SPUR THERAPEUTICS

Toward More™

January 2025

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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

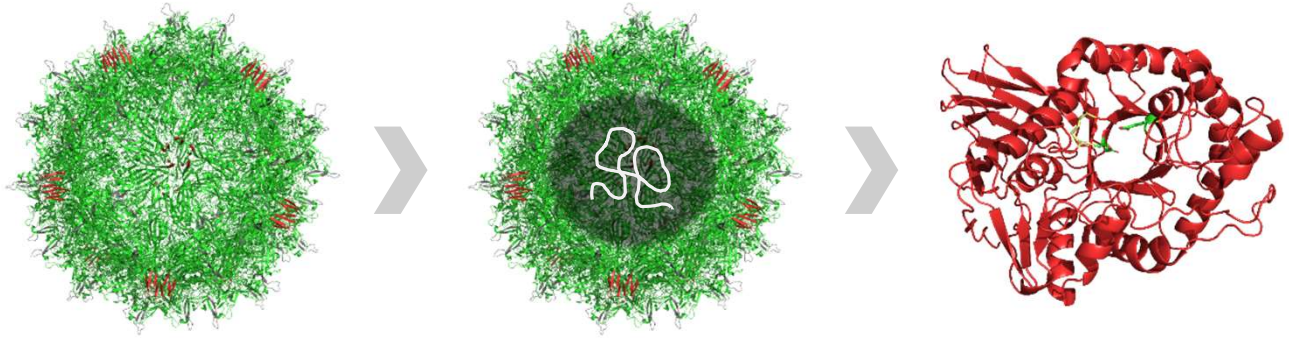
Value driven by delivering life-changing clinical outcomes for patients

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

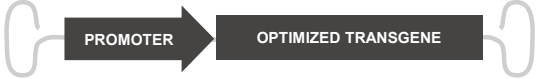
Optimizing every component of our product candidates



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

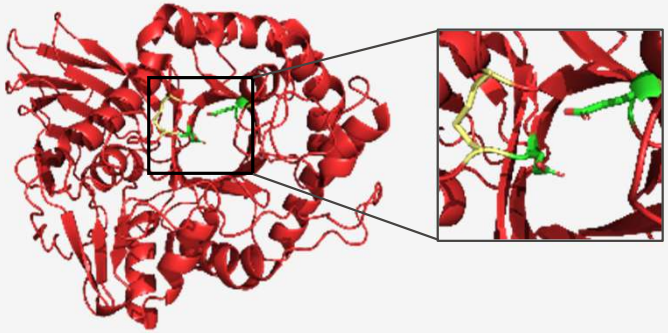
Disease Area	Program	Approximate Patient #	Research / Preclinical	Phase 1/2	Phase 3
GCase-mediated	**Gaucher Disease Type 1** FLT201	**~18K** US, UK, EU4, Israel			
	GBA1 Parkinson's Disease SPR301	**~190K** US, UK, EU4			
	Lewy Body Dementia	**>1M** US			
CNS	**Adrenomyeloneuropathy** SBT101	**~8K–10K** 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

VERTEX · Pfizer

Pam Foulds, MD, Chief Medical Officer

20+ years of medical and clinical leadership

Auregen · Aegerion Pharmaceuticals · Biogen · genzyme

Henning Stennicke, PhD, Chief Scientific Officer

25+ years of scientific leadership experience

novo nordisk · Sanford Burnham Prebys

Paul Schneider, Chief Financial Officer

25+ years of global financial, commercial and operational experience

Casebia Therapeutics · Aegerion Pharmaceuticals · Shire

Jay Bircher, Chief Technical Operations Officer

30 years of quality and technical operations experience

Abeona Therapeutics · BD · gsk · AMGEN

Nicole Jones, Chief People Officer

25+ years of global human resources experience

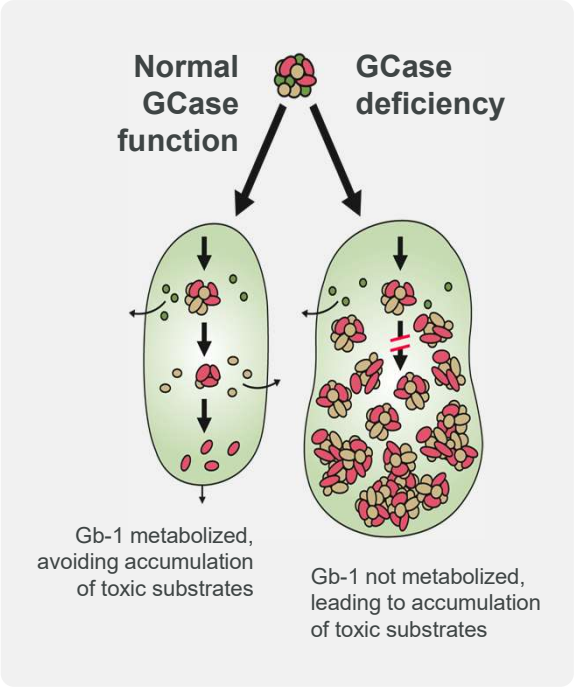
Alexion · MERCK · Fidelity

Chip McCorkle, VP, GC & Corporate Secretary

10 years of experience advising leading biopharmaceutical companies

Toward a new standard of care

Targeting a chronic, progressive, and debilitating condition



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

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

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 counts[1]

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 ERT[2]

65%

report **fatigue** despite treatment with ERT/SRT[3]

[1]Weinreb et al. 2013, † in those with severe symptoms before ERT. All percentages are approximate rounded to the nearest 5%; [2]De 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; [3]Wagner 2018.

