Poster #136

Individual participant outcomes after FLT201 AAV gene therapy for type 1 Gaucher disease: Two-year biomarker and clinical data

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Overview of GALILEO-1 and GALILEO-2 Trials

- FLT201 is an adeno-associated virus (AAV)-based investigational therapy designed to express GCase85, a recombinant variant of human GCase with extended half-life.
- GALILEO-1 was a first-in-human clinical trial of adult patients with GD1 who had been on a stable background therapy of ERT or SRT for at least 2 years. All participants have enrolled in GALILEO-2, the long-term follow up study.
- Six participants have received FLT201 at a low dose of 4.5 x 10^{11} vg/kg; 4 patients stopped ERT/SRT and have remained off to date; follow-up duration ranges from 20 to 29 months for all participants.
- The 3 individual cases are a sample of the highly relevant clinical and biochemical responses after switching to FLT201; results of the fourth patient are consistent.
- QoL (SF-36) results are presented for all 4 patients.

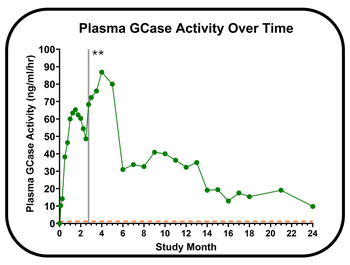
1

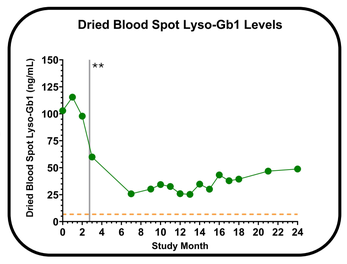
35-year-old male diagnosed at age 4 years

- p.[Val433Leu]; [Asn409Ser]
- 4 years of stable ERT treatment prior to enrollment
- Residual disease at study entry: bone/joint pain, fatigue, and low mental health QoL
- Last ERT dose Week 11
- Maintained normal hemoglobin and platelets throughout; maintained organ volumes (spleen: 1.82-2.01 MN; liver 1.12-1.12 MN)

Persistent GCase expression and reduction in toxic lyso-Gb1

Normal plasma GCase activity: 0.3-1.2 µmol/L/h



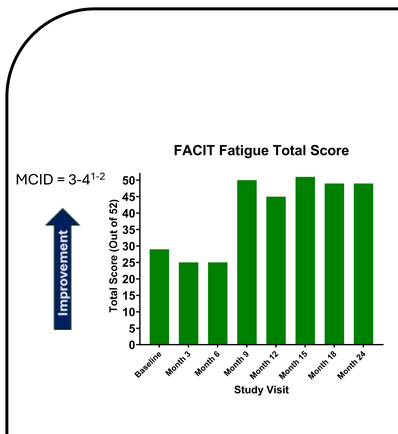


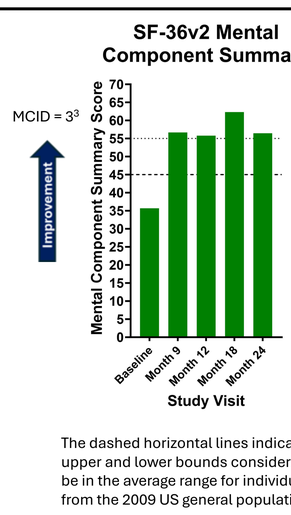
Normal DBS lyso-Gb1 activity: ≤6.8 ng/mL

Pathologic DBS lyso-Gb1 activity: > 12 ng/mL

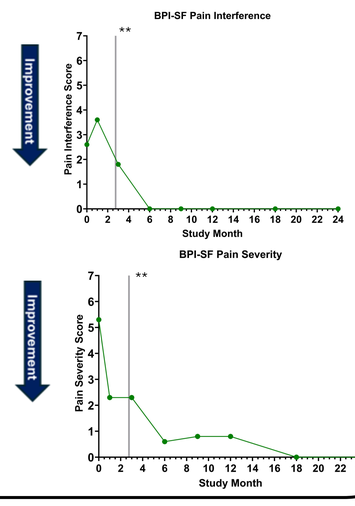
**Grey vertical lines on graphs represent the point at which each participant discontinued background ERT/SRT therapy

