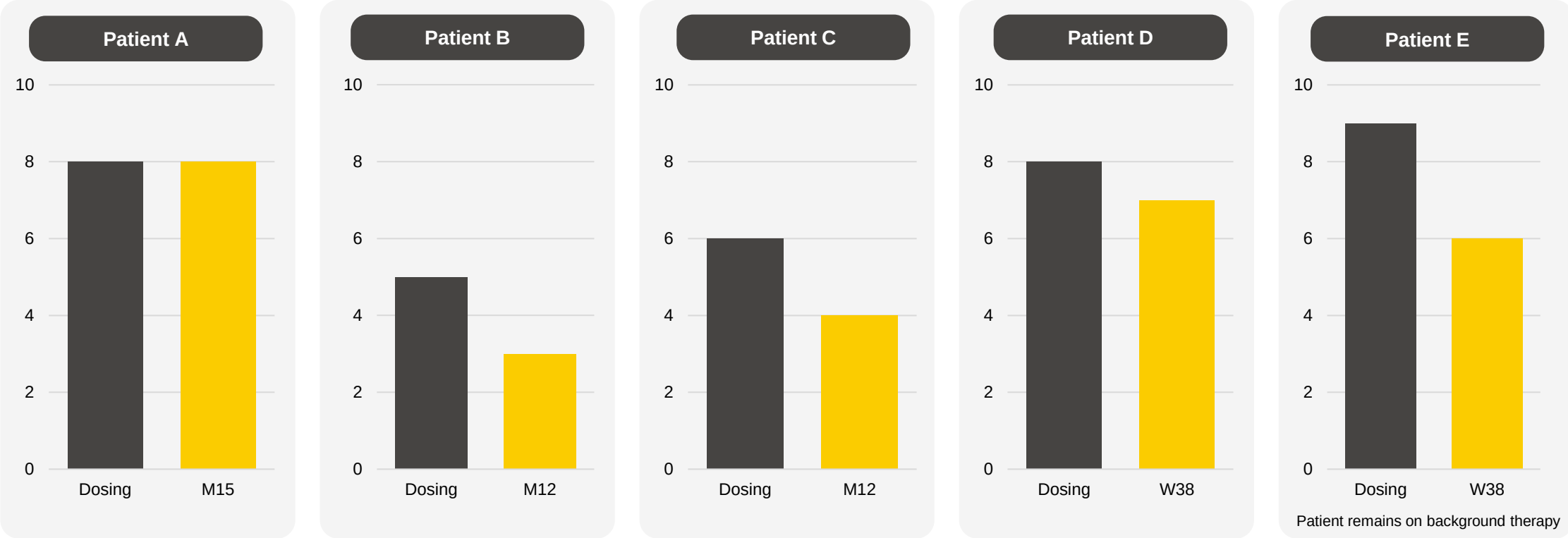
Data cut off Dec. 6, 2024

[1]Pastores et al. *Blood Cells, Molecules and Diseases.* 2014;53: 253–260

GALILEO-1 trial results:

Improvement or maintenance of bone marrow burden (BMB)

BMB correlates with bone necrosis, fractures, bone pain and joint replacements and remains one of the greatest unmet needs in Gaucher disease

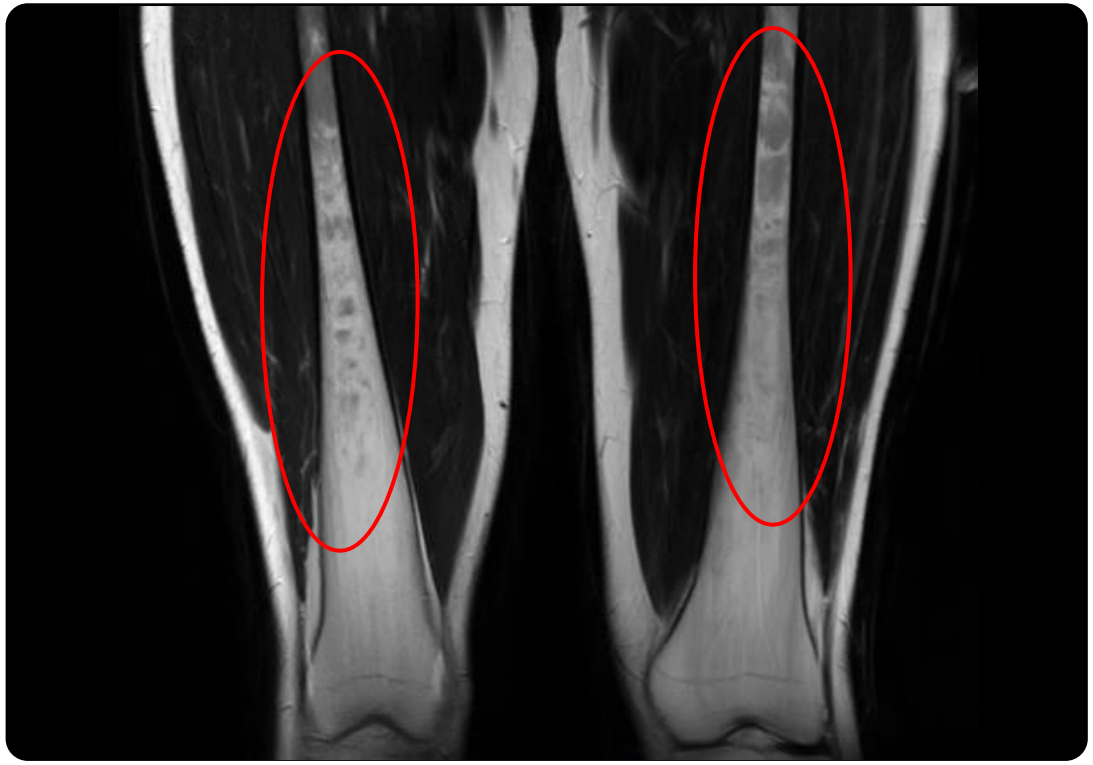


Patients A-D have been off their background therapies for 11.5-16 months.
Data as of Jan. 31, 2025

