Two-year follow up of FLT201 AAV gene therapy in adults with Type 1 Gaucher disease: Results from GALILEO-1 and GALILEO-2

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Unmet needs in GD1 despite long-term treatment

Although ERT/SRT are effective in alleviating many aspects of GD1, there are still unmet needs that remain

Prospective registry of 757 GD1 patients on ERT after 10 years[2]		
Persistence after 10 years ERT	**Non-Splenectomized**	**Splenectomized**
Bone pain	43%	63%
Splenomegaly	38%	N/A
Thrombocytopenia	23%	1%
Hepatomegaly	14%	19%
Anemia	12%	9%
Bone crisis	7%	17%

60% failed to achieve at least one of 6 therapeutic goals after 4+ years of ERT[1]

Many continue to exhibit **bone pain**, **organomegaly**, and **cytopenia** after 10 years of ERT[2]

25% have physical limitations after 2 years of ERT, primarily due to **bone disease**[3]

80% of individuals with severe bone marrow burden showed **no meaningful improvement after 8 years on ERT**[4]

65% report fatigue despite treatment with ERT/SRT[5]

GD1: Type 1 Gaucher disease; ERT: enzyme replacement therapy; SRT: substrate reduction therapy

1. Weinreb N, et al. *Am J Hematol.* 2008. 2. Weinreb N, et al. *J Inherit Metab Dis.* 2013. 3. Giraldo P, et al. *Qual Life Res.* 2005. 4. De Fost M, et al. *Blood.* 2006; Low ERT dose cohort.
5. Wagner V, et al, *J Genet Counsel*. 2018.

Avigbagene parvec (FLT201): Investigational AAV Gene Therapy for GD1

FLT201

- Novel human liver-tropic AAV capsid (AAVS3)
- Transgene encoding GCase85, a novel engineered variant of glucocerebrosidase
- GCase85 has similar catalytic properties to human GCase with *increased enzymatic stability*
  - **6-fold increase** in human serum
  - **20-fold increase** at lysosomal pH conditions
- Produces robust and sustained secretion of GCase into the bloodstream
- No changes in predicted immunogenicity compared to velaglucerase alfa

Preclinical studies demonstrate[1]

- High and durable expression with favorable tolerability out past 5 years
- Uptake in all disease-affected tissues
- Greater residence time in disease-affected tissues and organs compared to ERT
- Greater reduction of lyso-Gb1, a disease-causing substrate and biomarker, versus ERT in all disease-affected tissues

AAV: adeno associated virus; GCase: glucocerebrosidase; ERT: enzyme replacement therapy; LSP: liver specific promoter; Lyso-Gb1: glucosylsphingosine

1. Comper F, et al. Mol Ther. 2025.

GALILEO-1 / GALILEO-2 Overview

- **GALILEO-1**: First-in-human, open-label, multicenter study of FLT201
- **GALILEO-2**: Long-term follow-up study

Key Eligibility Criteria

- Adult ≥ 18 years of age
- Diagnosis of GD1 with deficient GCase activity ≤30% of normal in leukocytes at diagnosis
- ≥ 2 years ERT/SRT
- Negative for antibodies to AAVS3

Primary Objective

- To assess the safety and tolerability of FLT201 in GD1 adults

Secondary / Exploratory Objectives

- Impact on spleen, liver, Hb and platelets
- Biomarkers
  - Lyso-Gb1
  - Chitotriosidase
  - CCL18
- Bone disease / fatigue / pain
- Impact on HRQoL
- Viral shedding
- Immune response

AAV: adeno associated virus; CCL18: C-C motif chemokine ligand 18; GD1: Type 1 Gaucher disease; ERT: enzyme replacement therapy; Hb: hemoglobin; Lyso-Gb1: glucosylsphingosine; SRT: substrate reduction therapy

GALILEO-1 / GALILEO-2 Overview (cont.)

