

SPUR THERAPEUTICS

Toward MoreTM

December 2024

Legal Disclaimer

This presentation includes 'forward-looking statements' regarding the operations of Spur Therapeutics. Spur Therapeutics' actual results may differ from its expectations, estimates, and projections and, consequently, you should not rely on these forward-looking statements as predictions of future events. All statements other than statements of historical facts contained herein are forward-looking statements that reflect the current beliefs and expectations of management of Spur Therapeutics. These forward-looking statements involve significant risks and uncertainties that could cause the actual results to differ materially from those discussed in the forward-looking statements. Most of these factors are outside of the control of Spur Therapeutics and are difficult to predict. Factors that may cause such differences include, but are not limited to: the success, cost and timing of Spur Therapeutics' development activities; the commercialization and adoption of Spur Therapeutics' initial and future gene therapy candidates; Spur Therapeutics' ability to obtain and maintain regulatory authorization for its gene therapy candidates; Spur Therapeutics' ability to attract and retain talent; Spur Therapeutics' ability to compete with other companies developing gene therapy candidates; Spur Therapeutics' ability to continue to fund its operations; and economic downturns and political and market conditions beyond the control of Spur Therapeutics and their potential to adversely affect Spur Therapeutics' business, financial condition and results of operations. Spur Therapeutics cautions that the foregoing list of factors is not exclusive and readers should not place undue reliance upon any forward-looking statements, which speak only as of the date made. Spur Therapeutics does not undertake or accept any obligation or undertaking to release any updates or revisions to any forward-looking statements to reflect any change in its expectations or any change in events, conditions or circumstances on which any such statement is based.

The information in this presentation is disclosed for information purposes only and may not be relied upon by any recipient (which shall receive such information at their own risk). Certain information contained in this presentation relates to, or is based on, studies, publications, surveys and other data obtained from third-party sources and Spur Therapeutics' internal estimates and research. While Spur Therapeutics believes these third-party sources to be reliable as of the date of this presentation, they have not been independently verified, and Spur Therapeutics makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third party sources, and any and all liability for such third-party sources is specifically excluded. In addition, all of the market data included in this presentation involve a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, although Spur Therapeutics believes its own internal research is reliable, such research has not been verified by any independent source.

Toward the next generation of gene therapy

Our vision

To bring the transformative impact of genetic medicine to millions of patients around the world



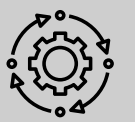
Our mission

To redefine what gene therapy can do



Our approach

To optimize every component of our product candidates, improving genetic expression and targeted delivery to realize outsized clinical results



Shifting paradigm from modality as innovation toward gene therapies that set new standards of care

First-generation gene therapies

Natural serotype capsids and wild-type transgenes

Serious diseases with therapies

Focused on leveraging modality to free people from chronic therapy

Comparable outcomes to standard of care and/or safety and durability issues limit uptake

Serious diseases with no therapies

Focused on providing a disease-modifying therapy where nothing exists

Value driven by delivering life-changing clinical outcomes for patients

Next-generation of gene therapies

Optimized capsids and transgenes

Serious diseases with therapies

Focused on delivering better efficacy than SoC with acceptable safety

One-time treatment is key benefit, but value driven by delivering better clinical outcomes for patients

Serious diseases with no therapies

Focused on providing a disease-modifying therapy where none exists

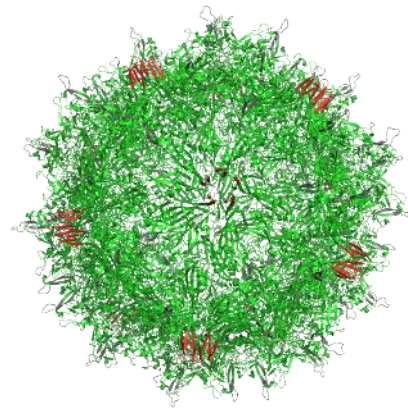
Value driven by delivering life-changing clinical outcomes for patients

Advancing the practice of genetic medicine

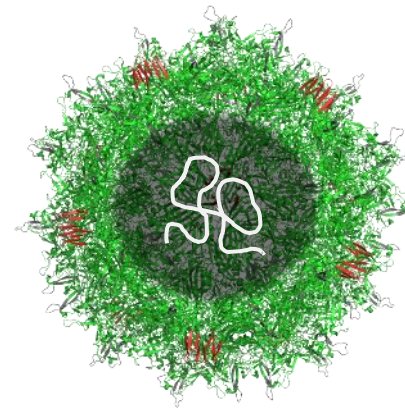
Targeting well-defined diseases

- Serious, chronic diseases
- High unmet need
- Right target with validated biology
- Consistent delivery of therapeutic protein highly likely to improve patient outcomes

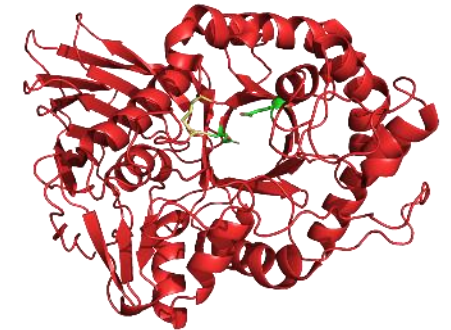
Optimizing every component of our product candidates



Selective Capsid
directed at
the right cells








Optimized Genome
through promoter design
and codon optimization



Engineered Therapeutic
for optimized
exposure and efficacy



Expanding our impact to more prevalent conditions

Disease Area	Program	Approximate Patient #	Research / Preclinical	Phase 1/2	Phase 3
GCase-mediated	Gaucher Disease Type 1 FLT201	~18K US, UK, EU4, Israel			
	GBA1 Parkinson's Disease SPR301	~190K US, UK, EU4			
	Lewy Body Dementia	>1M US			
CNS	Adrenomyeloneuropathy SBT101	~8K–10K US, UK, EU4			
Cardiovascular	Severe Chronic Heart Failure Subset: HFrEF	10K–20K Annually US, UK, Western Europe			

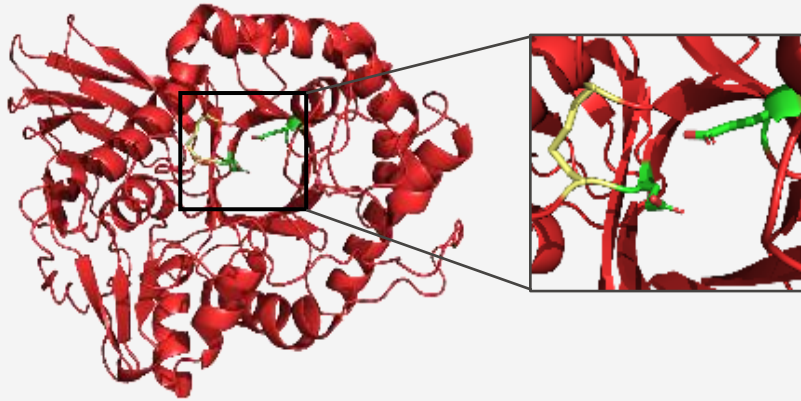
 Indicates potential for expansion

LSDs = lysosomal storage diseases; CNS = central nervous system; 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 adrenomyeloneuropathy (AMN) population from Turk et al *Int J Dev Neurosci* 2020: 80:52-72. Estimated GBA1-PD population is based on 5-15% of diagnosed PD patients, representing approximate number of patients with *GBA1* mutations. Lewy Body Dementia patient number from the Lewy Body Dementia Association. Estimated annual incidence of HFrEF based on company analysis.

GCase85: Core innovation drives highly differentiated profiles for our Gaucher and Parkinson's candidates



GCase85 structure

Two internal amino acid substitutions

- Does not impinge on the active site
- Minimizes 3D structural change

GCase85 dramatically increases half-life compared to wild-type GCase

	Lysosomal pH Half-life (minutes)	Human serum Half-life (minutes)
GCase-wt	388	24
GCase85	>8,639	143
Improvement	>21X	6X

Seasoned team to drive progress and execution

Michael Parini, Chief Executive Officer and Director



20+ years as a senior executive in leading biopharmaceutical companies



Pam Foulds, MD, Chief Medical Officer



20+ 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



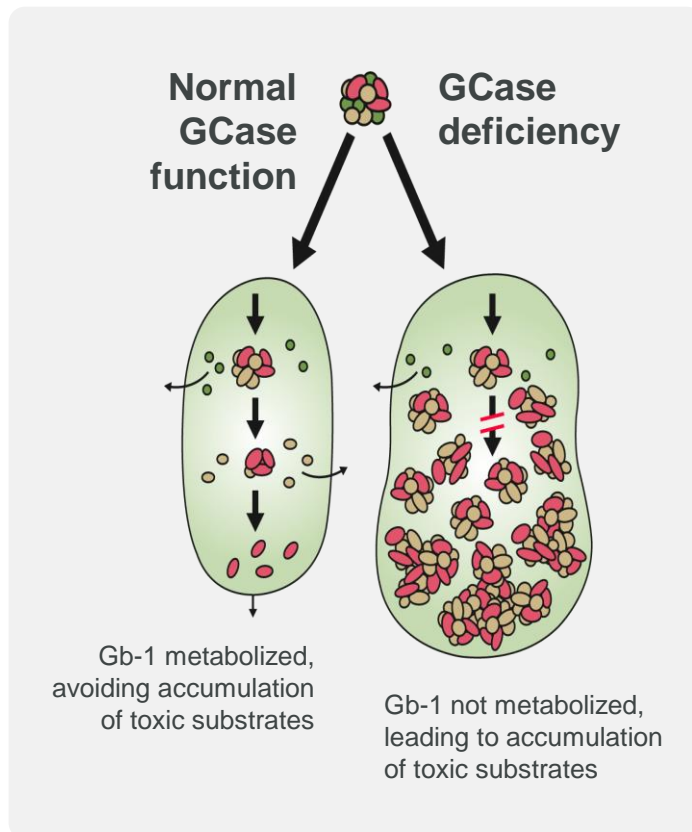
10 years of experience advising leading biopharmaceutical companies



FLT201 for Gaucher disease

Toward a new standard of care

Targeting a chronic, progressive, and debilitating condition



GCase = glucocerebrosidase; Gb-1 = glucosylceramide;
lyso-Gb1 = glucosylsphingosine