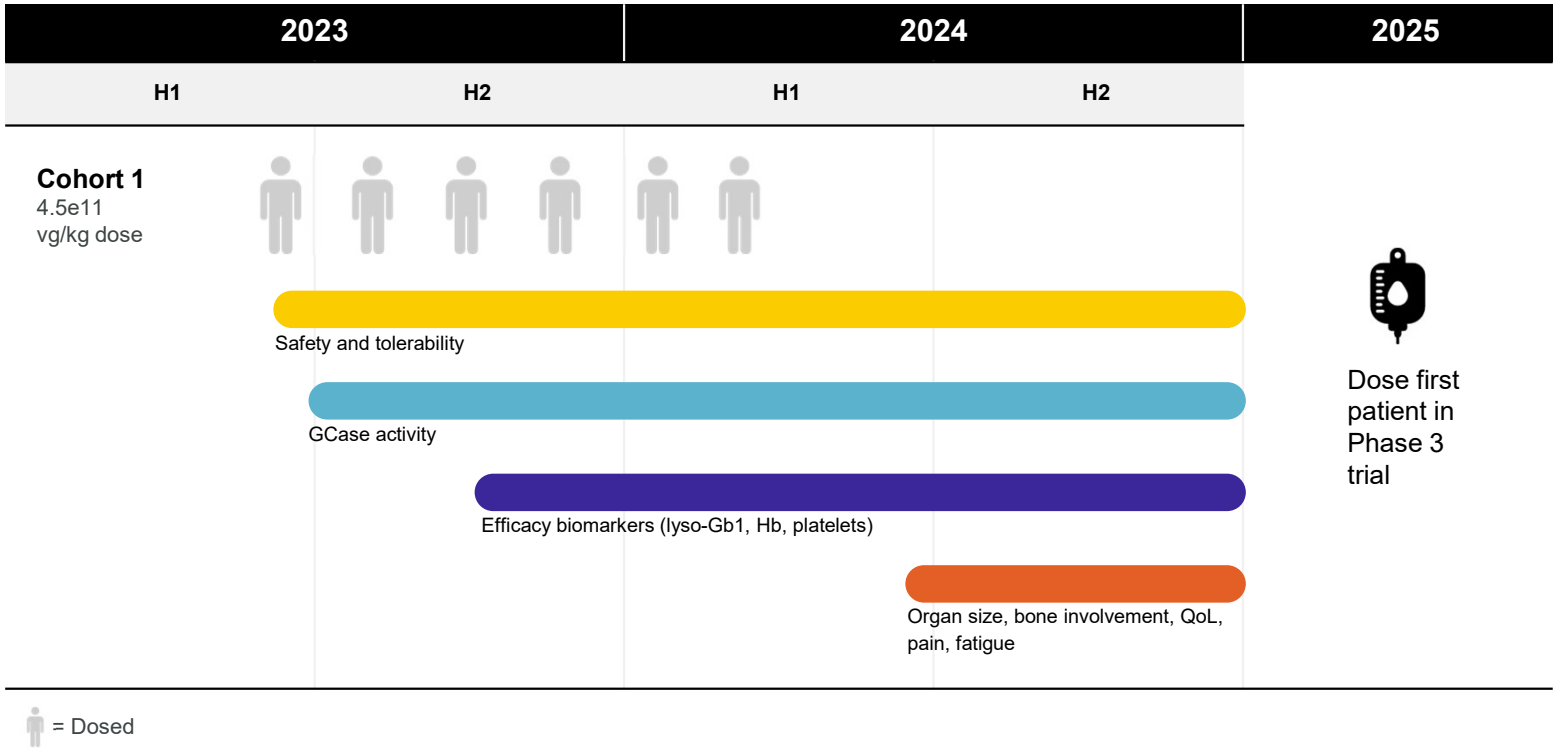
Completed dosing in Phase 1/2 dose-finding study

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

Patient population

Adults with Gaucher Type 1 on ERT or SRT

- Patients come off prior therapy
- IM regimen begins 3 weeks post-infusion; 4 weeks of tacrolimus and 4 weeks of prednisone, followed by slow taper off prednisone
- Patients roll into long-term follow-up study



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 efficacy[1]

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

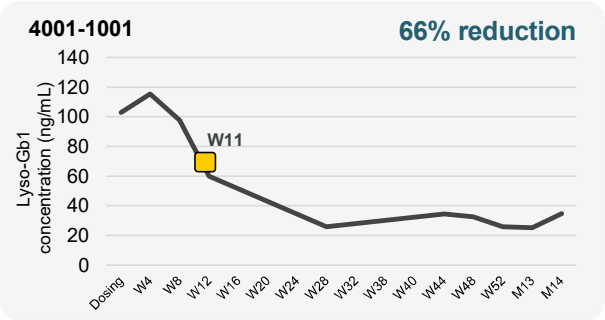
5/5 Maintenance or improvement in hemoglobin, platelets and organ volume

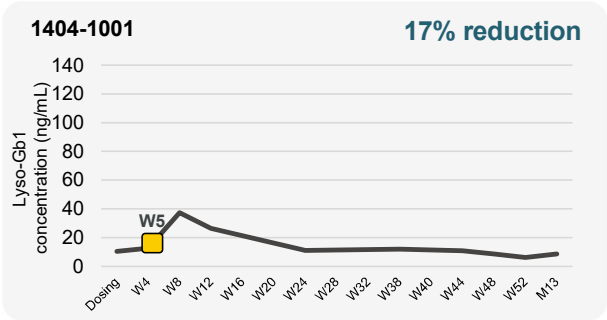
1/1 Clinically relevant improvement in patient-reported fatigue and pain in the one patient who entered trial with debilitating fatigue and pain

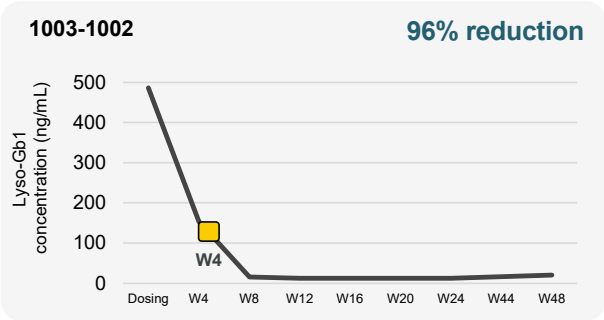
[1]One patient with detectable NAbs to AAVS3 below protocol cut-off excluded from efficacy analysis. Only patients with no detectable NAbs will be eiligible for Phase 3 trial.
NAbs = Neutralizing antibodies

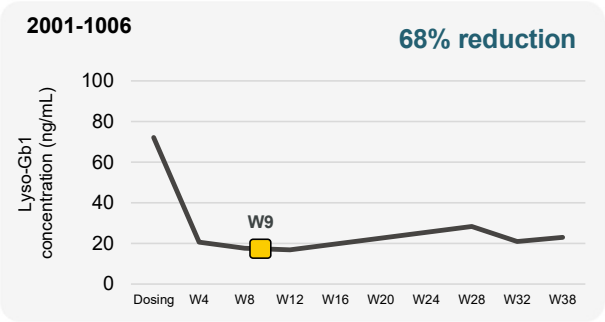
Dramatic reductions of toxic substrate in patients with persistently high levels despite prior treatment