- Six participants have received a single low dose of FLT201: 4.5 x 10^{11} vg/kg
- Prophylactic immune management regimen began 3 weeks post-infusion*
- Four participants have discontinued their SoC (ERT/SRT)
  - Discontinued between 4 to 11 weeks post FLT201 infusion, all remain off ERT/SRT 2 years later
- Two participants remain on their SoC
  - Patient 5 – No durable enzyme expression or sustained improvements in lyso-Gb1; likely attributable to a heightened and less regulated immune response due to a confluence of contributing factors impacting transgene expression.
  - Patient 6 – No apparent GCase expression, detectable pre-existing AAVS3 NAbs at a titer below exclusion cut-off. GALILEO-3 will focus on patients with no detectable AAVS3 NAbs.
- All participants have enrolled in the long-term follow up study: GALILEO-2
- Patient follow-up ranges between 20 to 29 months after FLT201 dosing

*Prophylactic immune regimen consisted of oral steroids prednisolone/prednisone and/or oral tacrolimus

AAV: adeno associated virus; GD1: Type 1 Gaucher disease; ERT: enzyme replacement therapy; GCase: glucocerebrosidase; Hb: hemoglobin; Lyso-Gb1: glucosylsphingosine; NAb: neutralizing anti-body; SoC: standard of care; SRT: substrate reduction therapy

Data cut off as of November 20, 2025

Baseline Characteristics

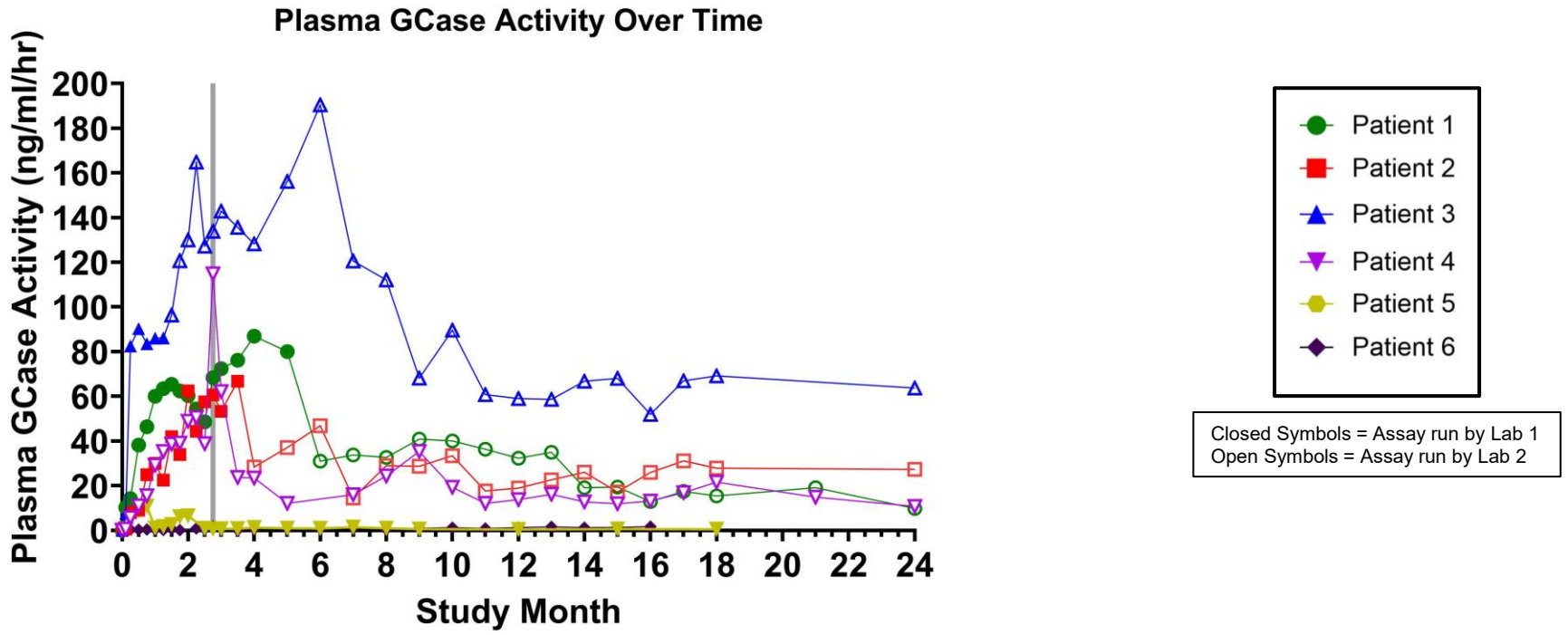
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age / Gender	35 / M	25 / M	24 / M	30 / F	24 / M	58 / F
Age at diagnosis	4	3	16	15	20	15
GBA1 Variant	p.Val433Leu; p.Asn409Ser	p.Asn409Ser; p.Leu483Pro	p.Gln112Valfs*32; p.Leu422fs; p.Leu483Pro; p.Ala495Pro	p.Asn409Ser; p.Leu483Pro	p.Asn409Ser; p.Leu29Alafs*18	p.Asn409Ser; p.Trp223Arg
Duration of SoC	4 years	22 years	9 years	14 years	4 years	24 years
Therapy at entry	ERT	SRT	SRT	ERT	SRT	SRT
Plasma GCase activity (µmol/L/h)	0.1	0.09	0.04	<0.1[#]	0.5	<0.1
DBS Lyso-Gb1 (ng/mL)	102.9	10.3	383.3	72.2	257.0	52.6
Hemoglobin (g/dL)	15.1	15.2	14.5	13.3	17.0	12.6
Platelet count ($x10^3$/mL)	200	213	124	176	167	113
Spleen volume (MN)	1.82	1.32	2.67	2.01	8.09	5.78
Liver volume (MN)	1.12	1.06	0.80	0.77	1.10	0.92
Total BMB Score	7	7	11	11	13	7