SPUR THERAPEUTICS

Gaucher disease

- Mutations in *GBA* gene cause deficiency of GCase enzyme needed to metabolize Gb-1 in the lysosome, resulting in accumulation of toxic substrate lyso-Gb1
- Affects multiple organs, leading to enlarged organs, fatigue, bone pain, and lung dysfunction
- Type 1 most common form of disease, affecting ~94% of Gaucher patients

High ongoing unmet need

- Many patients experience debilitating symptoms despite treatment
- Physicians and patients cite fatigue and bone pain as top ongoing unmet medical needs
- Approved therapies come with heavy life-long treatment burden
- Significant burden and cost for patients as well as on healthcare system

Significant market opportunity

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

Current standard of care still means debilitating symptoms and diminished quality of life

- Short half-life of wildtype GCase limits ERT's ability to reach and penetrate deeper tissues
- Patients on biweekly ERT infusions are uncovered for most of their 2-week period

After 10+ years on ERT, up to **60%** still experience symptoms, including bone pain, lung dysfunction, enlarged organs, fatigue, and low platelet counts¹



enlarged liver

55%

still have moderately enlarged livers †



enlarged spleen

60%

still have moderately or severely enlarged spleens †



low blood counts

50%

still have moderately or severely low platelet counts †

80%

of individuals with severe BMB showed no meaningful improvement after 8 years on ERT²

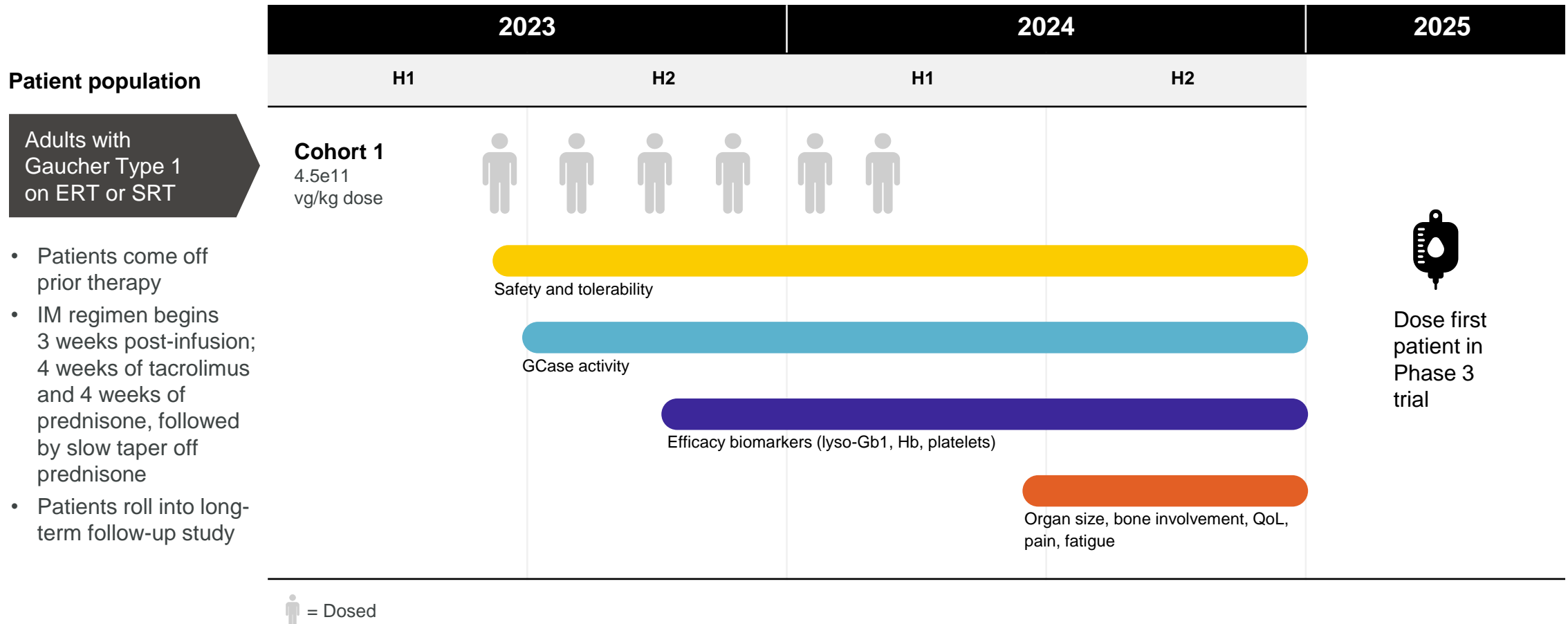
65%

report **fatigue** despite treatment with ERT/SRT³

¹Weinreb et al. 2013, † in those with severe symptoms before ERT. All percentages are approximate rounded to the nearest 5%; ²De Fost 2006; low ERT dose cohort; score of 6 or higher defined as severe BMB; meaningful improvement defined as decrease in BMB score of at least 2 points; ³Wagner 2018.

Completed dosing in Phase 1/2 dose-finding study

GALILEO-1 is a first-in-human, open-label, multicenter study of FLT201



GALILEO-1 trial of FLT201: What have we learned?

Highly compelling efficacy and safety data support 4.5e11 vg/kg dose for Phase 3

Clean safety

6/6 Favorable safety and tolerability in all patients dosed

Well-defined population

Sizable Gaucher disease type 1 patient population of at least 50% NAb negative and available for treatment with FLT201

Compelling efficacy¹

5/5 Dramatic improvements in lyso-Gb1 levels in four patients with persistently high levels and maintenance of low levels in the one patient who entered trial with a well-controlled level

5/5 Improvement in bone marrow burden

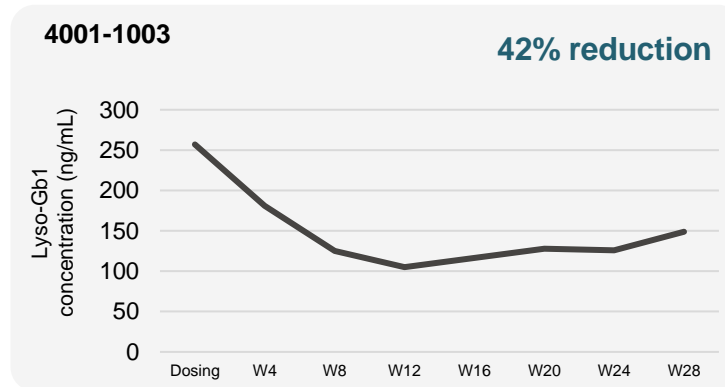
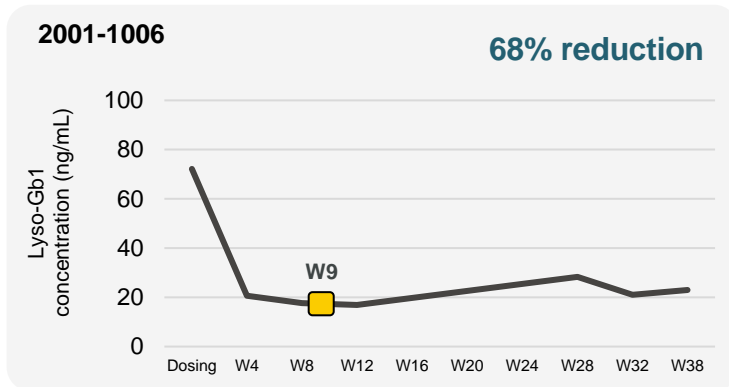
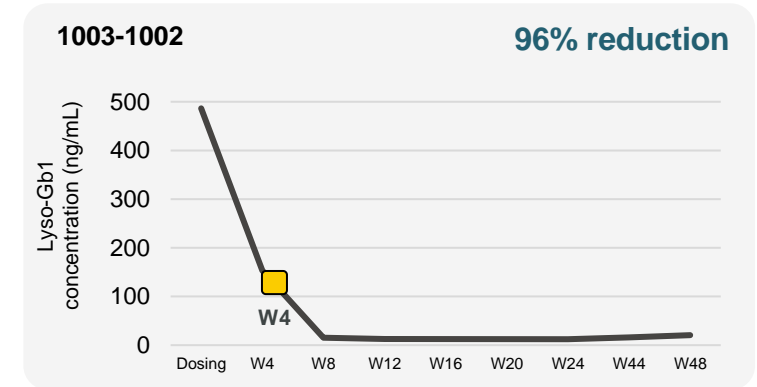
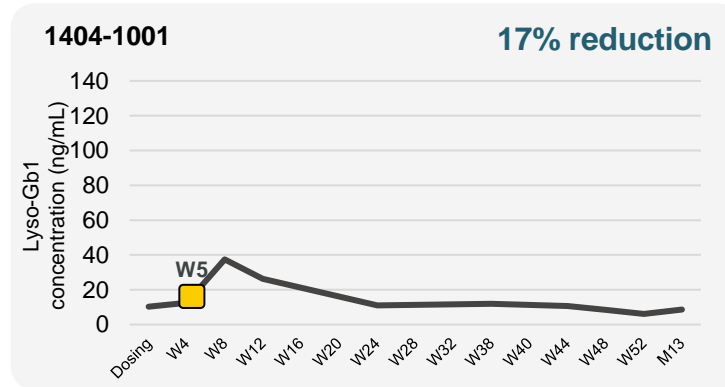
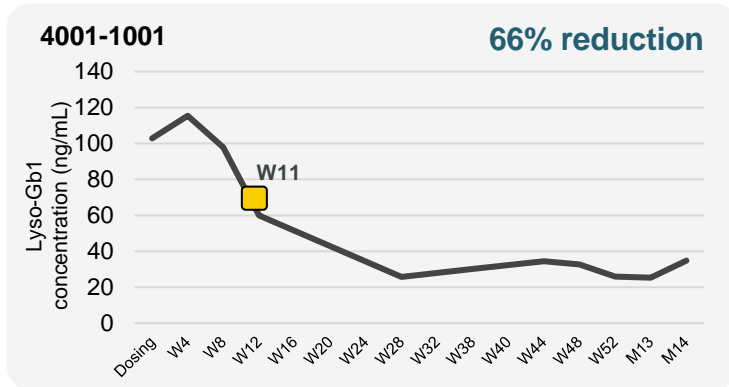
5/5 Maintenance or improvement in hemoglobin, platelets and organ volume

1/1 Clinically relevant improvement in patient-reported fatigue and pain in the one patient who entered trial with debilitating fatigue and pain

¹One patient with detectable NAb to AAVS3 below protocol cut-off excluded from efficacy analysis. Only patients with no detectable NAb will be eligible for Phase 3 trial.
NAbs = Neutralizing antibodies