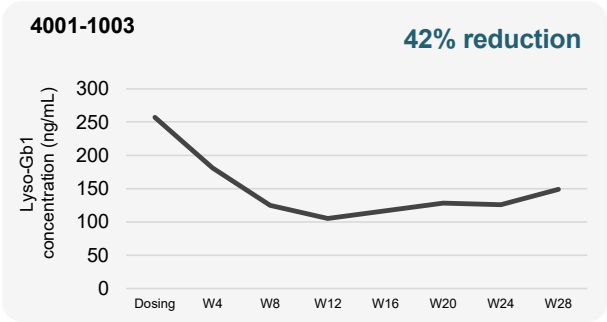
Dried blood spot lyso-Gb1 concentration over time











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

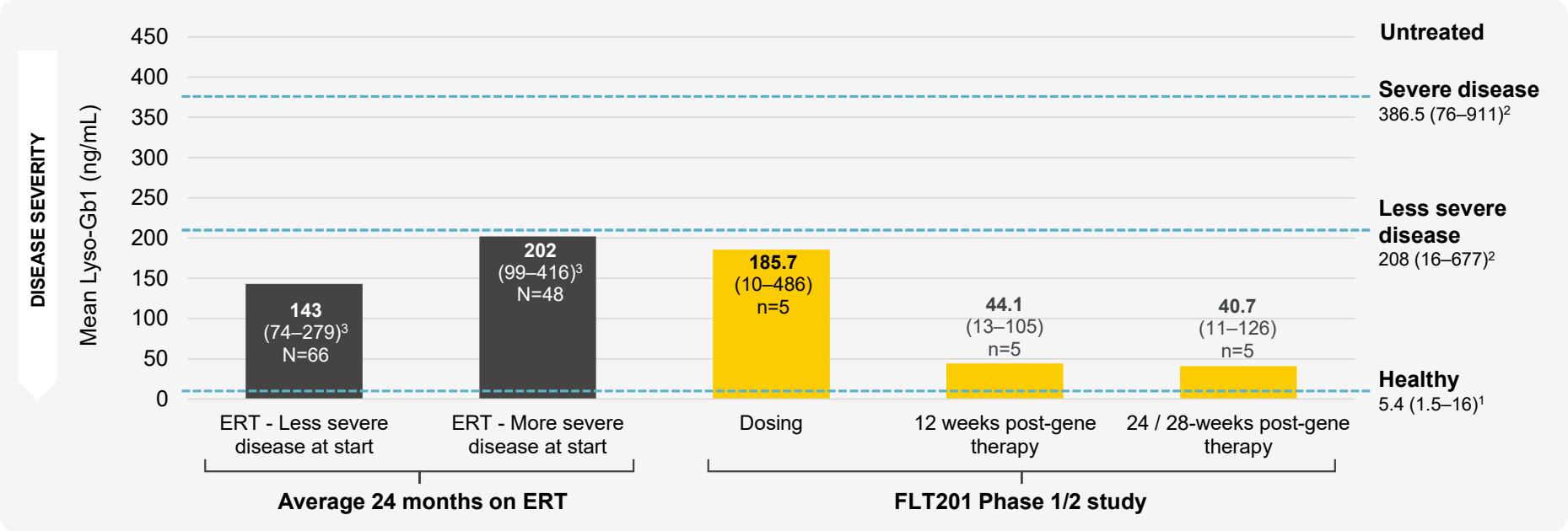
- Highly correlated with outcomes in hemoglobin, platelets, spleen and bone
- Gaucher-specific, highly sensitive

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



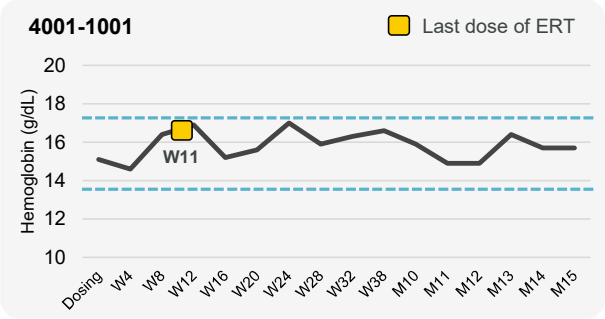
Mean DBS lyso-Gb1 concentration (range); measured in different populations at different timepoints

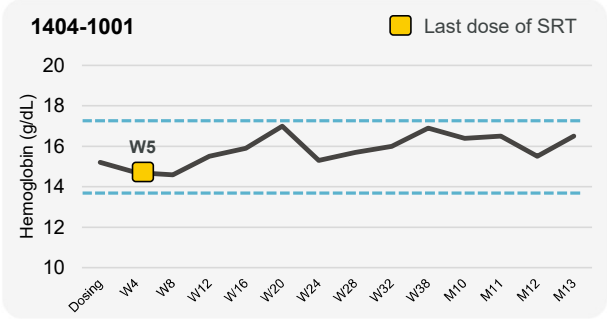
[1] Median value and range (Dinur 2022); [2] Curado 2023; [3] Dinur 2021