[#] Below lower limit of quantification

BMB: bone marrow burden; DBS: dried blood spot; ERT: enzyme replacement therapy; GBA1: glucosylceramidase beta 1; GCase: Glucocerebrosidase; lyso-Gb1: Glucosylsphingosine; MN: Multiples of normal; SoC: standard of care; SRT: substrate reduction therapy

Substantial increases in GCase activity observed

- Plasma GCase activity shows a substantial increase from baseline in the 4 patients who discontinued their SoC
- A similar picture has been seen with GCase activity from Dried Blood Spots



Grey vertical line = time at which last participant discontinued background ERT/SRT therapy (Week 11)

Data cut off as of November 20, 2025

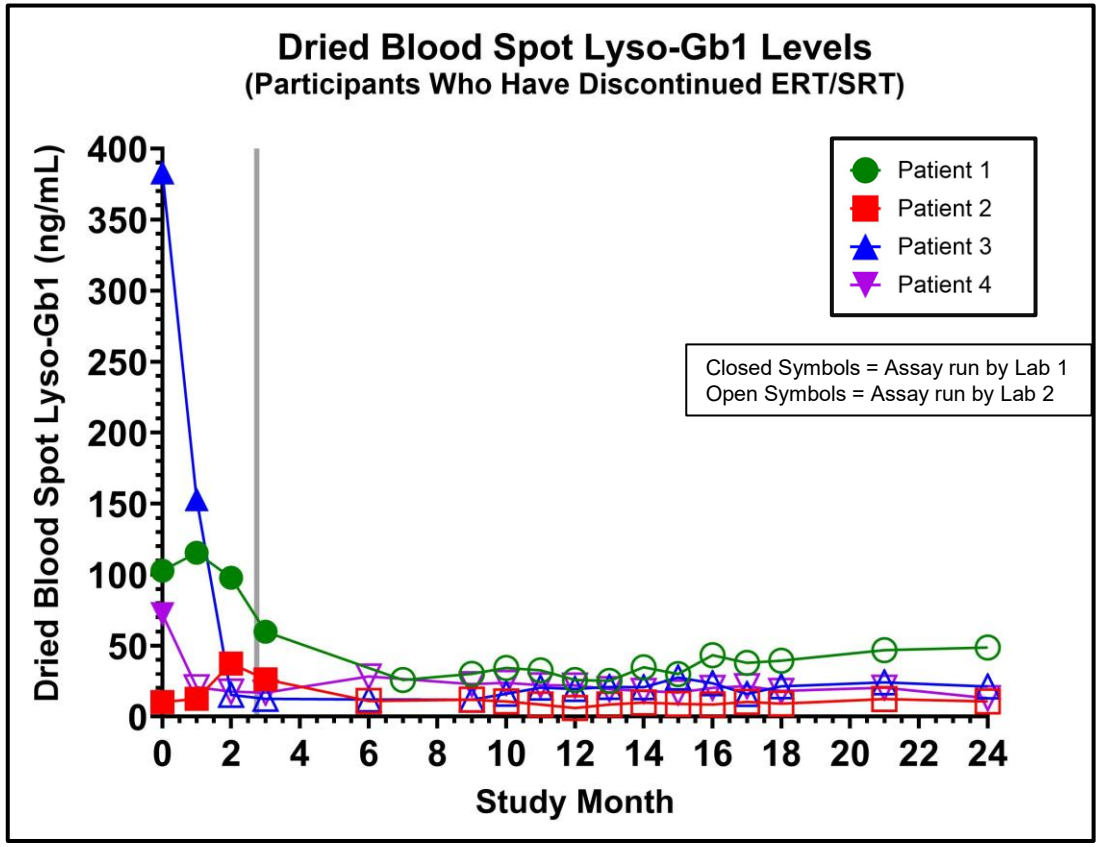
GCase: glucocerebrosidase; SoC: standard of care