Dramatic reductions of toxic substrate in patients with persistently high levels despite prior treatment

Dried blood spot lyso-Gb1 concentration over time



Lyso-Gb1 is one of best predictors of disease severity and clinical response

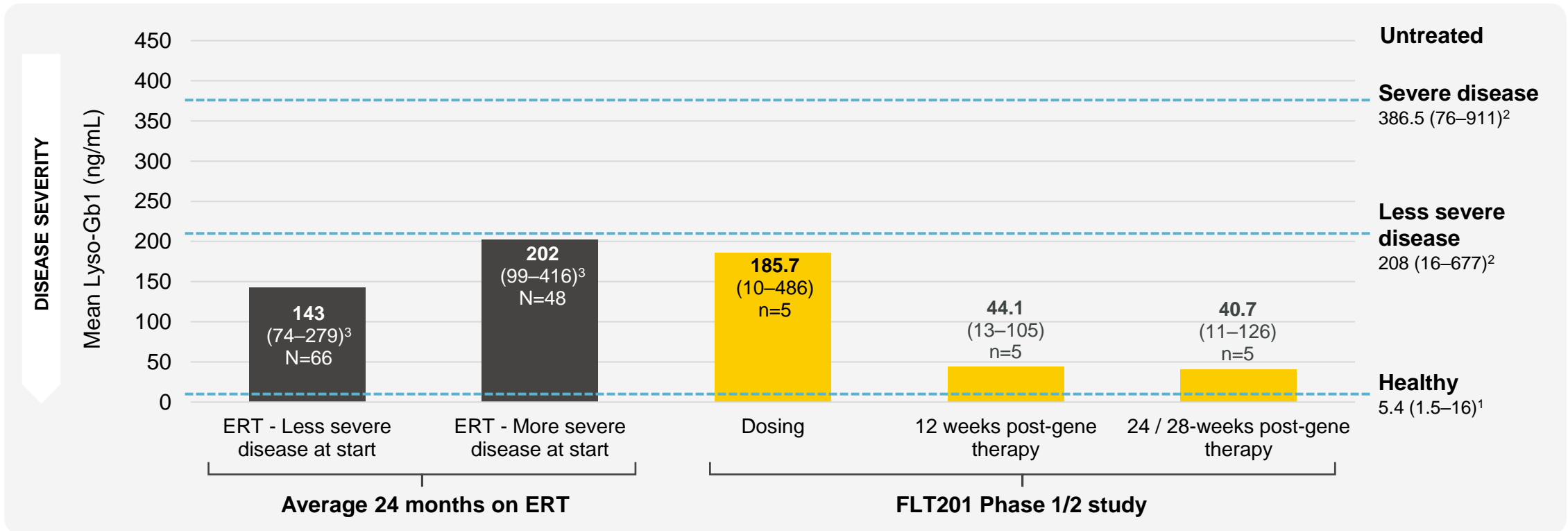
- Highly correlated with outcomes in hemoglobin, platelets, spleen and bone
- Gaucher-specific, highly sensitive

■ Last dose of ERT/SRT

Data cut off Sep. 27th, 2024

FLT201 reduces lyso-Gb1 to near-normal levels

FLT201 drives lyso-Gb1 lower relative to ERT



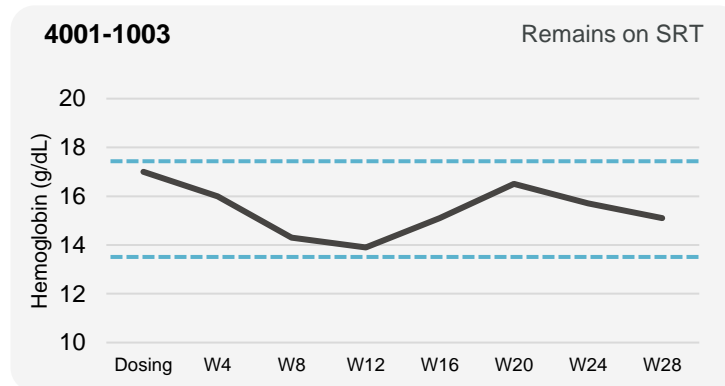
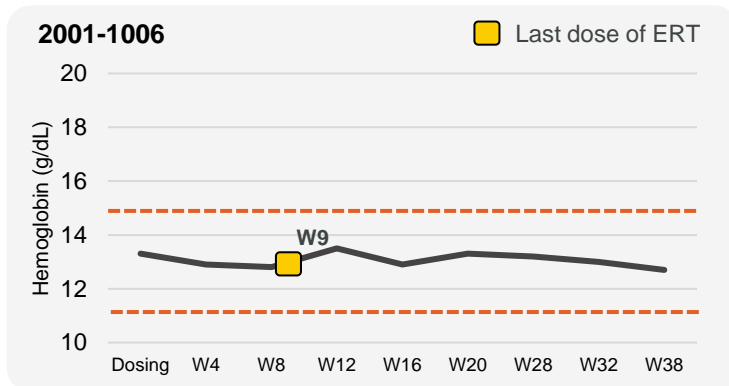
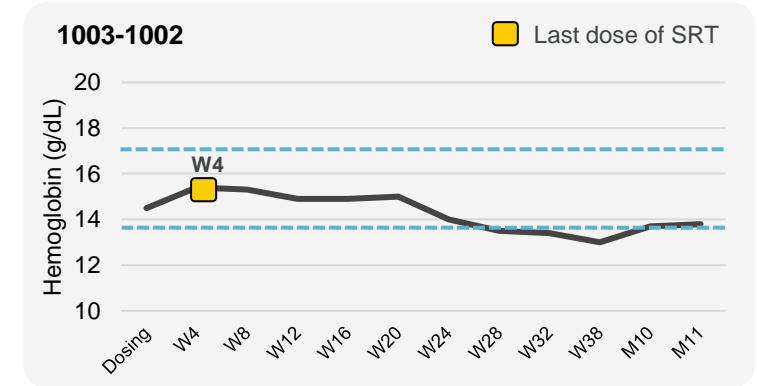
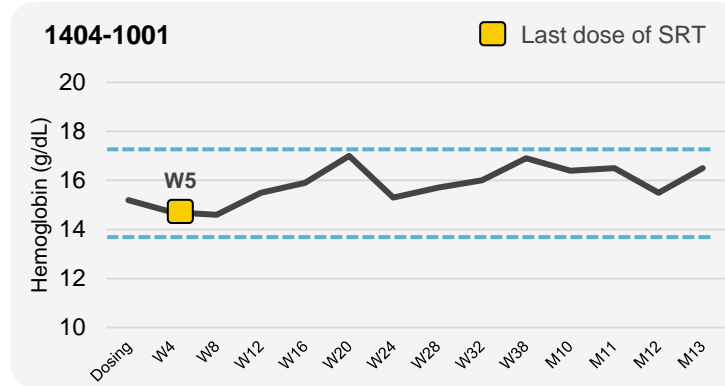
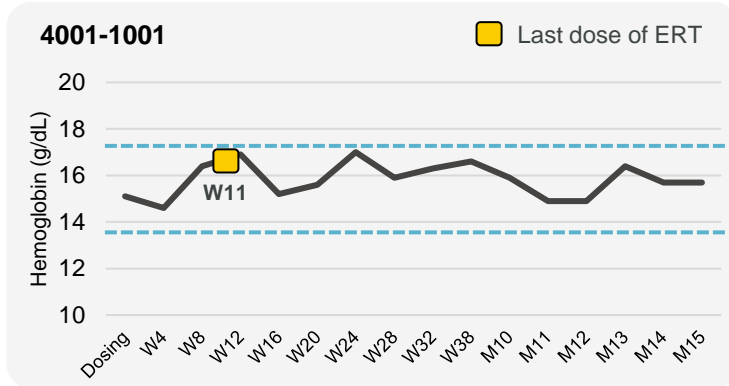
Mean DBS lyso-Gb1 concentration (range); measured in different populations at different timepoints