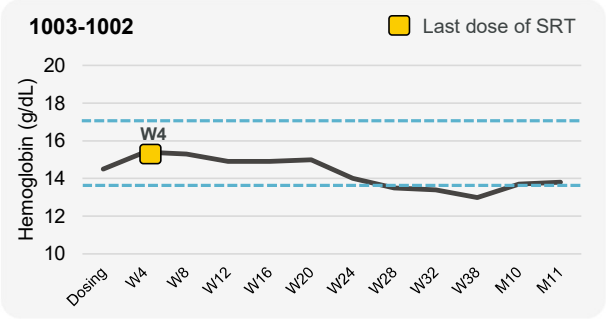
Data cut off Sep. 27th, 2024

Sustained hemoglobin maintenance observed after withdrawal of ERT or SRT

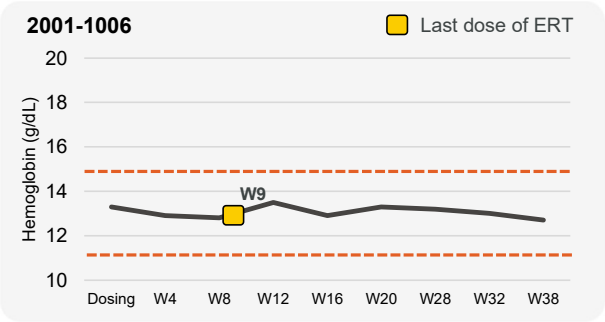
Hemoglobin concentration over time

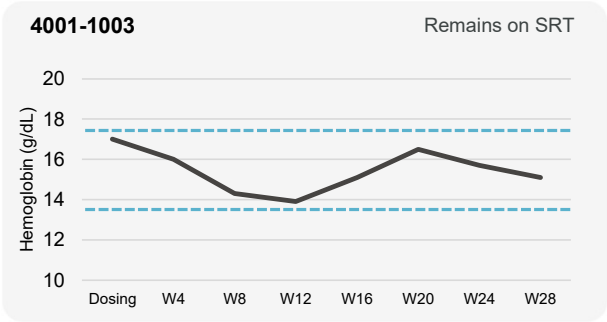






Patient recently diagnosed with iron deficiency unrelated to FLT201





Normal Hb [male] 13.8-17.2 g/dL

Normal Hb [female] 11.0-15.5 g/dL

Data cut off Sep. 27th, 2024

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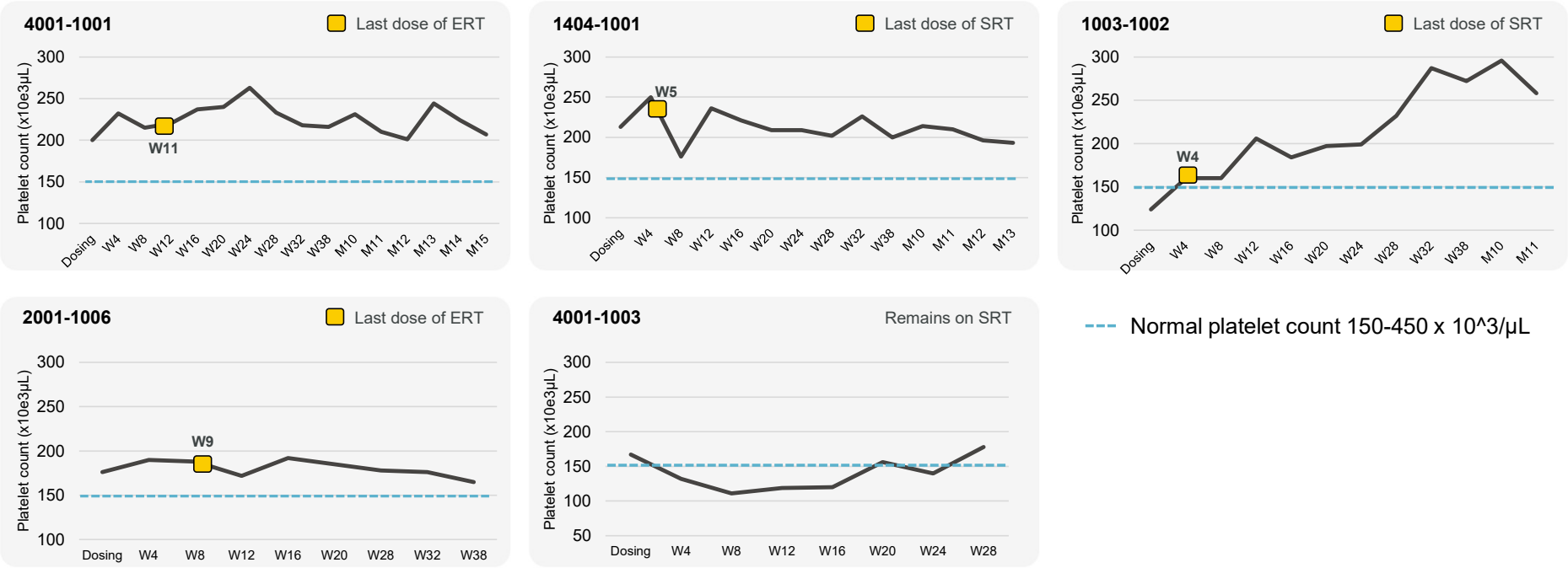
Sustained improvement or maintenance of platelets observed after withdrawal of ERT and SRT