Substantial and durable reductions in lyso-Gb1 observed

Lyso-Gb1 is a reliable and validated biomarker for GD[1] and highly correlated to disease severity[2] and treatment response[3]

- Lyso-Gb1 levels were maintained or reduced in all participants who discontinued their SoC
- Despite many years of treatment participants with elevated lyso-Gb1 had reductions as early as month 1 following FLT201 administration

For more detail visit **Poster #379**
Lyso-Gb1 Dynamics as a Surrogate Biomarker in Type 1 Gaucher Disease Treated with FLT201 AAV Gene Therapy



Grey vertical line = time at which last participant discontinued background ERT/SRT therapy (Week 11)

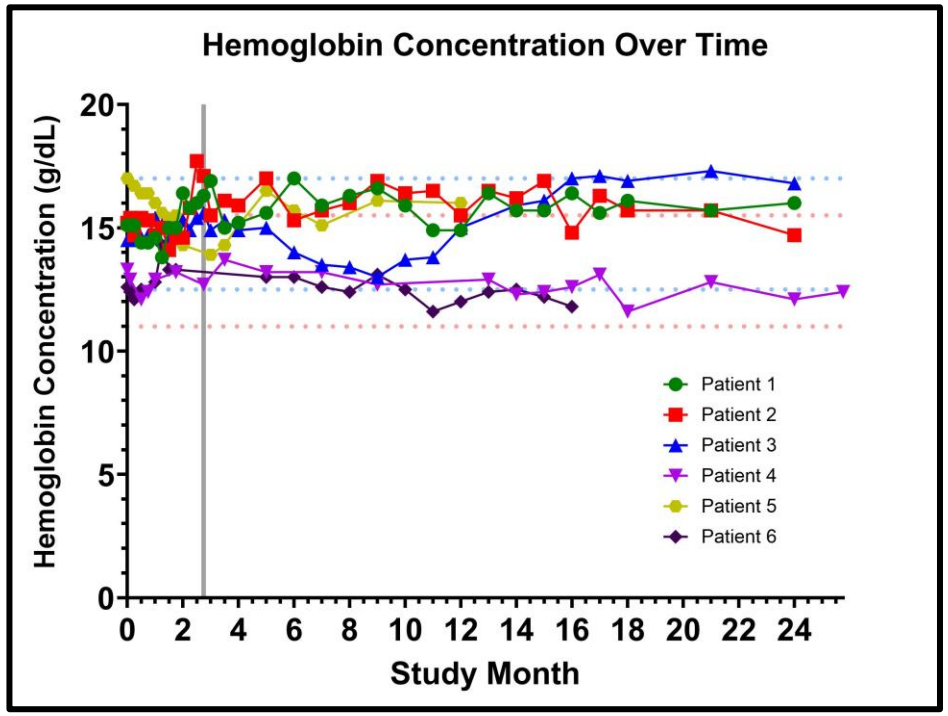
DBS: dried blood spot; ERT: enzyme replacement therapy; GD: Gaucher disease; Lyso-Gb1:glucosylsphingosine; SoC: standard of care; SRT: substrate reduction therapy