¹ Median value and range (Dinur 2022); ² Curado 2023; ³ Dinur 2021

Data cut off Sep. 27th, 2024

Sustained hemoglobin maintenance observed after withdrawal of ERT or SRT

Hemoglobin concentration over time



Patient recently diagnosed with iron deficiency unrelated to FLT201

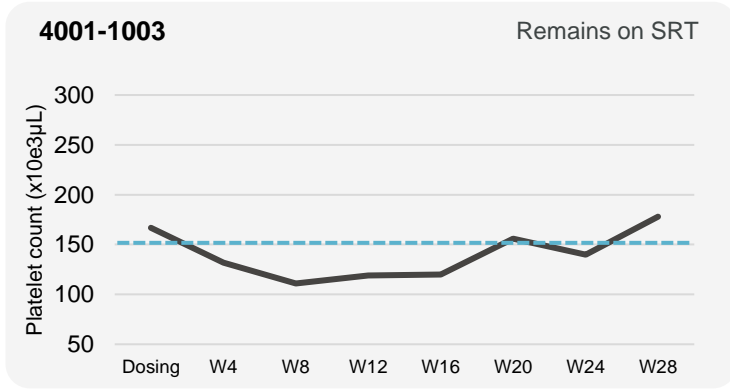
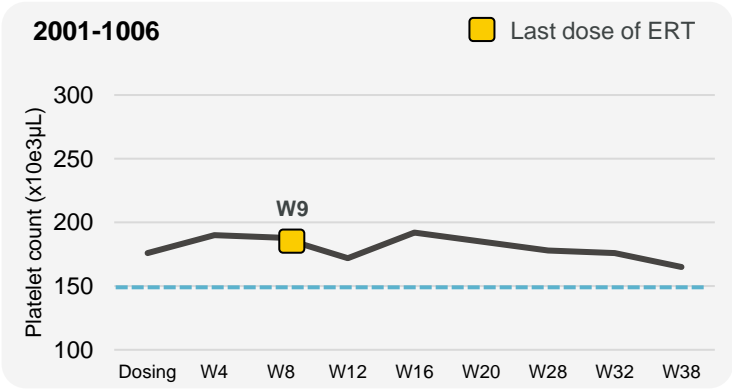
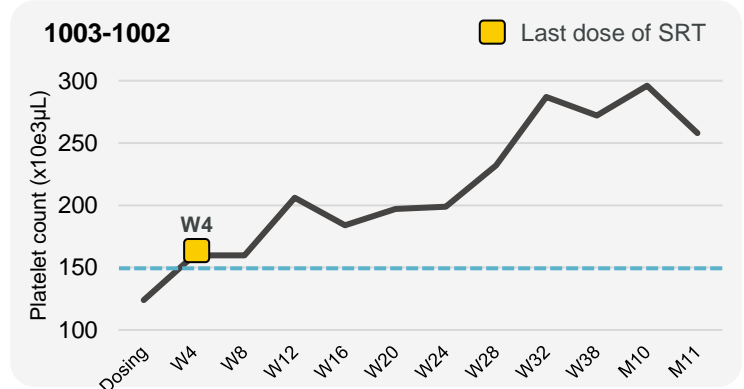
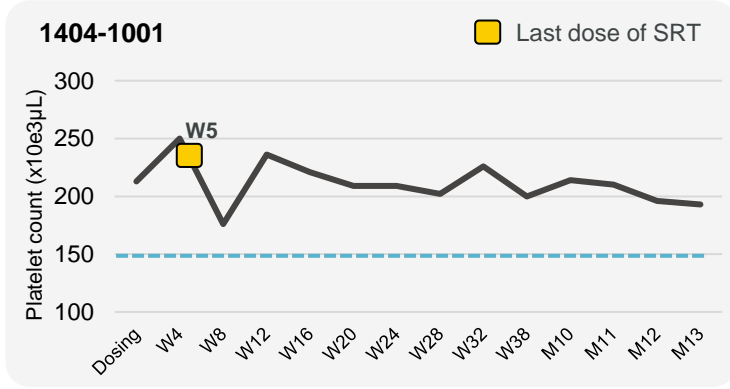
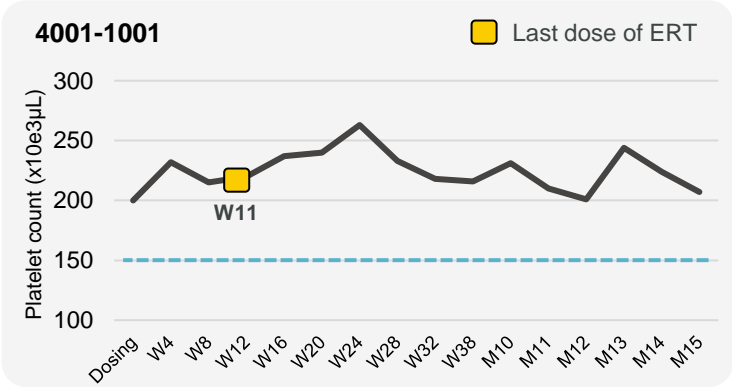
- Normal Hb [male] 13.8-17.2 g/dL
- Normal Hb [female] 11.0-15.5 g/dL

Data cut off Sep. 27th, 2024

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

Ongoing unmet need
50%
of patients have low platelets after 10+ years on ERT¹

Platelet count over time



--- Normal platelet count 150-450 x 10³/µL

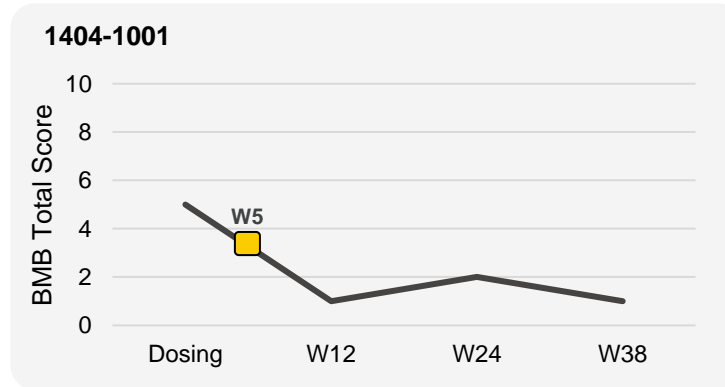
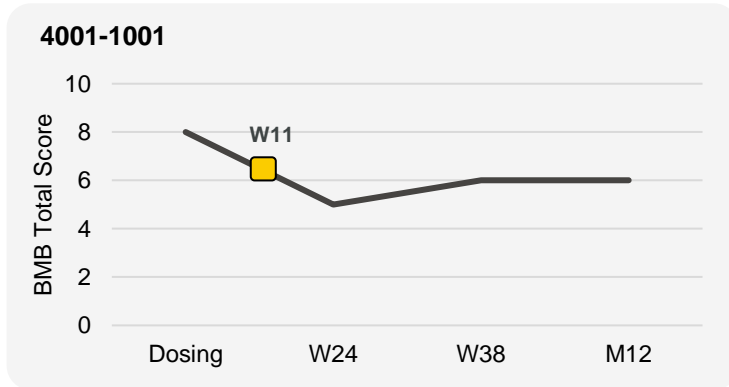
Data cut off Sep. 27th, 2024

¹Weinreb et al. 2013; in those with severe symptoms before ERT; rounded to the nearest 5th percentile

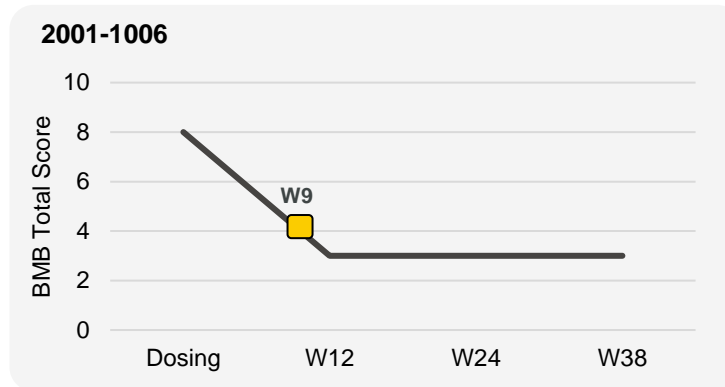
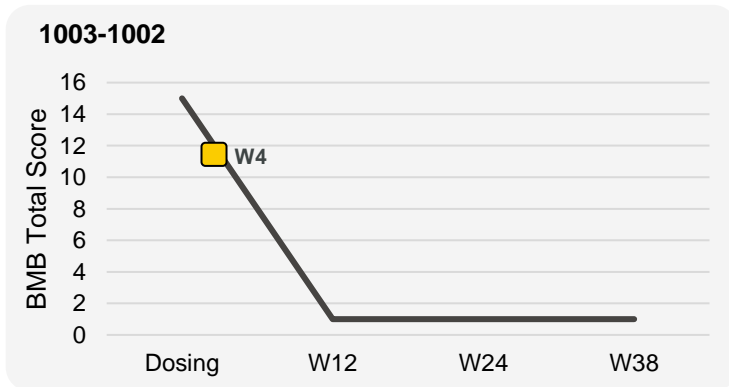
Substantial decreases in bone marrow burden show FLT201 penetrating difficult-to-reach tissues

No meaningful improvement in **80%** of those with severe BMB after 8 years on ERT^{1,2}

BMB score by MRI over time



- Improvements even in patients with severe bone involvement²
- BMB correlated with bone cell death, fractures, bone pain and joint replacements

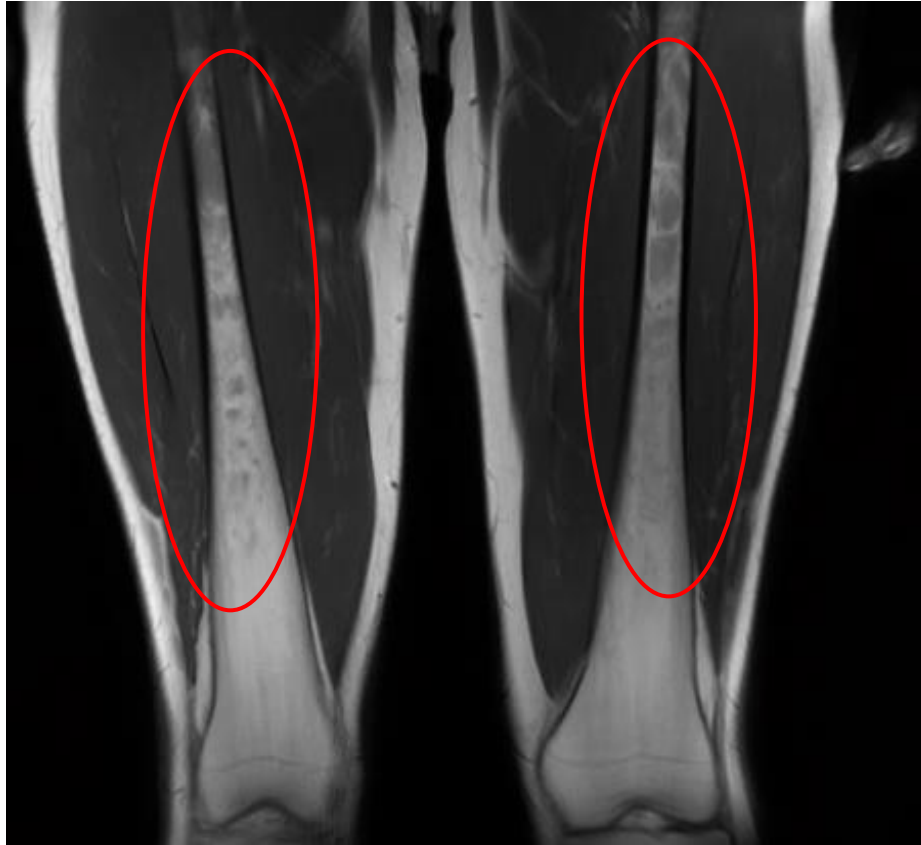


¹Meaningful improvement defined as decrease in BMB score of at least 2 points; ²De Fost 2006; low dose ERT cohort; rounded to the nearest 5th percentile; score of 6 or higher defined as severe BMB