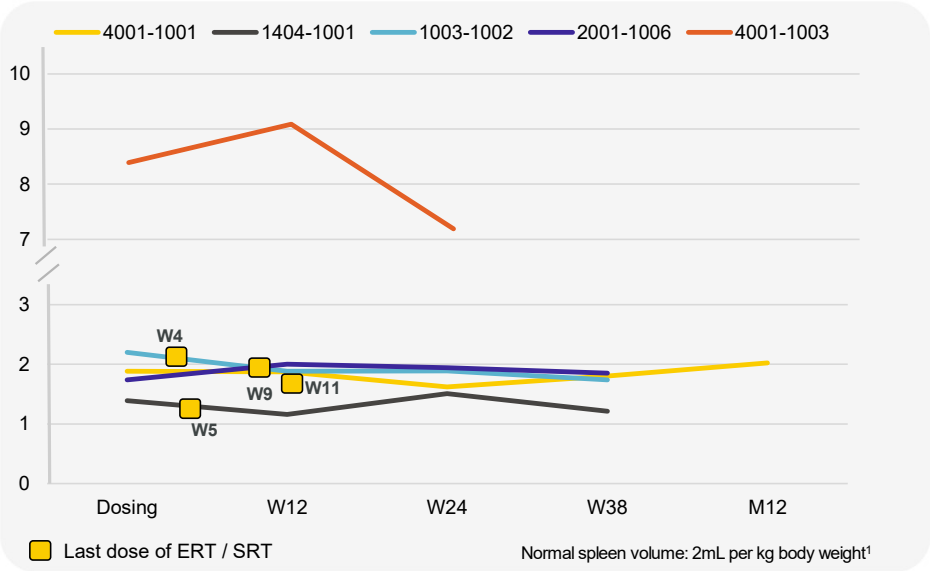
Platelet count over time



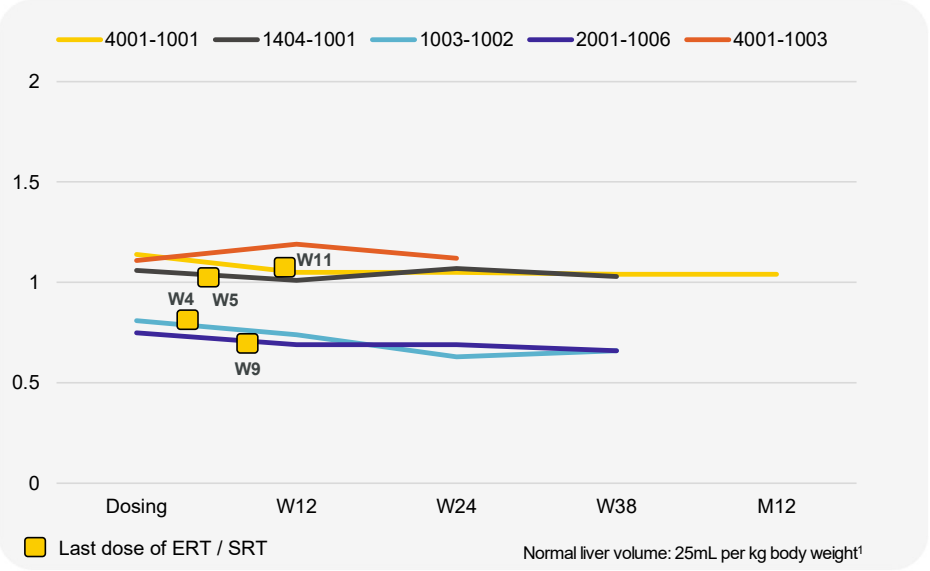
Data cut off Sep. 27th, 2024

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

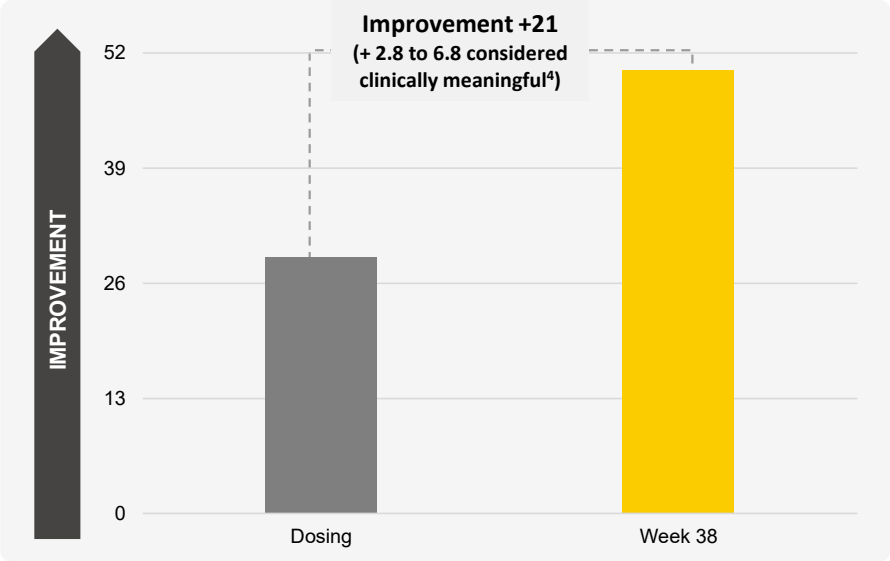


[1]Pastores et al Blood Cells, Molecules and Diseases 2014;53: 253–260
Data cut off Sep. 27th, 2024

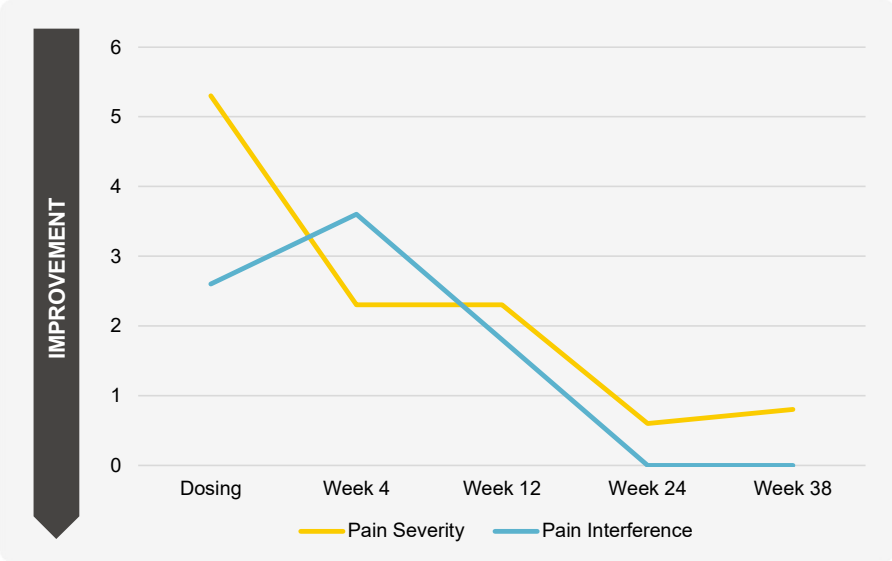
Clinically meaningful improvement in fatigue and pain leading to improved functioning

Patients ranked fatigue #1 and pain #2 as most important symptoms[1]

FACIT fatigue scale (0–52)[2]



Pain severity and interference (0-10)[3]



[1]Zion 2016; [2]FACIT = Functional Assessment of Chronic Illness Therapy; [3]Measured by Brief Pain Inventory Short Form; [4]Greenbaum 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

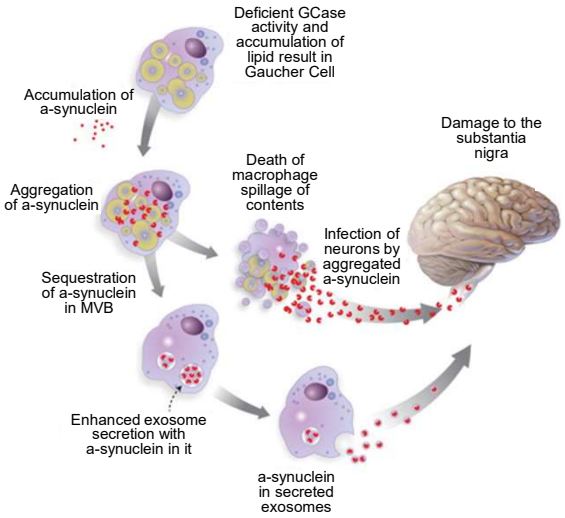
- Infusions well tolerated; no infusion-related reactions
- Treatment-related adverse events were mild to moderate
- No dose-limiting toxicities
- Any ALT elevations deemed related to therapy were mild and managed with immune therapy with no impact on efficacy
- AEs related to immune management consistent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