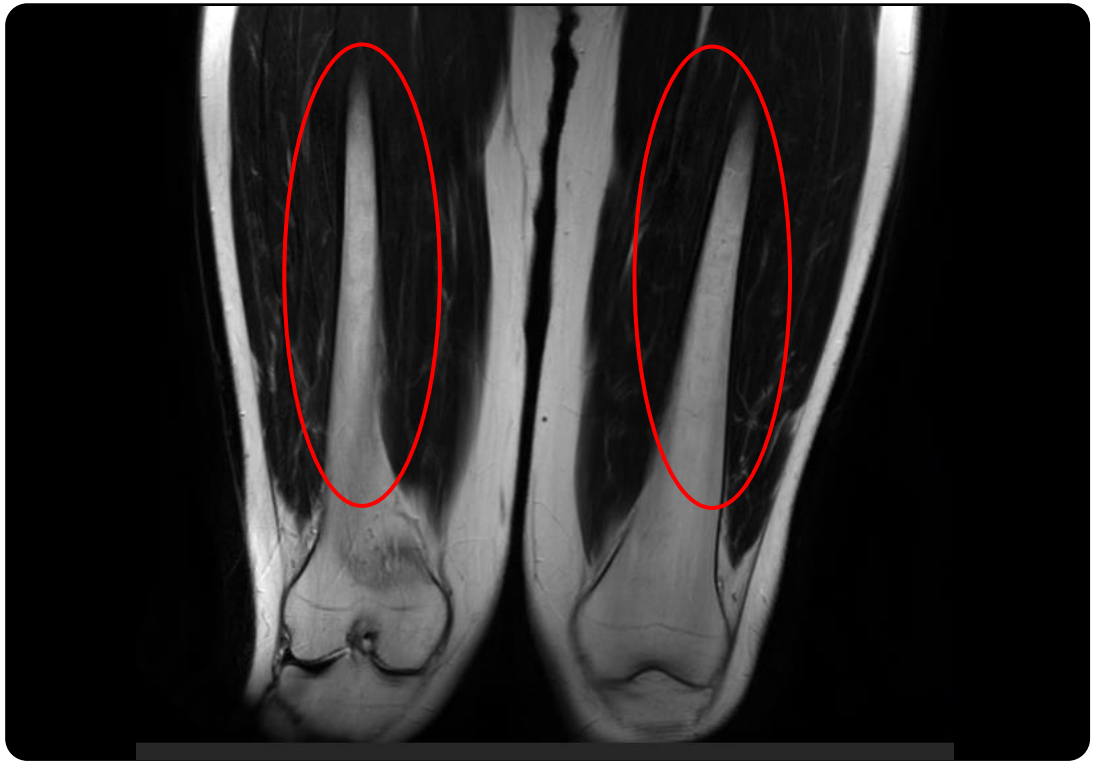
GALILEO-1 trial results:

Clinically meaningful improvement in patient with significant bone disease

MRI shows clearance of diseased cells and reappearance of healthy fatty marrow



Baseline femur score: 3

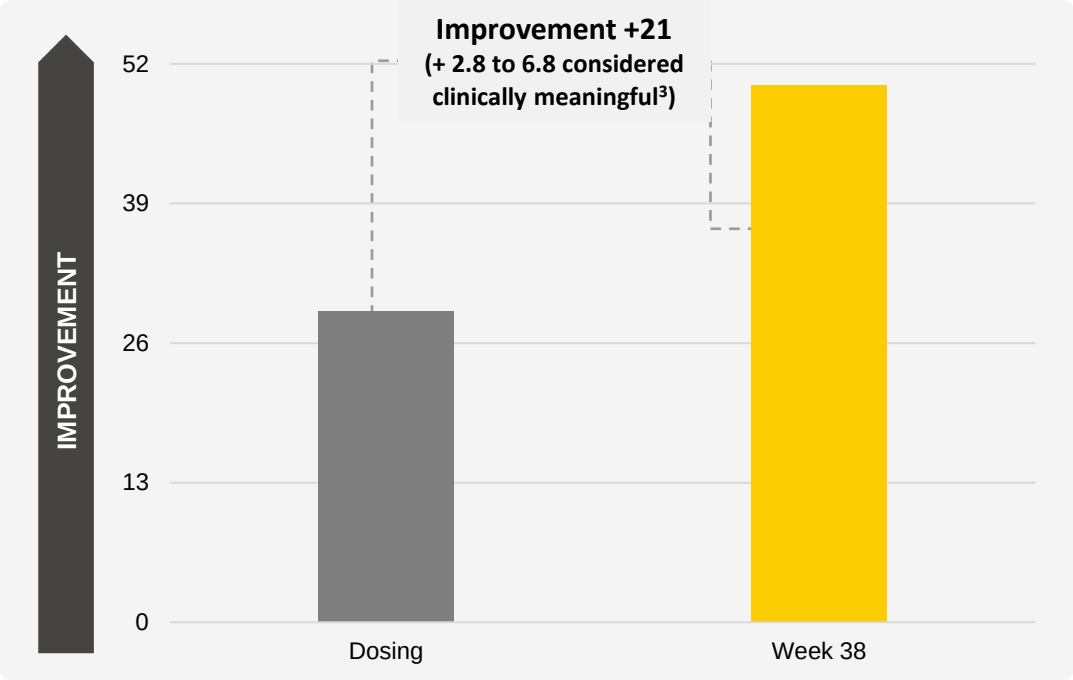


Month 12 femur score: 1

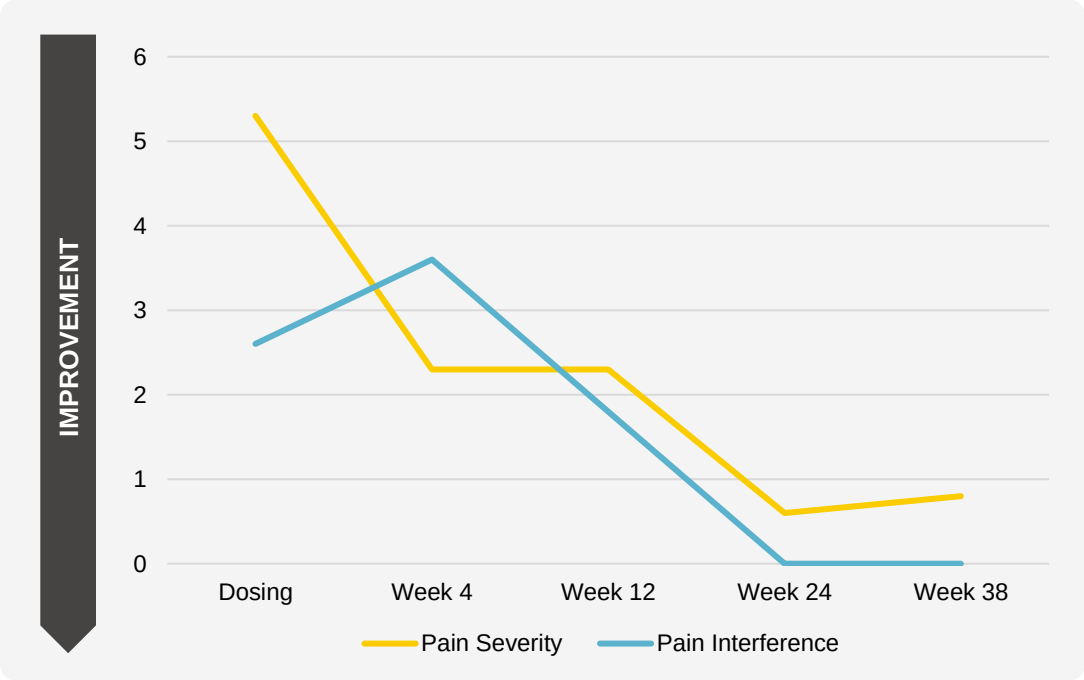
GALILEO-1 trial results:

Substantial improvement in fatigue and pain leading to improved functioning

FACIT fatigue scale (0–52)[1]



Pain severity and interference (0-10)[2]



Data cut off Sep. 27, 2024
[1]FACIT = Functional Assessment of Chronic Illness Therapy; [2]Measured by Brief Pain Inventory Short Form; [3]Greenbaum 2020; clinically meaningful in cancer, lupus, HUS, RA

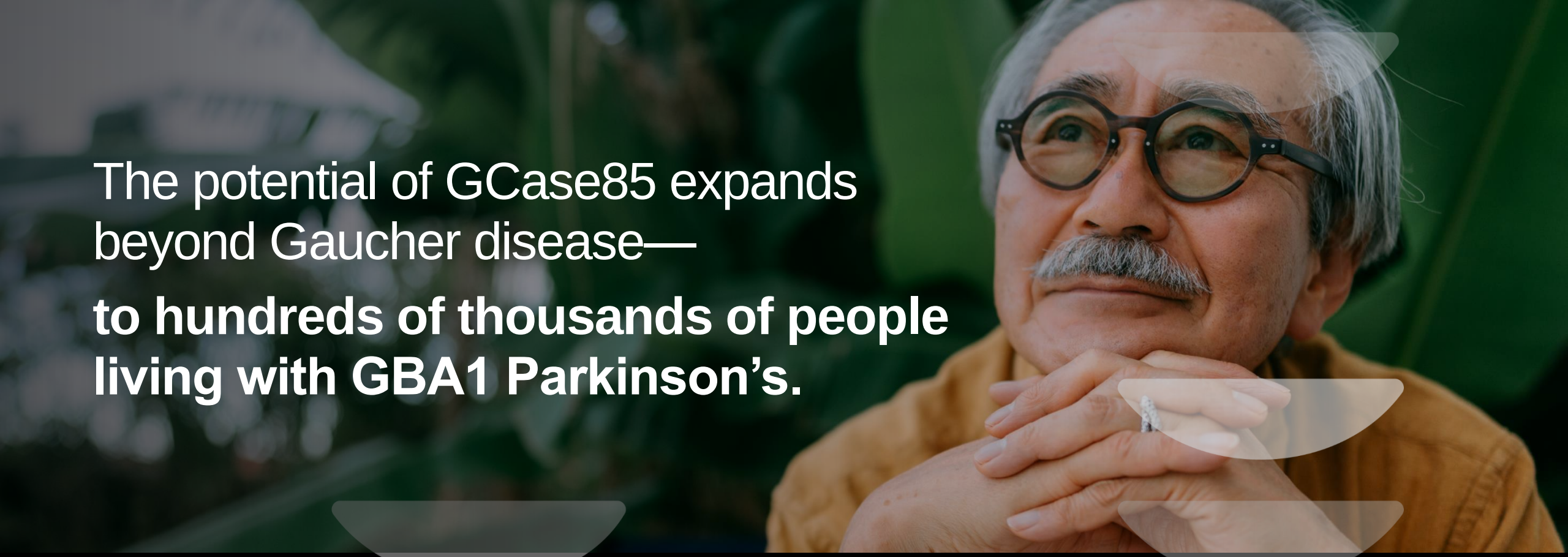
GALILEO-1 trial results:

Well tolerated, with a favorable safety profile

- No dose-limiting toxicities
- Two cases of ALT elevations above normal range deemed related to therapy
  - Spontaneously resolved or managed with immune therapy
  - No impact on efficacy
- Transient anti-GCase antibodies in two patients with no impact on clinical parameters
- ADRs related to immune management consistent with known profile

Summary of Adverse Drug Reactions for FLT201 and Immune Management (n≥2)	
Adverse Drug Reactions (ADR)	# events (# patients)
FLT201	
Elevated alanine aminotransferase (ALT)	7 (6)
Fatigue	4 (3)
Activated partial thromboplastin time prolonged	2 (2)
Anti-GCase neutralizing antibodies	2 (2)
Prednisone	
Hyperglycemia	3 (3)
Weight increase	2 (2)
Panic attack	2 (1)
Tacrolimus	
Diarrhea	4 (4)

Data cut off Dec. 6, 2024

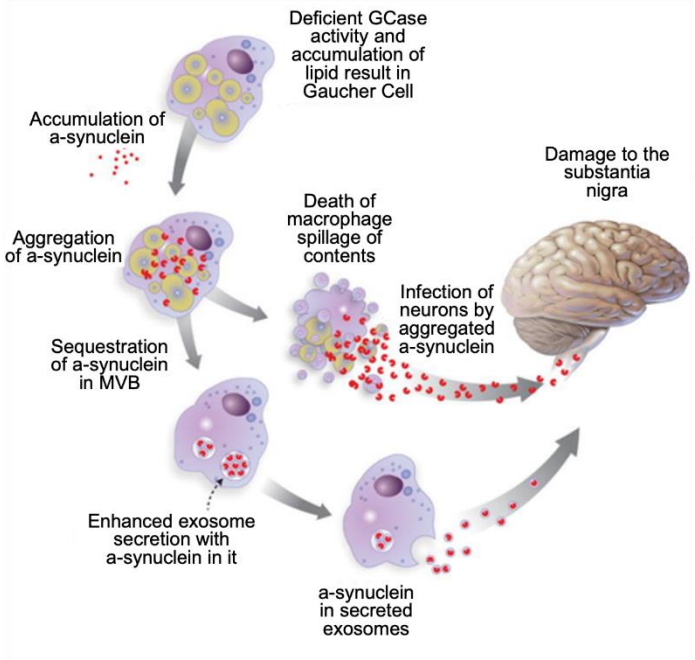


The potential of GCase85 expands beyond Gaucher disease—

to hundreds of thousands of people living with GBA1 Parkinson’s.

A debilitating disease with a clear, unmet need

GBA1 Parkinson's disease
GCase deficiency leads to accumulation of α-synuclein, a hallmark of Parkinson's



Progressive, neurodegenerative condition with no disease-modifying therapy

5-15%

of people with Parkinson's disease have *GBA1* mutations[1]

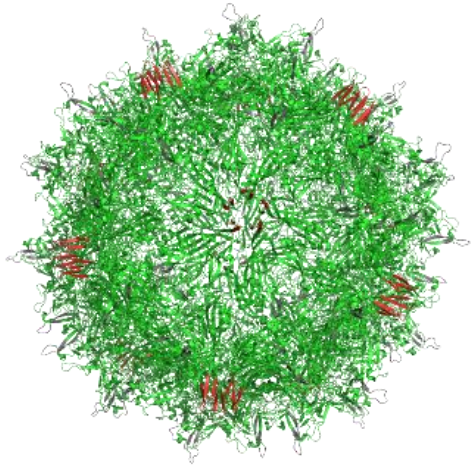
~190K people

have GBA1 Parkinson's in the U.S., U.K., and EU4

[1]*Cells* 2022, 11(8), 1261; https://doi.org/10.3390/cells11081261

SPR301: A potentially disease-modifying treatment for GBA1 Parkinson's with a highly differentiated profile

AAV9 capsid is known for effective transduction of brain cells at low doses



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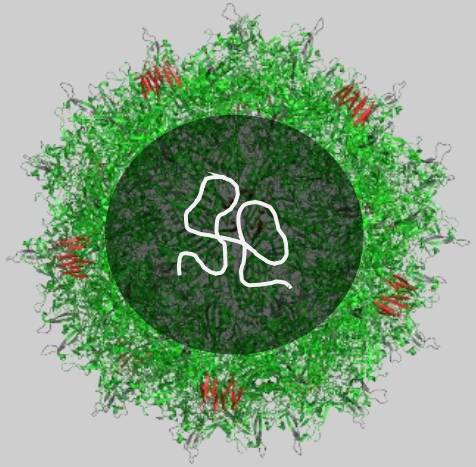
Optimized genome boosts neuronal cell expression while minimizing harmful astrocyte and microglia activation to increase therapeutic window