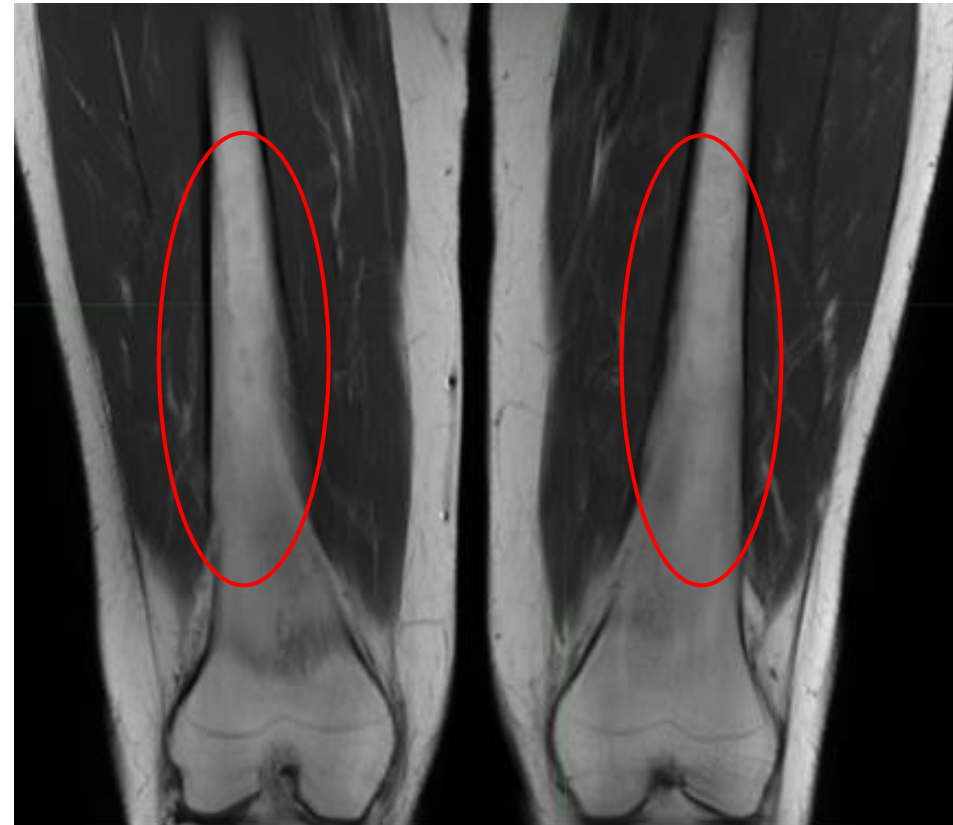
■ Last dose of ERT/SRT

BMB reaches near normal in patient with severe bone disease

BMB at baseline = 15



BMB at 24 weeks = 1

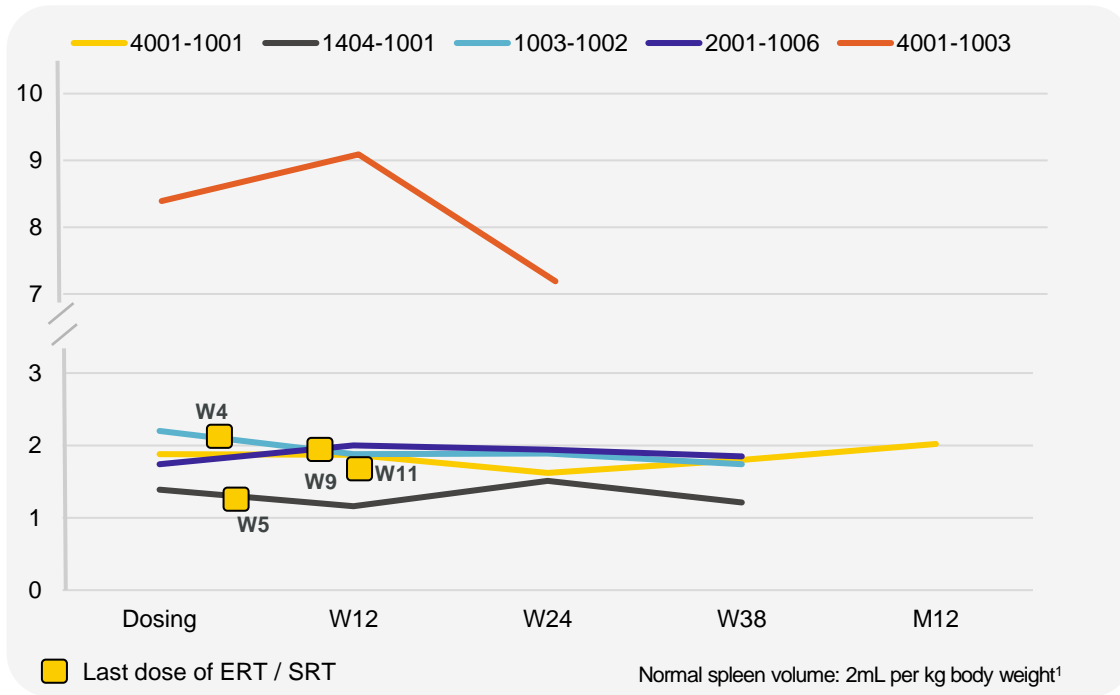


MRI shows:

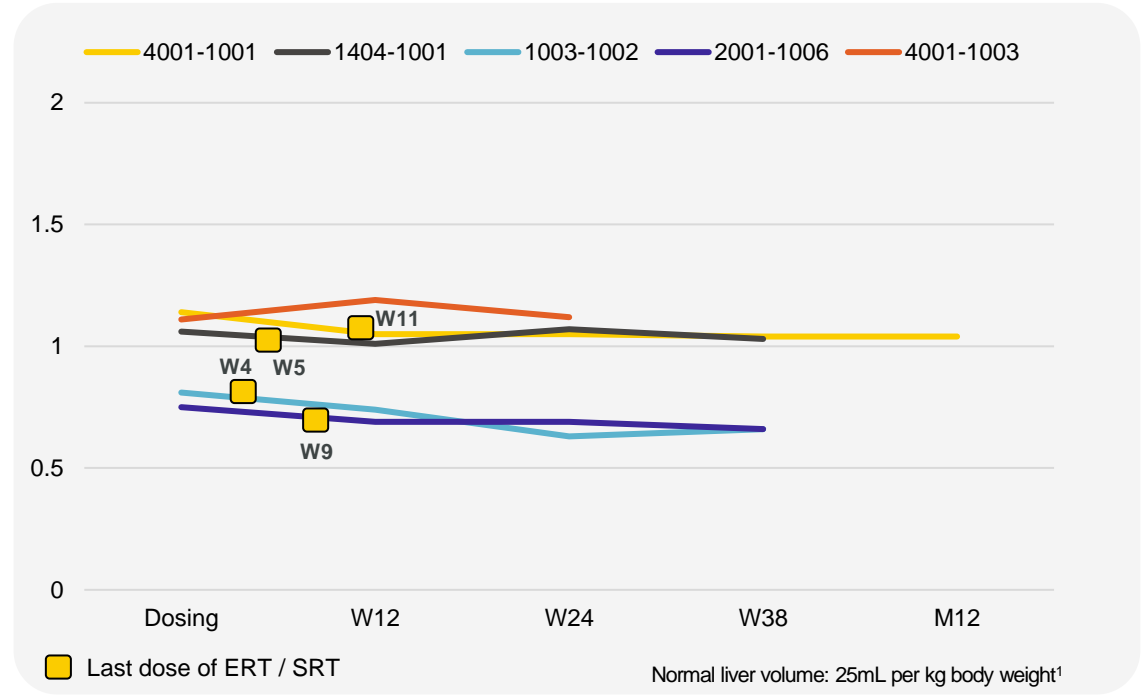
- Clearance of diseased Gaucher cells
- Reappearance of healthy fatty marrow

Maintenance of spleen and liver volume observed post withdrawal of ERT and SRT

Spleen volume by MRI as a multiple of normal



Liver volume by MRI as a multiple of normal

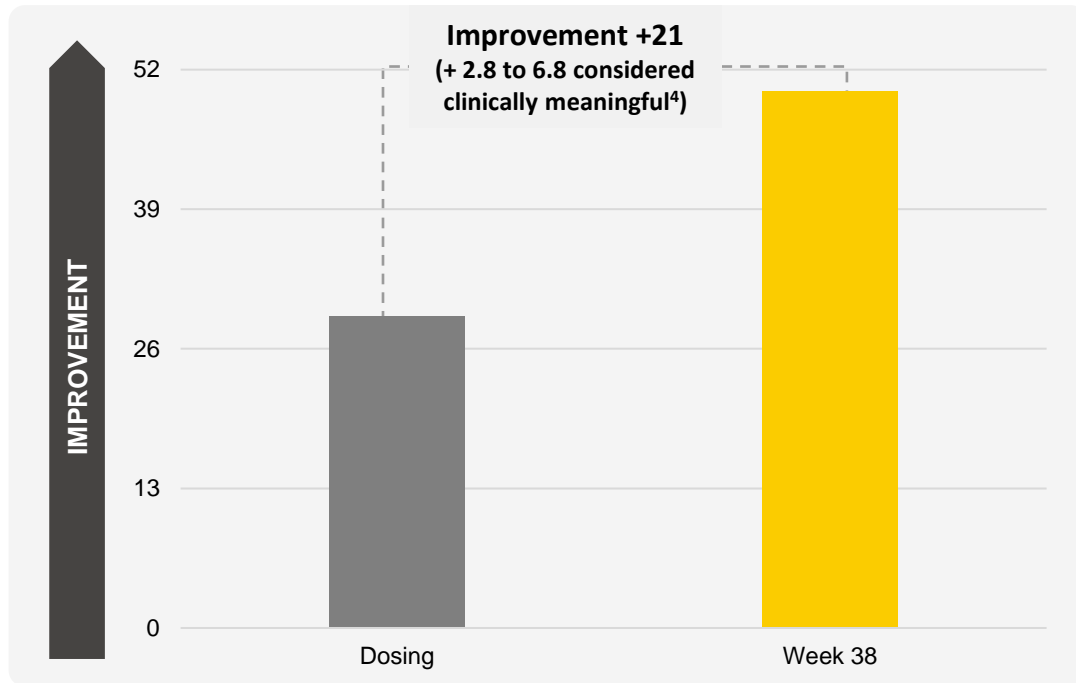


¹Pastores et al Blood Cells, Molecules and Diseases 2014;53: 253–260
Data cut off Sep. 27th, 2024