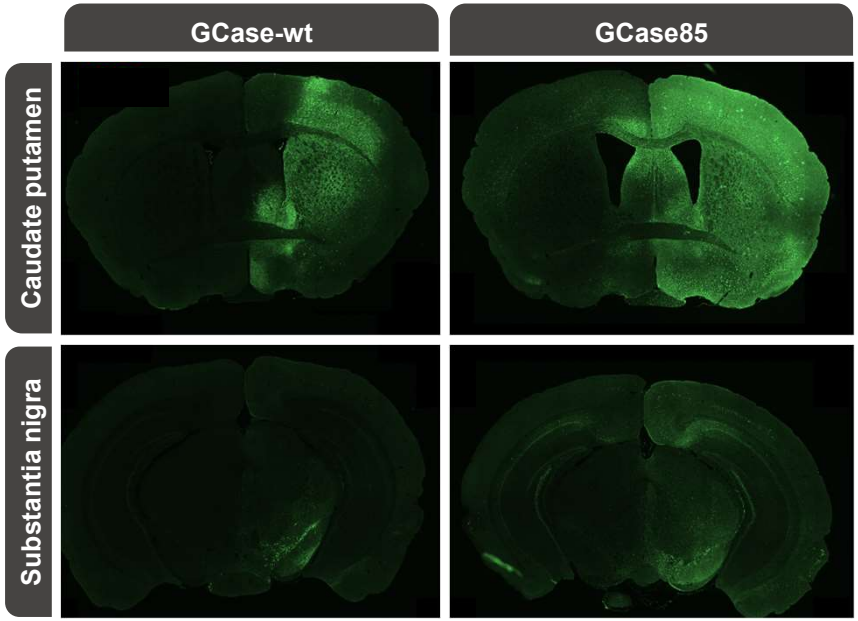


†*Cells* 2022, 11(8), 1261; https://doi.org/10.3390/cells11081261

GBA1 Parkinson's disease	• *GBA1* 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 *GBA* mutation
High ongoing unmet need	• No disease-modifying therapies exist for PD • Symptomatic treatments become less effective over time
Substantial, well-defined patient population	**5-15%** of people with PD have *GBA1* mutations† **~190K** patients with GBA1-PD in US, UK, and EU4

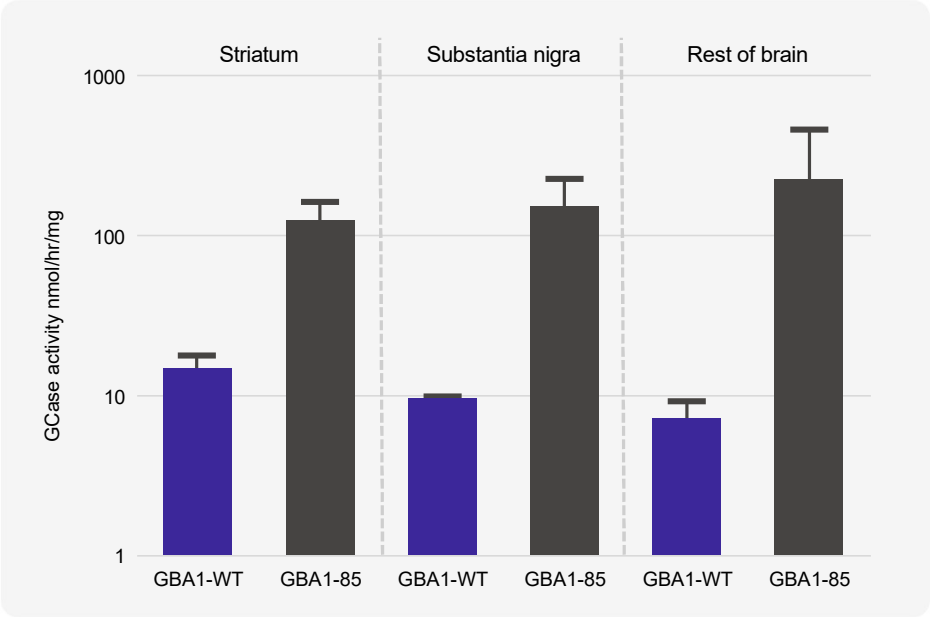
GCase85 shows greater brain distribution and higher enzyme levels than delivery of wildtype GCase *in vivo*

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.

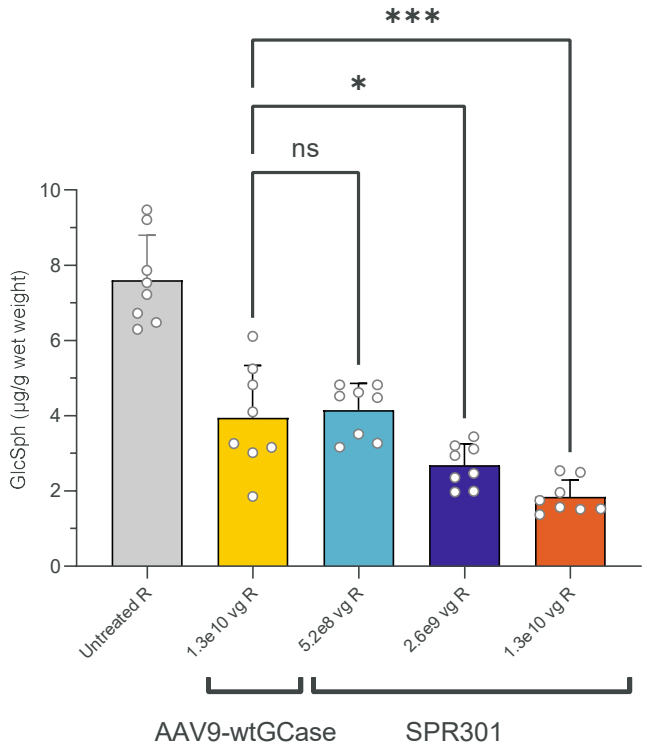
GCase activity in brain regions



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 ± SD.