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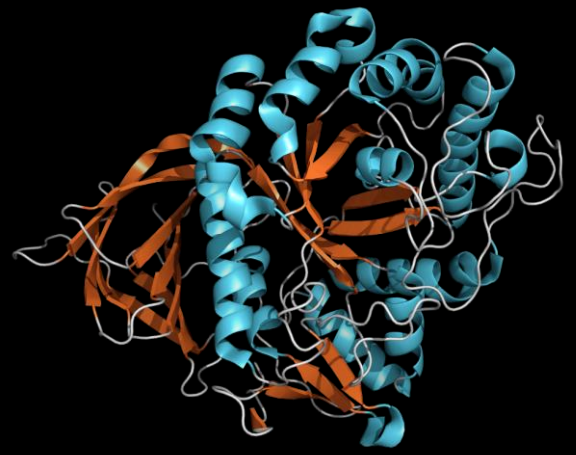
Engineered *GBA1* transgene encodes engineered GCase85, which offers dramatically longer half-life and more stability in the brain



Achieving broad distribution at low doses

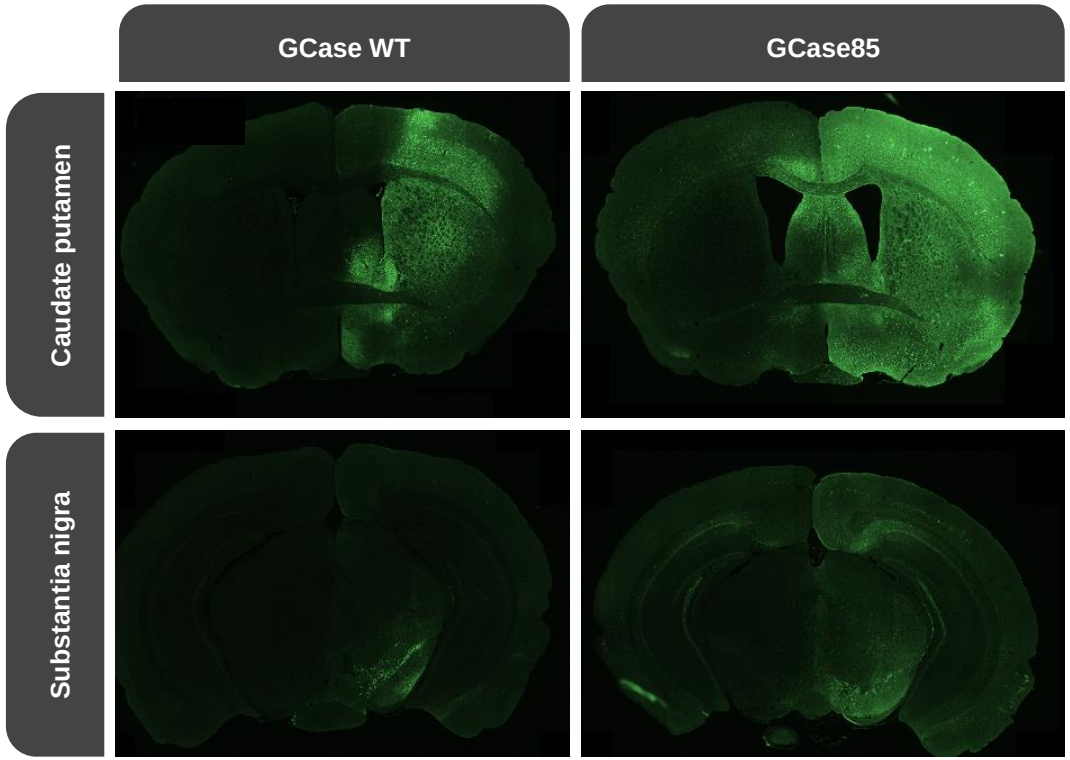
Data from ongoing preclinical studies

SPR301 preclinical study results:

Superior distribution throughout the brain compared to wildtype

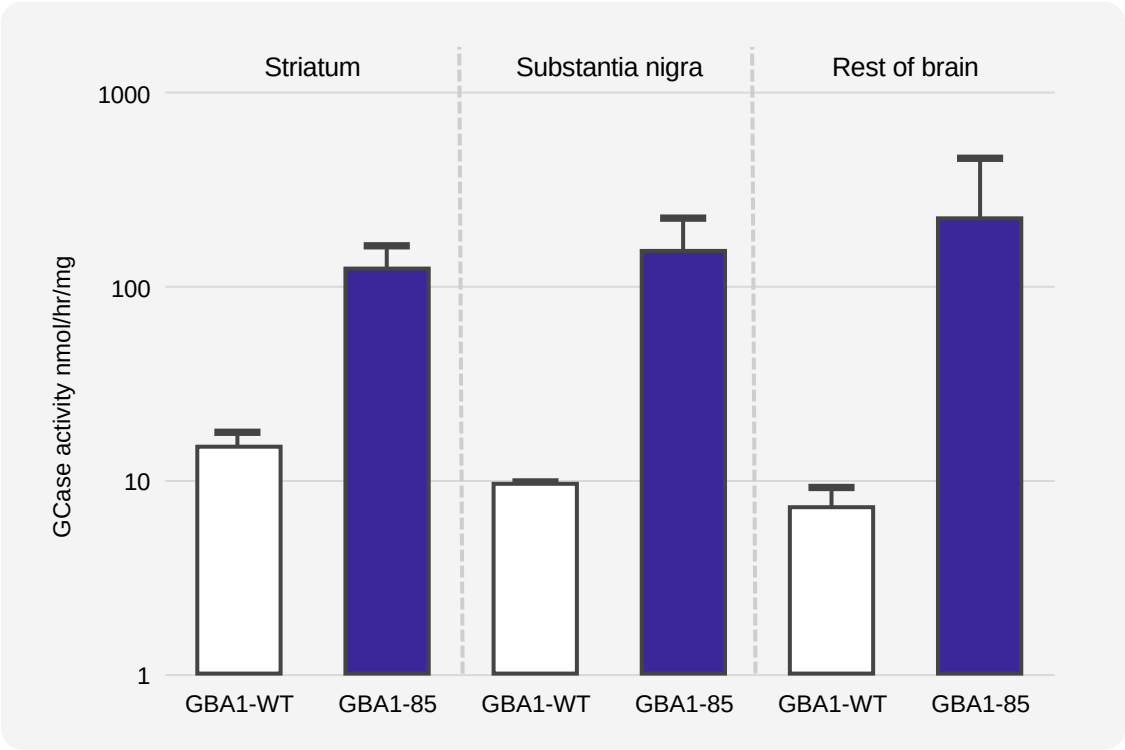
GCase85 distributes broadly and cross-corrects non-transduced cells