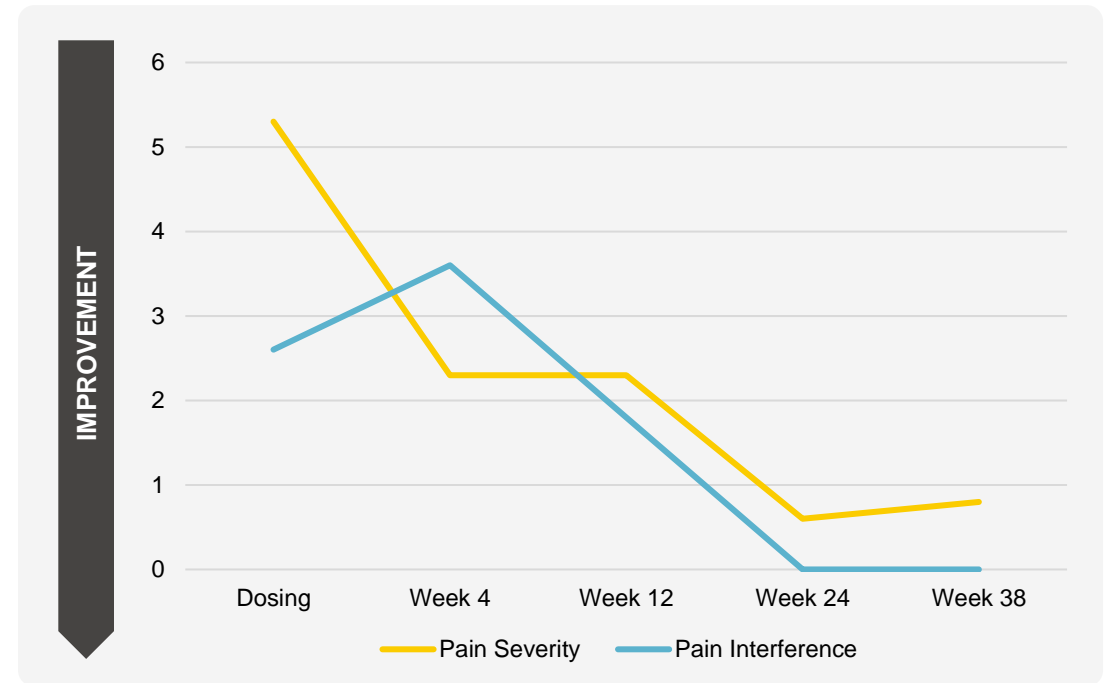
Clinically meaningful improvement in fatigue and pain leading to improved functioning

Patients ranked fatigue #1 and pain #2 as most important symptoms¹

FACIT fatigue scale (0–52)²



Pain severity and interference (0-10)³



¹Zion 2016; ²FACIT = Functional Assessment of Chronic Illness Therapy; ³Measured by Brief Pain Inventory Short Form; ⁴Greenbaum 2020; clinically meaningful in cancer, lupus, HUS, RA
Data cut off Sep. 27th, 2024

FLT201 has been well tolerated, with clean safety profile to date

- Infusions well tolerated; no infusion-related reactions
- Treatment-related adverse events were mild to moderate
- No dose-limiting toxicities
- Any ALT elevations deemed related to therapy were mild and managed with immune therapy with no impact on efficacy
- AEs related to immune management consistent with known profile of prednisone and tacrolimus

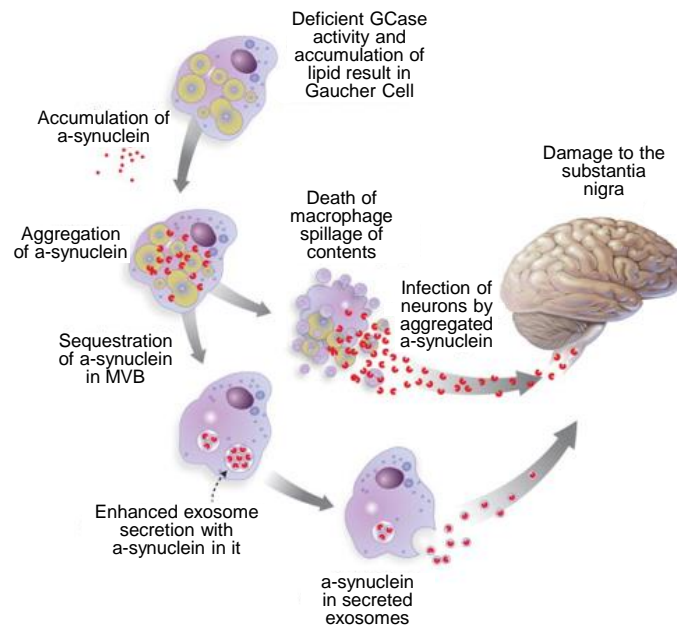
Data cut off Sep. 27th, 2024



Toward a disease-modifying treatment

GCase85 provides opportunity for a best-in-class gene therapy for GBA1 Parkinson's disease

GCase deficiency leads to formation of Lewy bodies (α -synuclein aggregates) and death of dopaminergic neurons via multiple mechanisms

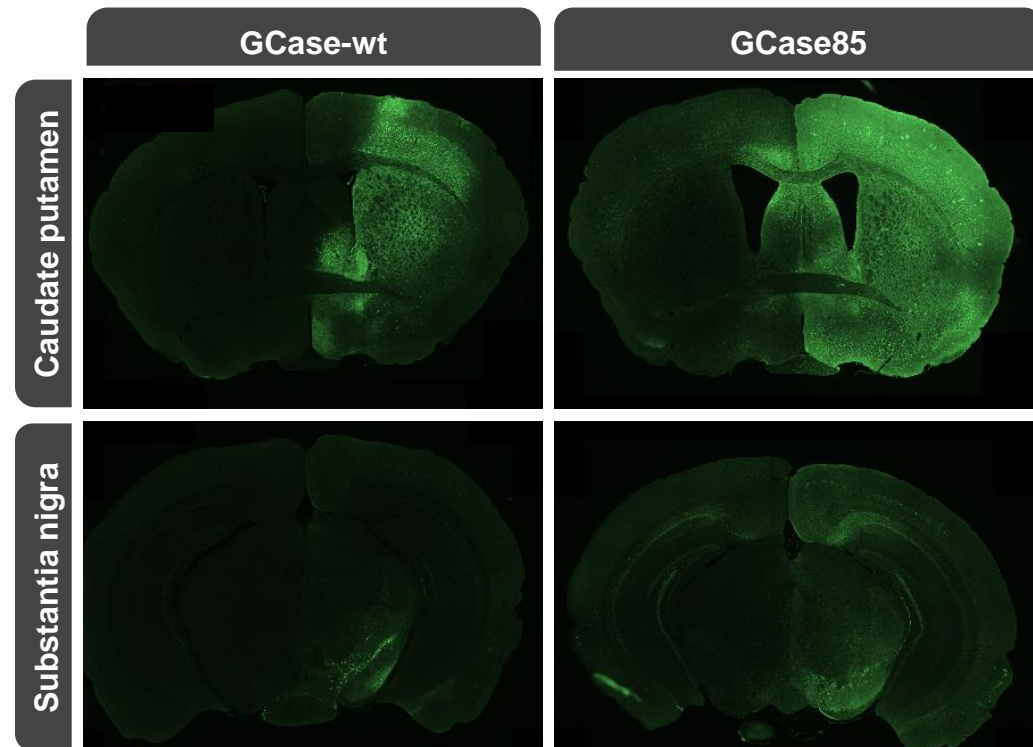


†Cells 2022, 11(8), 1261; <https://doi.org/10.3390/cells11081261>

<p>GBA1 Parkinson's disease</p>	<ul style="list-style-type: none"> • <i>GBA1</i> mutations are most common genetic risk factor for developing PD • Associated with earlier onset, more severe disease and increased risk of progression to dementia • Evidence of reduced GCase activity, even in patients without a known <i>GBA</i> mutation
<p>High ongoing unmet need</p>	<ul style="list-style-type: none"> • No disease-modifying therapies exist for PD • Symptomatic treatments become less effective over time
<p>Substantial, well-defined patient population</p>	<p>5-15% of people with PD have <i>GBA1</i> mutations†</p> <p>~190K patients with GBA1-PD in US, UK, and EU4</p>

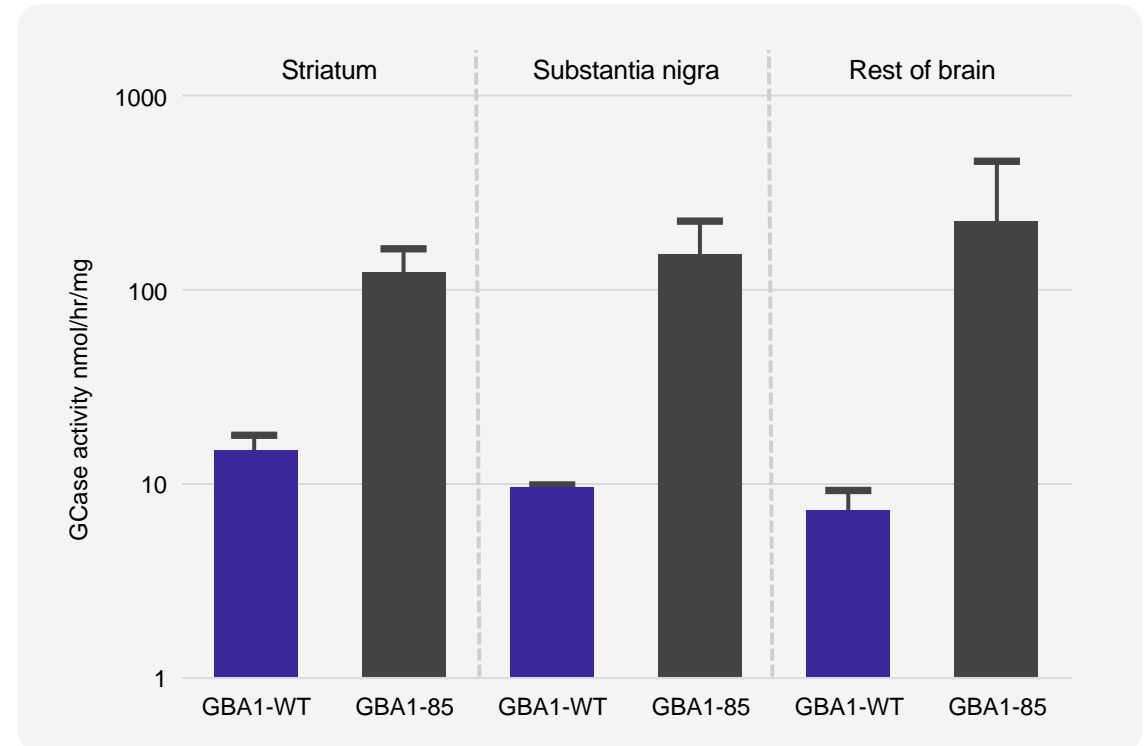
GCase85 shows greater brain distribution and higher enzyme levels than delivery of wildtype GCase *in vivo*