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

Lyso-Gb1 levels in GCase-deficient CBE mice



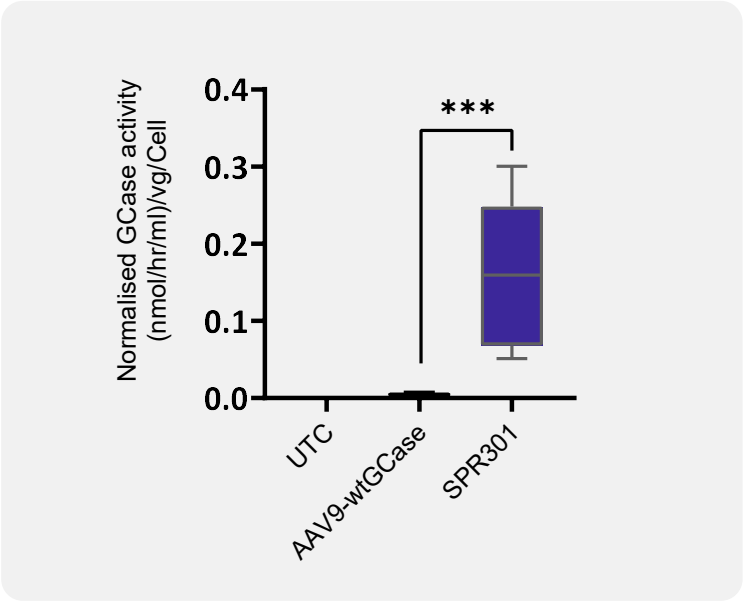
Wider therapeutic window, with 25-fold lower dose showing equivalent lyso-Gb1 reduction as high-dose AAV9-wtGCase

Dose-dependent response

*p≤0.05, ***p<0.001

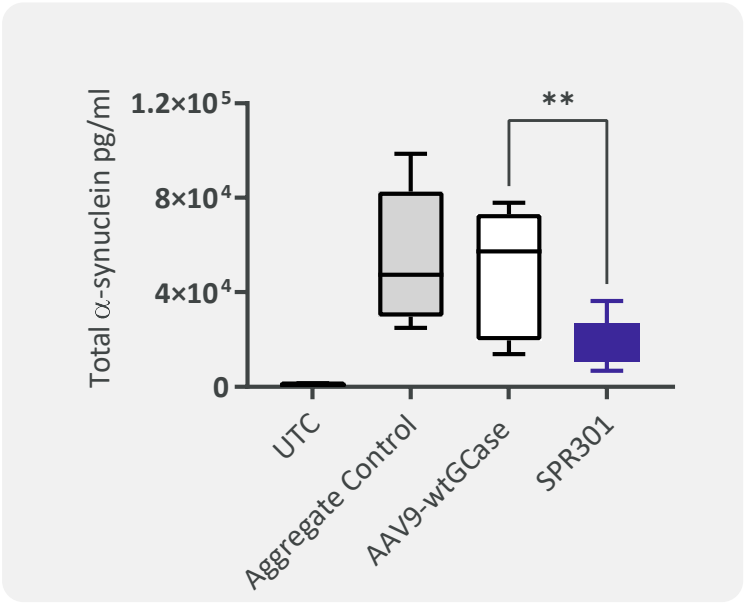
SPR301 more effectively reduces α-synuclein accumulation in neuronal cells than wildtype GCase *in vitro*

Greater GCase activity



Tested in the surrogate disease model, SH-SY5Y plus α-synuclein (4µg/ml), with vectors at MOI 10^6; 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 ± SEM. T-test analysis vs. AAV9-wtGCase; ****p<0.001.*

Greater α-synuclein reduction



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.*

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

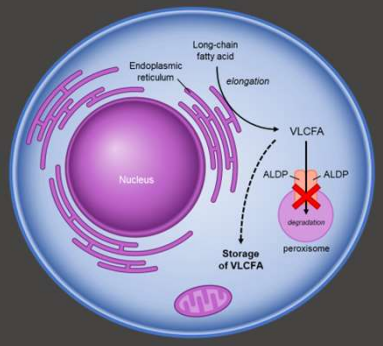
SBT101 alters underlying cause of disease in pre-clinical experiments supporting advancement to clinic

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.

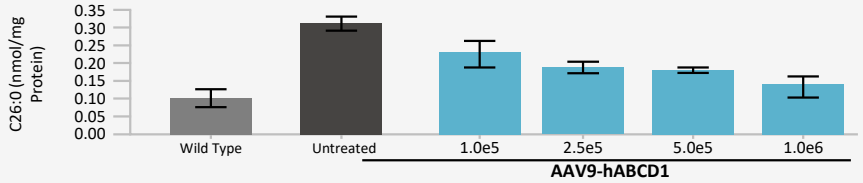
Mutation in this gene leads to:

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



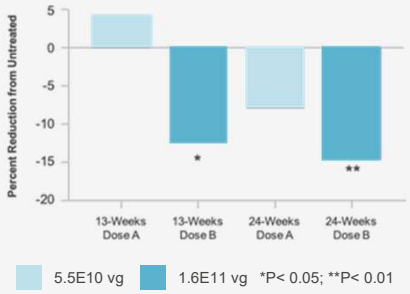
Pre-clinical proof-of-concept and safety demonstrated