Distribution in the brain



Representative coronal sections of animals injected with either AAV9-GBA1-WT or AAV9-GBA1-85 labeled for GCase, n=4. Dosed AAV9 at 1.3e10 vg per mouse by unilateral injection of the right hemisphere striatum.

Activity in brain regions

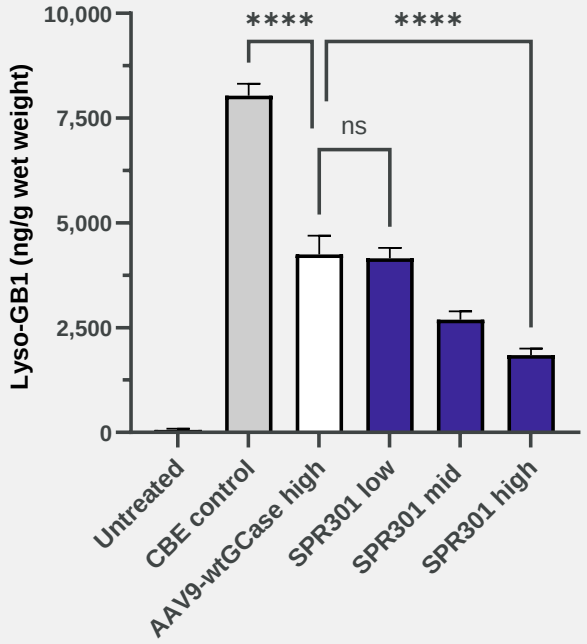


Injected with indicated AAVs, samples dissected from striatum, substantia nigra, or the rest of the brain. The GCase activity is normalized for VG, n=3, data denoted as mean ± SD.

SPR301 preclinical study results:

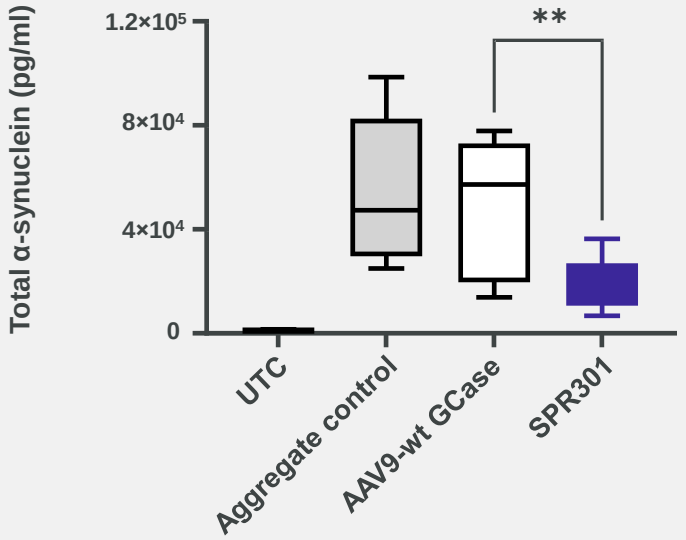
Potential for greater efficacy with a favorable safety profile

Wider therapeutic window, with 25-fold lower dose showing equivalent lyso-Gb1 reduction as high-dose AAV9-wtGCase



CB57BL/6J (n=8) was treated with CBE 100 mg/kg i.p. daily for 15 days either alone or in combination with a single dose of AAV9 control (1.3e10 vg), AAV9-wt GCase (1.3e10 vg) or a series of increasing doses of SPR301 in 5-fold steps from low (5.2e8 vg) to medium (2.6e9 vg) to high (1.3e10 vg). All vector doses were administered directly to the putamen as a single injection. Ordinary one-way ANOVA; ***p=0.0002 and ****p<0.0001

Higher, sustained activity levels in the brain more effectively reduce α-synuclein in neuronal cells compared to wildtype