GCase distribution in the brain



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

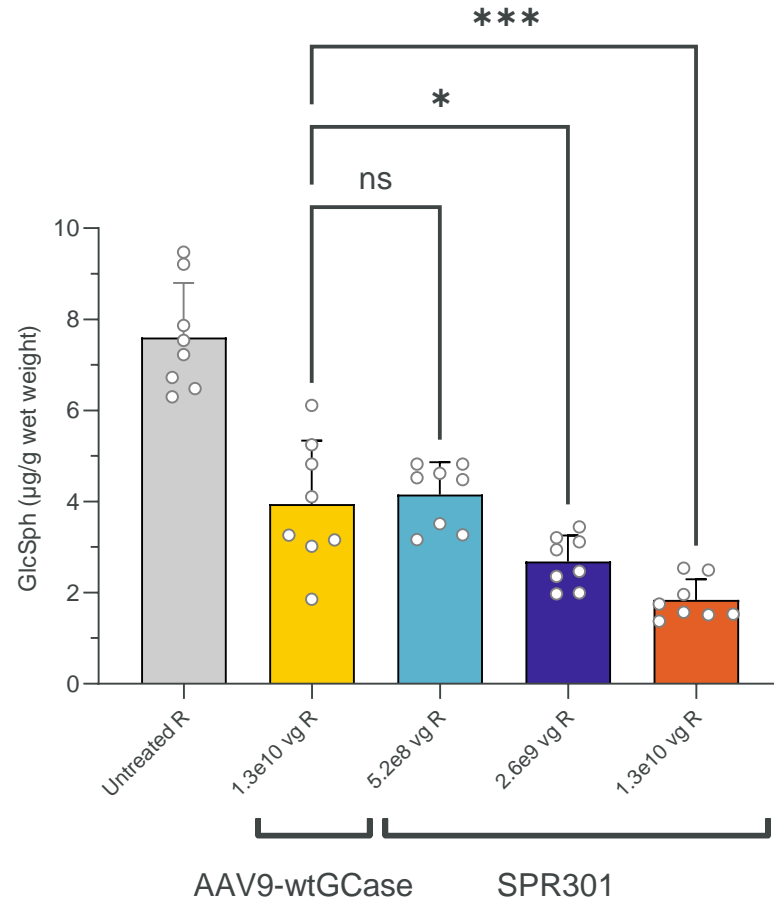
GCase activity in brain regions



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 \pm SD.

SPR301 shows superior substrate reduction, potentially allowing for better efficacy at doses with favorable safety

Lyso-Gb1 levels in GCCase-deficient CBE mice

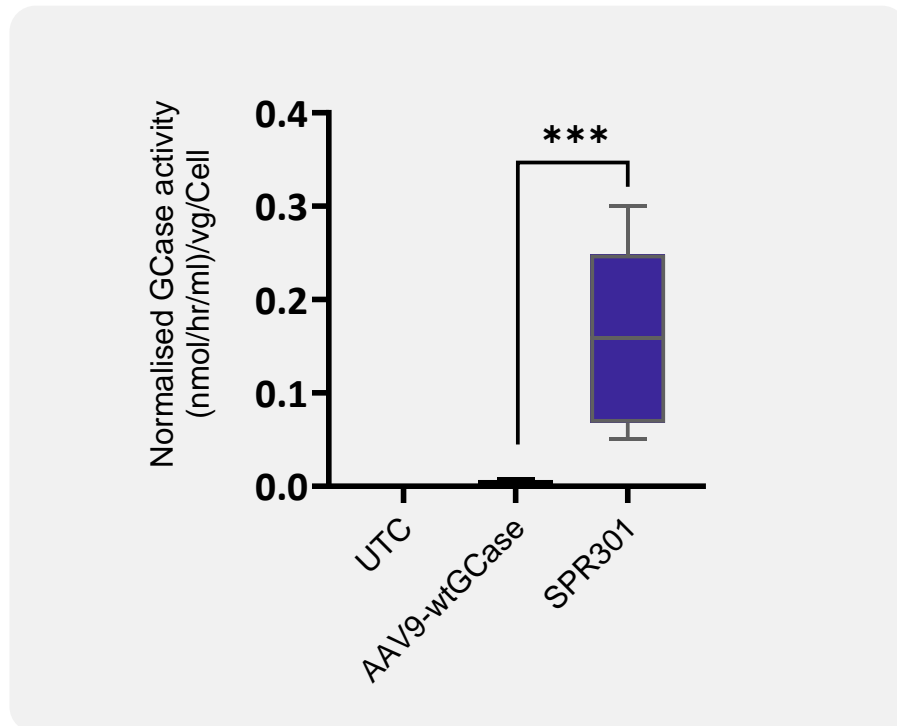


Wider therapeutic window, with 25-fold lower dose showing equivalent lyso-Gb1 reduction as high-dose AAV9-wtGCCase

Dose-dependent response

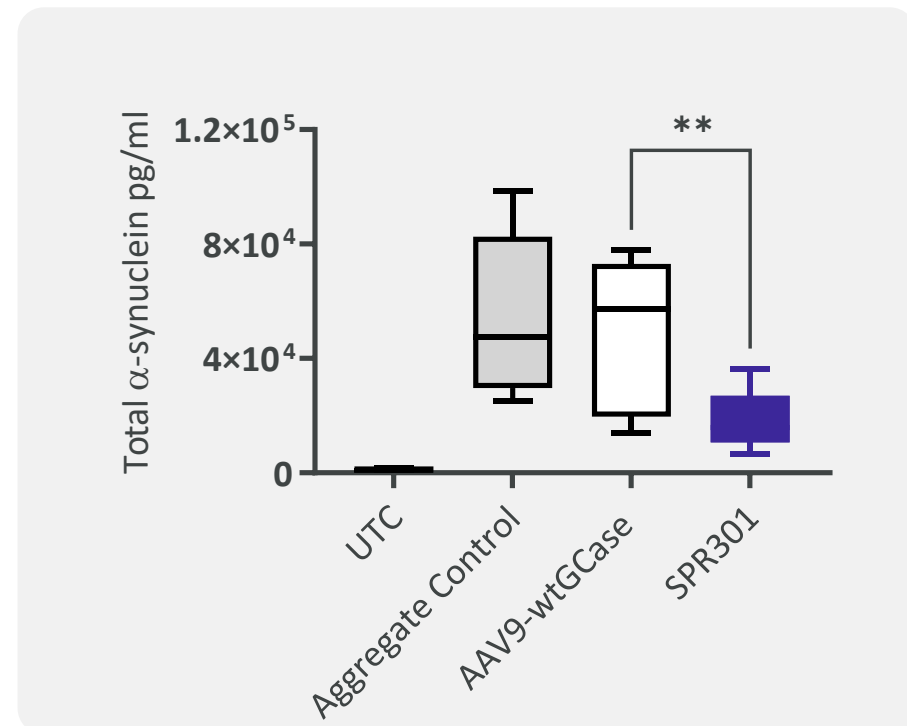
SPR301 more effectively reduces α -synuclein accumulation in neuronal cells than wildtype GCCase *in vitro*

Greater GCCase activity



Tested in the surrogate disease model, SH-SY5Y plus α -synuclein (4 μ g/ml), with vectors at MOI 10⁶; SH-SY5Y cells were pre-treated with GBA gene therapy for 24h before challenging them for 24h with recombinant α -Synuclein aggregate; n=7, data denoted as mean \pm SEM. T-test analysis vs. AAV9-wtGCCase; *** p <0.001.

Greater α -synuclein reduction



Tested in the surrogate disease model, SH-SY5Y plus α -synuclein (4 μ g/ml), with vectors at MOI 2.5x10⁵; 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 \pm SEM. T-test analysis vs. AAV9-wtGCCase; ** p <0.01.

SBT101 for Adrenomyeloneuropathy (AMN)

Toward a first-in-class gene therapy

AMN is a devastating neurodegenerative disease with no current treatments



Adrenomyelo-neuropathy (AMN)

- Caused by mutations in single X-linked gene *ABCD1*
- Default phenotype of X-ALD
- Characterized by progressive muscle weakness and sensory loss, leading to loss of mobility, increased risk of falls, incontinence, and debilitating pain

High ongoing unmet need

- No approved treatments and few in development
- Standard of care is symptom control with physical therapy and mobility aids
- Patients become wheelchair dependent within 10-12 years of myelopathy onset

Well-defined and motivated patient population

8-10K
Men diagnosed in US, UK, and EU4

~28
Typical age of onset in men

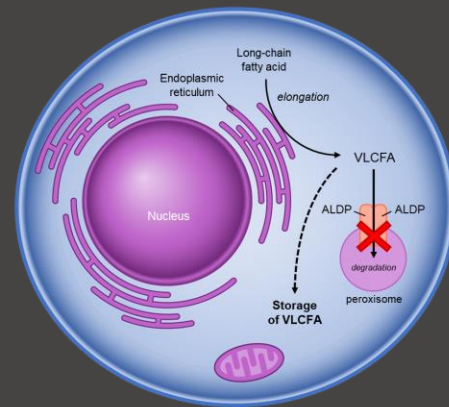
SBT101 alters underlying cause of disease in pre-clinical experiments supporting advancement to clinic

Disease mechanism of action

- Mutation in **ABCD1** gene results in impaired peroxisomal β -oxidation and overproduction of Very Long-chain Fatty Acids (VLCFA)
- The ABCD1 gene on the X chromosome encodes the peroxisomal ALD protein.