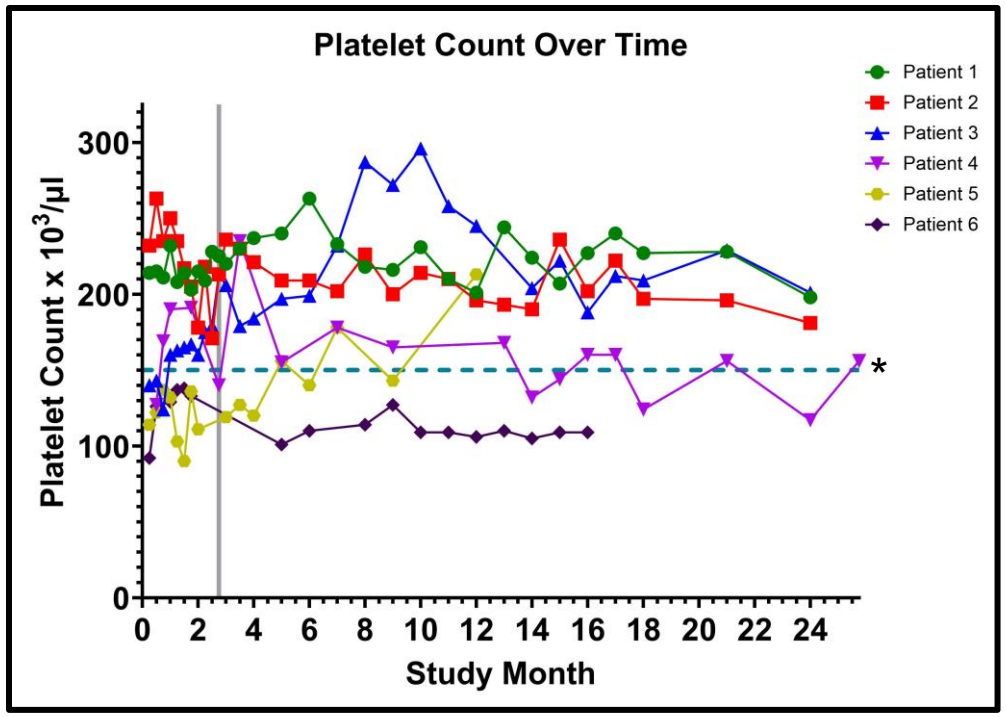
Data cut off as of November 20, 2025

1. Rolfs A., et al, *PlosOne,* 2013, 2. Revel-Vilk S., *Int J. Mol Sci* 2020, 3. Peterschmitt et al. 2023

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

Hemoglobin and platelet levels have improved or remained in the normal range following administration of FLT201





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

Normal platelet count 150-450 x 10^3/µL

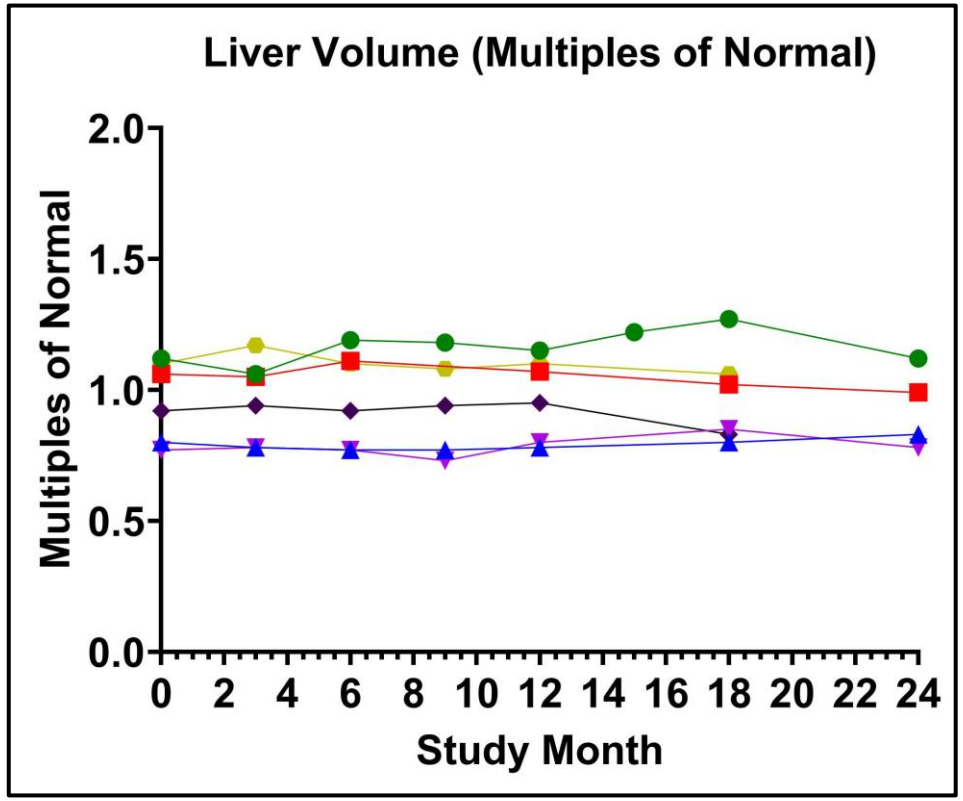
*One participant experienced a transient drop in hemoglobin due to a newly diagnosed iron deficiency. Once iron supplements were initiated, hemoglobin levels returned to normal.