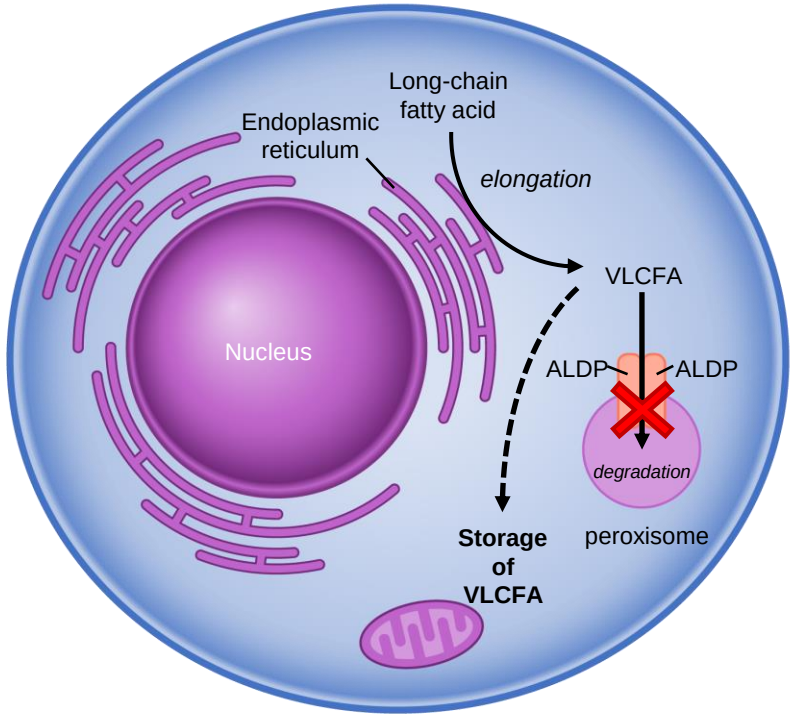
Tested in the surrogate disease model, SH-SY5Y plus α-synuclein (4µg/ml), with vectors at MOI 2.5x10^5; SH-SY5Y cells were pre-treated with *GBA* gene therapy for 24h before challenging them for 24h with recombinant α-synuclein aggregate; N=3 (n=6-10), data denoted as mean ± SEM. T-test analysis vs. AAV9-wtGCase; **p<0.01.

AMN is another neurodegenerative condition with no disease-modifying treatment available.

At least, not yet.

A progressive, devastating condition without a true treatment

Adrenomyeloneuropathy (AMN)
Caused by a mutation in X-linked gene *ABCD1*



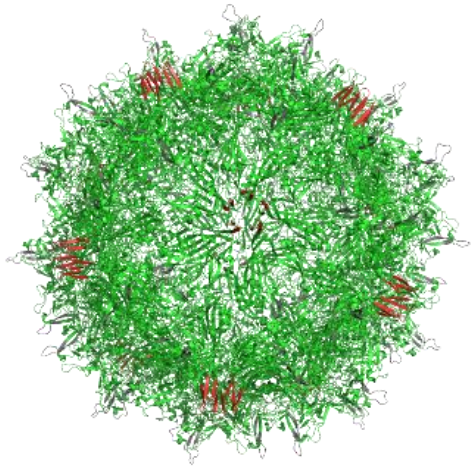
Progressive, neuro-degenerative condition with no disease-modifying therapy, leading to mobility loss, risk of falls, sensory loss, and debilitating pain

8K-10K

men diagnosed in the U.S., U.K., and EU4

SBT101: A potential first-in-class gene therapy for AMN

AAV9 capsid is ideal for spinal targeting



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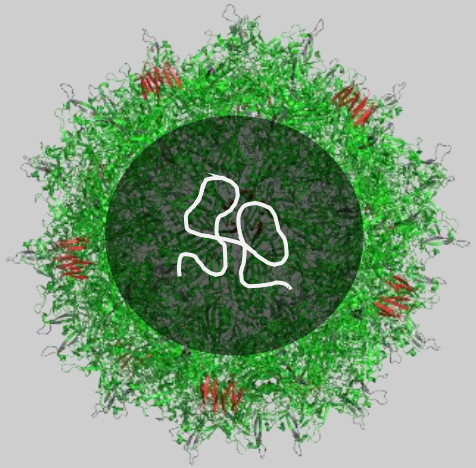
Selected promoters drive higher levels of expression in the spine



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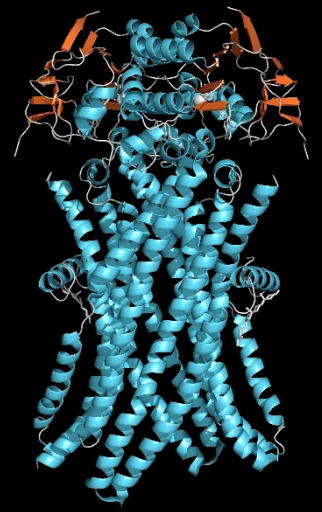
Key therapeutic gene is a copy of the human *ABCD1* gene to produce the missing enzyme



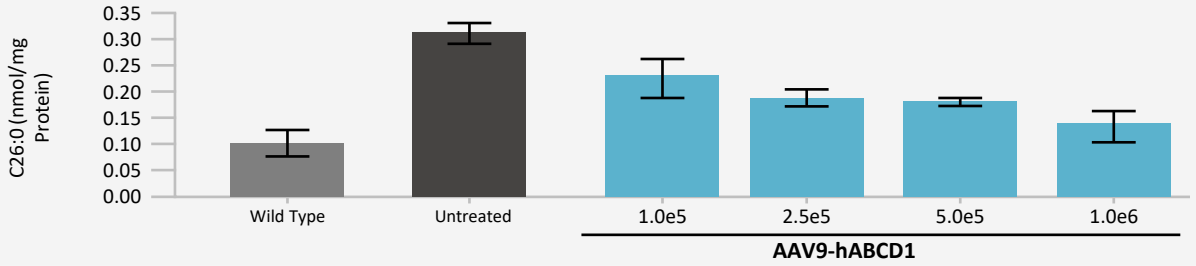
Achieving elevated expression and decreasing toxic substrates