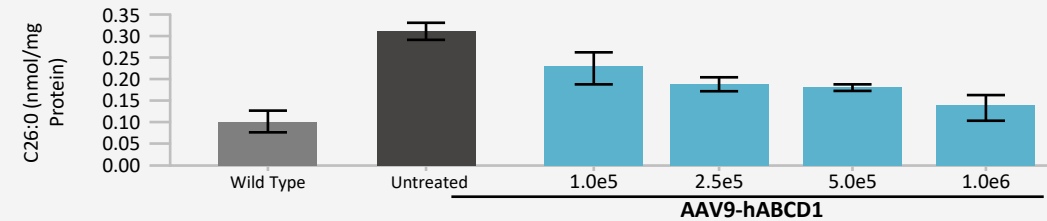
Mutation in this gene leads to:

1. Blockade of degradation of VLCFAs
2. Accumulation of VLCFA inside the cell
3. Cell stress and dysfunction
4. Disruption of the myelin/axon relationship
5. Dying back of axons



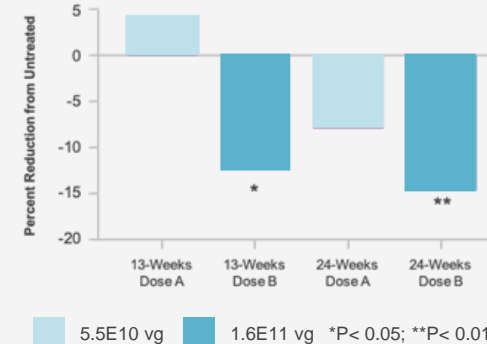
Pre-clinical proof-of-concept and safety demonstrated

AAV9-ABCD1 lowers VLCFA to wild-type levels *in vitro*



Dose-responsive ABCD1 expression and VLCFA lowering *in vivo*

Spinal cord levels

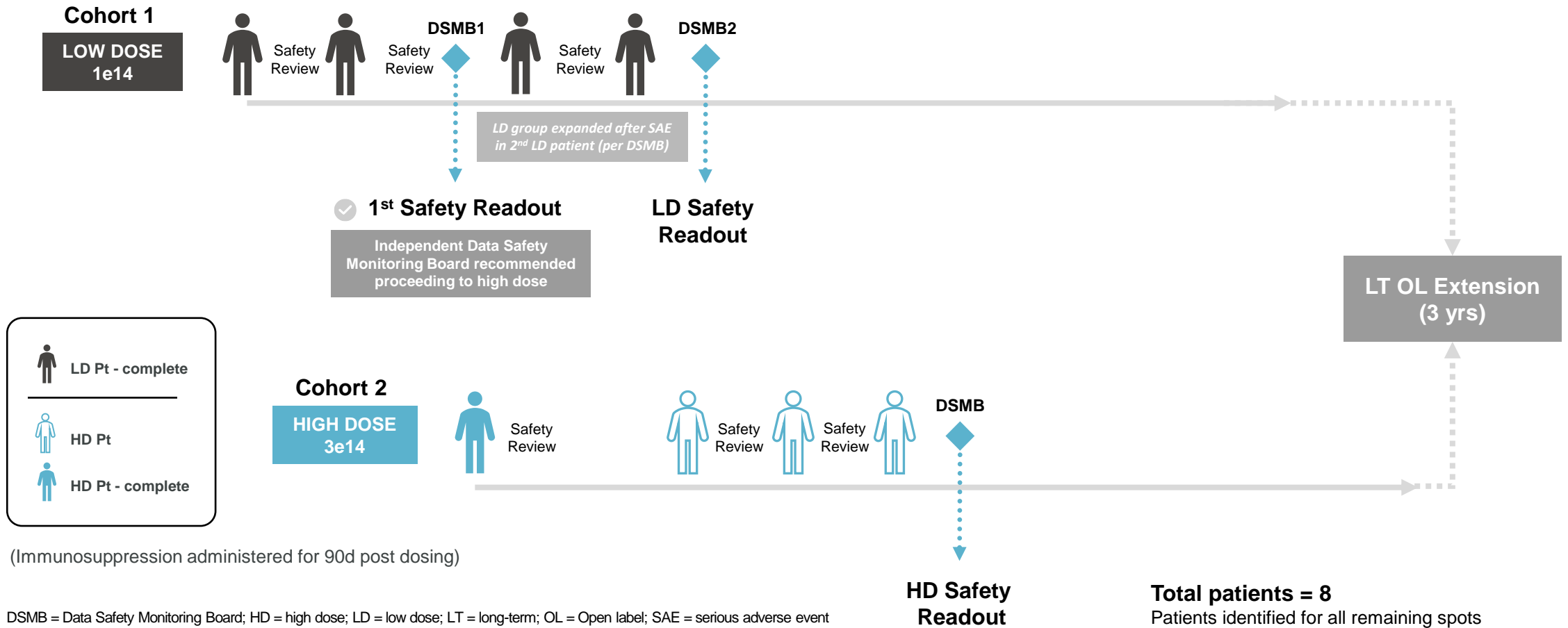


Biodistribution/safety *in vivo*

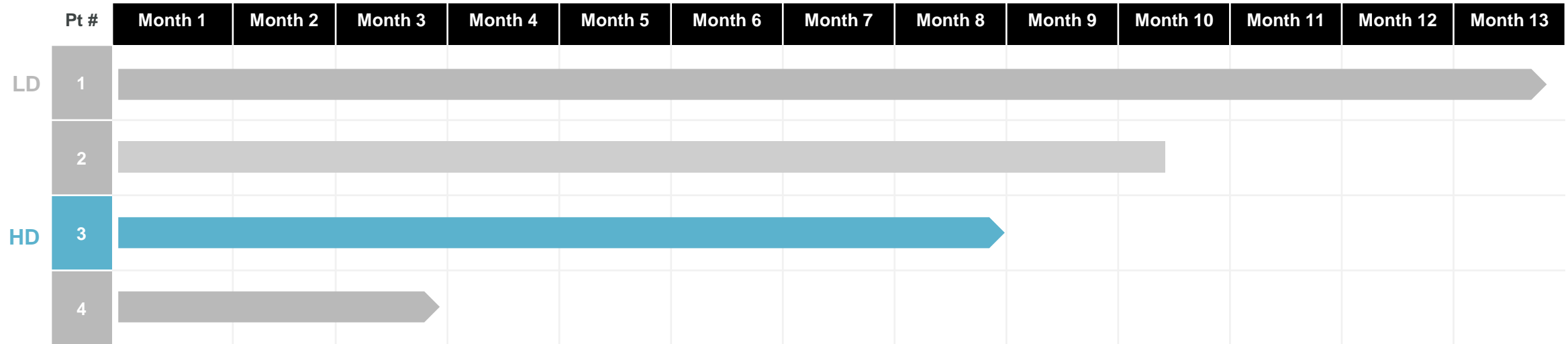
- Target biodistribution and expression (>50% neurons) achieved with delivery over 6 hours
- Distribution/expression throughout spinal cord and DRG
- Distribution persists 12M+
- Safety demonstrated through 12 months in pilot tox and GLP tox

Ongoing PROPEL Phase 1/2 trial in AMN

First-in-human, open-label study



Preliminary safety update



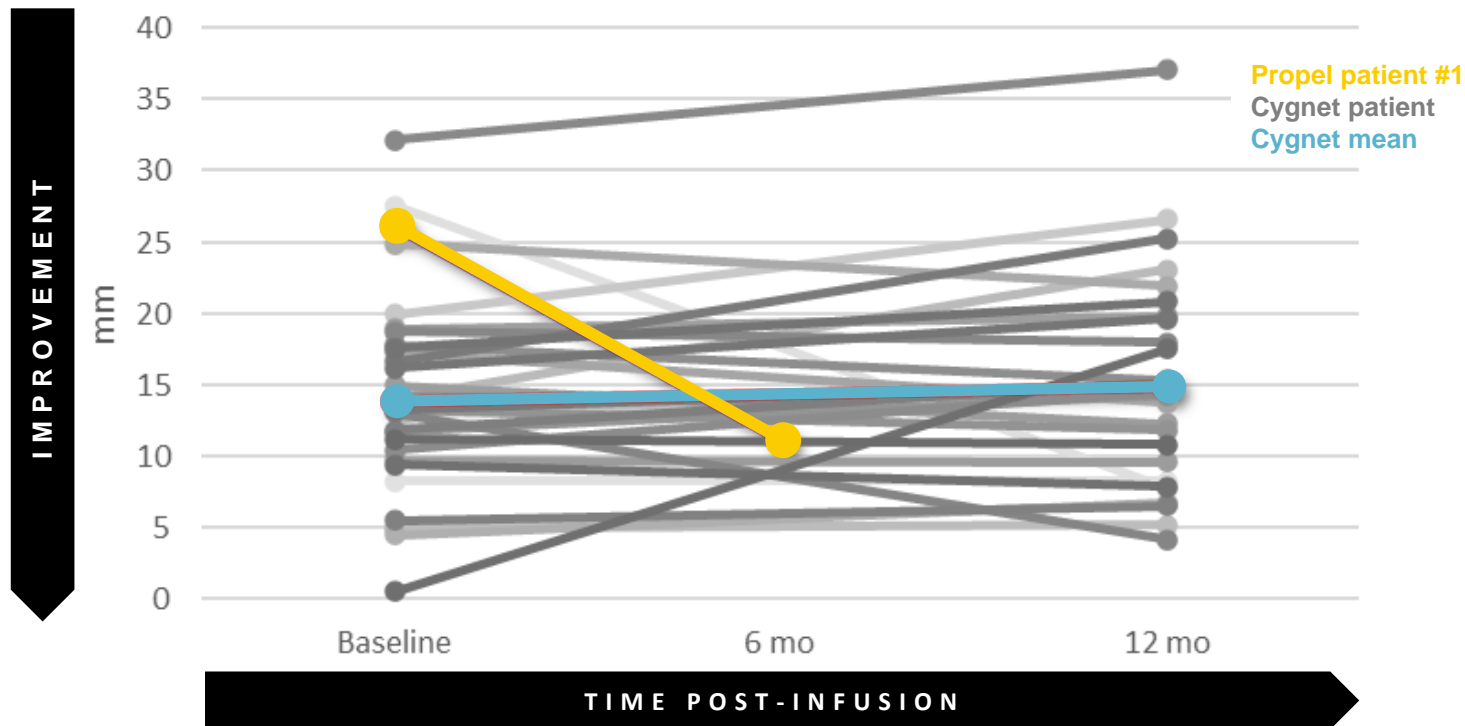
Safety

- 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

Data cut off June 30, 2024

First patient in PROPEL trial shows improvement in body sway, an early predictor of disease progression

Sway Average Amplitude AP Eyes Closed Feet Together



- Average body sway amplitude in PROPEL patient 1 (yellow line) from baseline to month 6 versus patients in CYGNET natural history study from baseline to month 12
- Body sway is correlated to risk of falls, ability to ambulate, and is a top concern for AMN patients

N=29. Baseline assessments >50 mm excluded. Only patients with paired assessments shown
Low dose 1e14vg/pt. AP = anteroposterior; data as of January 2024

Advancing the next generation of gene therapies

A potential first-
and best-in-
class gene
therapy for
Gaucher
disease
backed by
compelling
clinical data



Extending
the impact of
our more stable
GCase85
into GBA1
Parkinson's
disease



A potential first-
in-class gene
therapy for
AMN, a
devastating
CNS disorder
with no
approved
treatments



Ambitious
research
strategy to
move gene
therapy into
more prevalent
conditions



Thank you

SPUR THERAPEUTICS

© 2024 Spur Therapeutics