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



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

Spinal cord levels

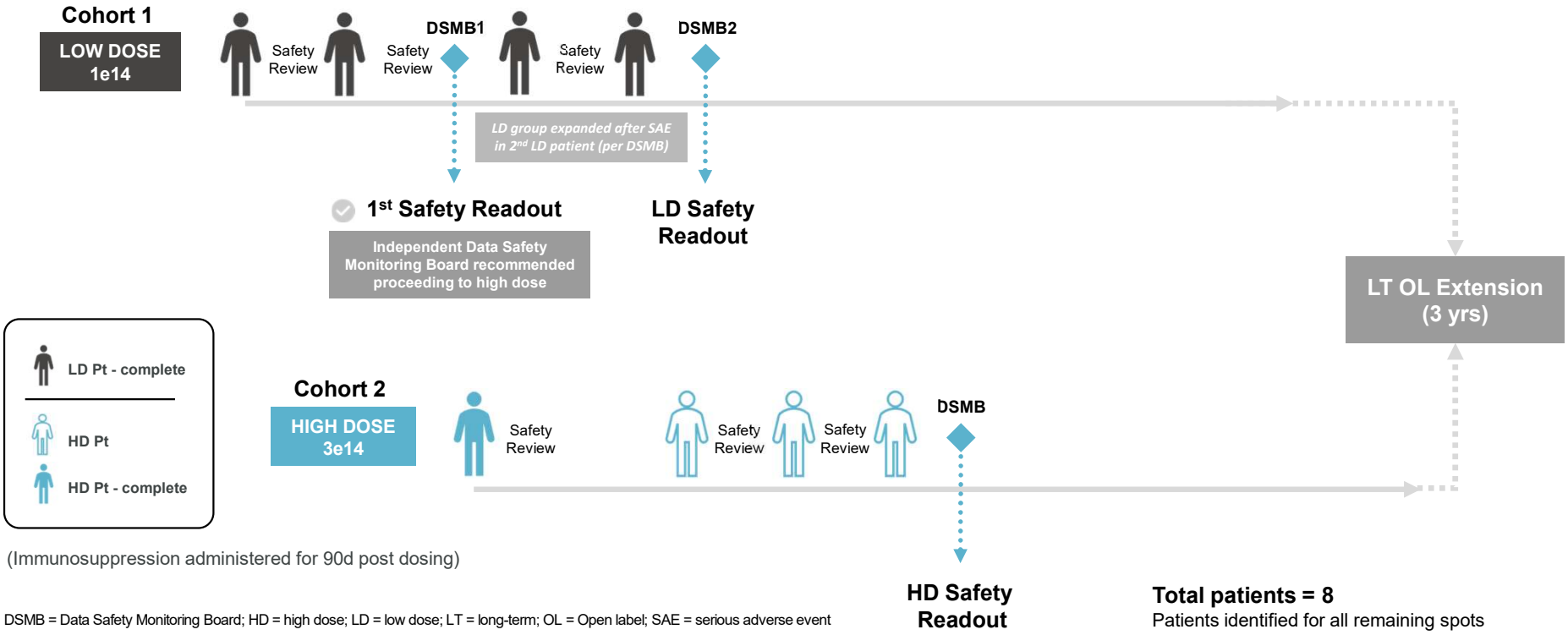


Biodistribution/safety *in vivo*

- 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

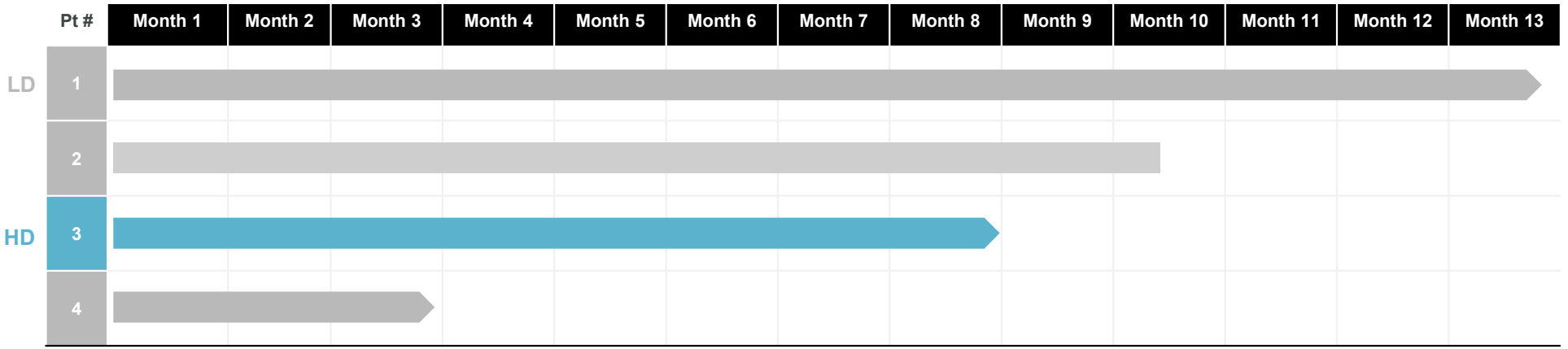


(Immunosuppression administered for 90d post dosing)

DSMB = Data Safety Monitoring Board; HD = high dose; LD = low dose; LT = long-term; OL = Open label; SAE = serious adverse event

Total patients = 8
Patients identified for all remaining spots

Preliminary safety update



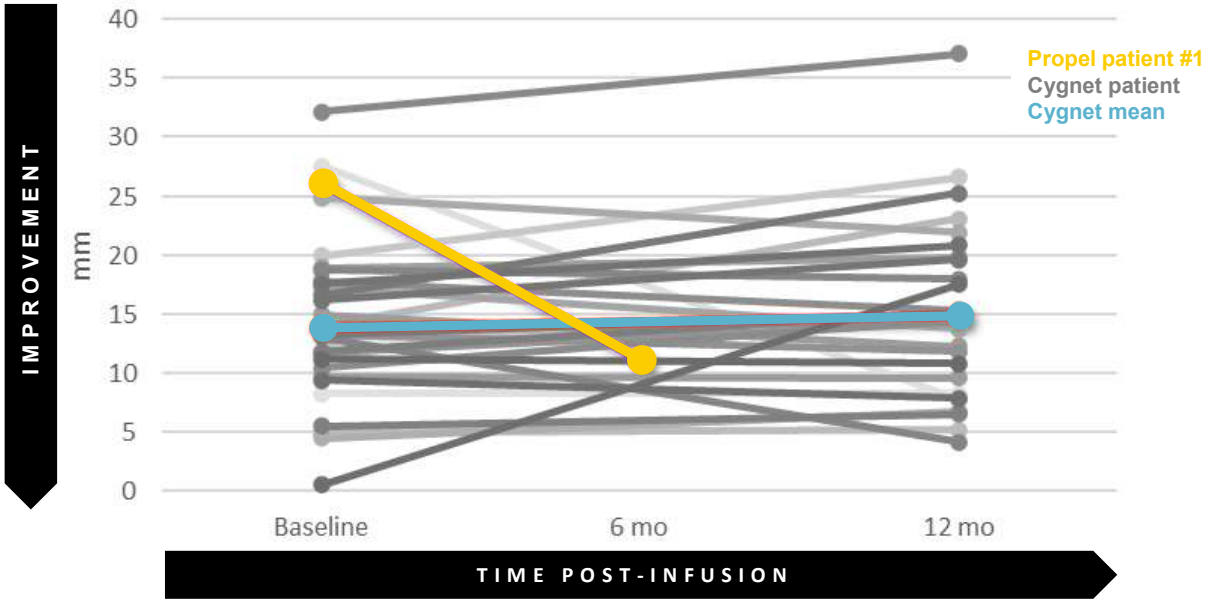
Safety

- 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

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Thank you

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