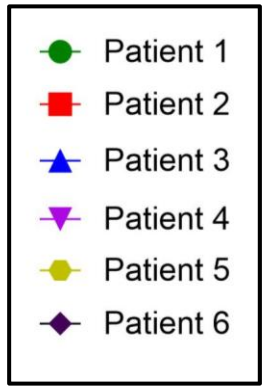
*local sample from unscheduled visit

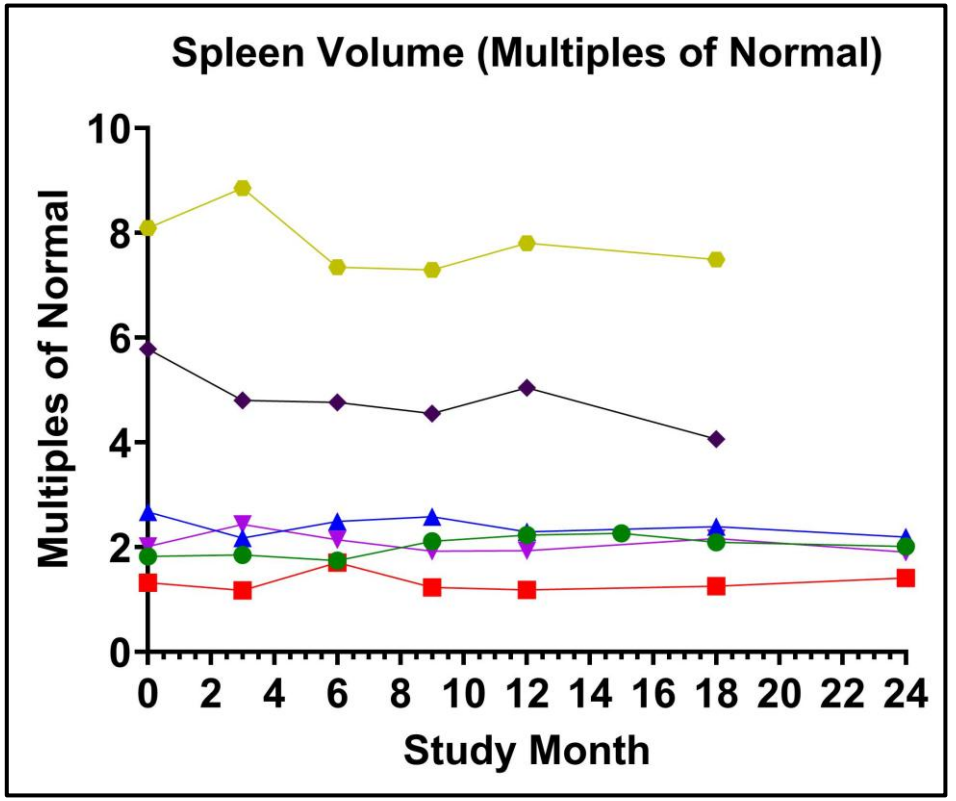
Grey vertical line = time at which last participant discontinued background ERT/SRT therapy (Week 11)

Data cut off as of November 20, 2025

Spleen and liver volumes have remained stable following administration of FLT201







Data cut off as of November 20, 2025

FLT201 continues to be well-tolerated with favorable safety profile

- Infusions were well tolerated; with no infusion-related reactions
- ADRs were mild to moderate
- No dose-limiting toxicities
- 2 cases of ALT elevations above normal range (≤2 x ULN*) deemed related to therapy
  - These spontaneously resolved or were managed with immune therapy
- Transient anti-GCase antibodies in 2 patients
- ADRs related to immune management consistent with known profile

* Central lab values

Summary of ADRs (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)

Adverse Drug Reactions with 2 or more reports

ADR: adverse drug reaction; ALT: alanine aminotransferase; GCase: glucocerebrosidase; ULN: upper limit of normal.

Data cut off as of November 20, 2025

Conclusions

Safety

- FLT201 shows a favorable safety and tolerability profile with a single low dose of 4.5 x 10^{11} vg/kg.
- Infusions well tolerated with no infusion-related reactions
- ADRs were mild to moderate

Efficacy

- Clinical parameters and key biomarkers showed sustained improvement or maintenance up to 26 months to date after the withdrawal of ERT/SRT
- All participants who discontinued ERT/SRT remain off their background therapy

Conclusion

- FLT201 shows potential for meaningful improvements in clinical outcomes over the existing standard of care with a single infusion.
- Continuous expression of GCase85, which is more stable than recombinant human GCase, ensures constant exposure to enzyme
- Preparation for GALILEO-3 (Phase 3) is underway, enrolment scheduled to start in early 2026

ADR: adverse drug reaction; ERT: enzyme replacement therapy; GCase: glucocerebrosidase; SRT: substrate reduction therapy.

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