Data from preclinical studies

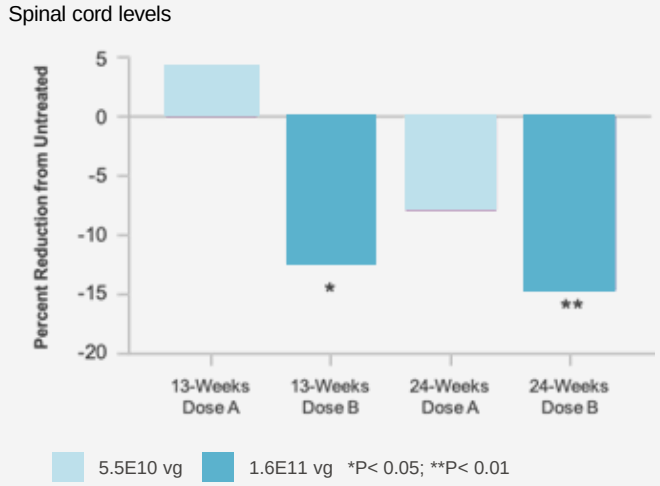
SBT101 alters underlying cause of disease in pre-clinical experiments supporting advancement to clinic

Preclinical proof-of-concept and safety demonstrated

AAV9-ABCD1 lowers VLCFA to wt levels *ex vivo* in mixed mouse ABCD-/- Glial Cell Culture



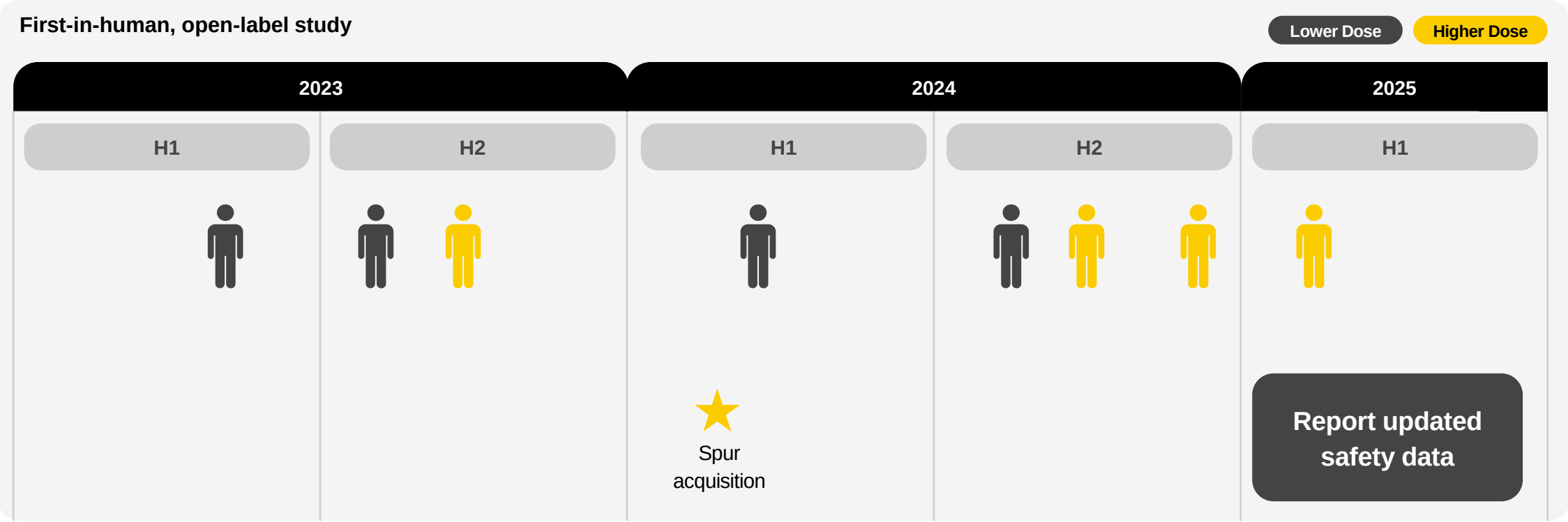
SBT-101 dose response and VLCFA lowering in ABCD1 -/- mice



Biodistribution/safety in NHP

- Target biodistribution and expression (>50% neurons) achieved with delivery over 6 hours
- Distribution/expression throughout spinal cord and DRG
- Distribution persists 12M+
- Safety demonstrated through 12 months in pilot tox and GLP tox

Ongoing PROPEL Phase 1/2 trial in AMN



Well tolerated in all patients

Patient 2 died of causes unrelated to drug; no changes to trial protocol or safety monitoring per DSMB and regulators

Moving toward more

- Optimizing every component of our product candidates to realize outsized clinical results at lower doses
- Advancing gene therapy candidates with the potential to set new standards of care in Gaucher disease, GBA1 Parkinson's disease, and AMN
- Ambitious research strategy to move gene therapy into more prevalent diseases

Creating more impact for more people.

A team known for making an impact

Michael Parini

Chief Executive Officer and Director

- 20+ years as a senior executive in leading biopharmaceutical companies

Pam Foulds, MD

Chief Medical Officer

- 25+ years of medical and clinical leadership

Henning Stennicke, PhD

Chief Scientific Officer

- 25+ years of scientific leadership experience

Paul Schneider

Chief Financial Officer

- 25+ years of global financial, commercial, and operational experience

Jay Bircher

Chief Technical Operations Officer

- 30 years of quality and technical operations experience

Nicole Jones

Chief People Officer

- 25+ years of global human resources experience

Chip McCorkle

VP, GC & Corporate Secretary

- 10 years of experience advising leading biopharmaceutical companies

Help us spur gene therapy **forward.**