Highly clinically relevant improvements in fatigue, pain, and mental health





The dashed horizontal lines indicate the upper and lower bounds considered to be in the average range for individuals from the 2009 US general population



Case discussion

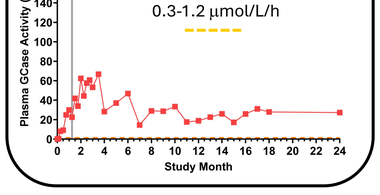
- FLT201 resulted in a rapid rise in GCase expression, followed closely by reductions in lyso-Gb1 and clinical improvements thereafter
- Maintenance of hemoglobin and platelets levels are highly relevant at the 2-year mark, as worsening would have been seen with a lack of adequate enzymatic control
- Significant improvements in patient-reported outcome measures are consistent and highly meaningful

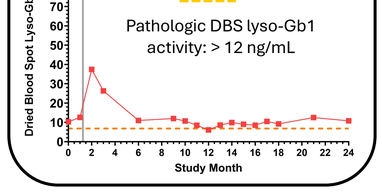
2

25-year-old male diagnosed at age 3 years

- p.[Asn409Ser]; [Leu483Pro]
- 22 years of stable ERT/SRT treatment prior to enrollment
- Disease fairly well controlled
- Last SRT dose Week 5
- Maintained normal hemoglobin and platelet levels throughout; maintained organ volumes (spleen: 1.32-1.41 MN; liver 1.06-0.99 MN)
- Maintained normal pain, fatigue, and mental health scores

Persistent GCase expression and maintenance of low lyso-Gb1





**Grey vertical lines on graphs represent the point at which each participant discontinued background ERT/SRT therapy

Case discussion

- FLT201 is responsible for the maintenance of the low lyso-Gb1 as, without adequate enzymatic control, levels would rapidly worsen as seen during a forced treatment break during ERT shortage (**Figure 1**)[4]

Effect on lyso-Gb1 of a forced treatment break (FTB) in ERT[4]

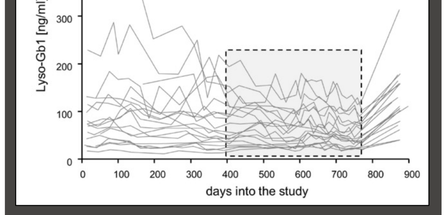


Figure 1. Lyso-Gb1 values in a cohort of 19 routinely monitored Gaucher patients. The box denotes a subset of measurements over a ~12-month period for assessments in coefficients of variation.[4]

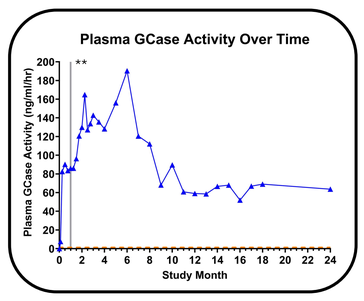
3

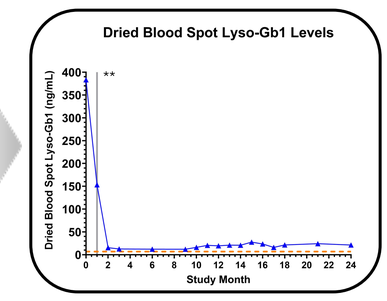
24-year-old male diagnosed at age 16 years

- p.[Gln112ValfsTer32]; [Leu422ProfsTer4; Leu483Pro; Ala495Pro]
- 9 years of stable ERT/SRT treatment prior to enrollment
- Residual disease at study entry: marked/severe bone marrow infiltration, thrombocytopenia
- Last SRT dose Week 4
- Maintained normal pain, fatigue, and mental health scores

Persistent GCase expression and drastic reduction in toxic lyso-Gb1

Normal plasma GCase activity: 0.3-1.2 µmol/L/h



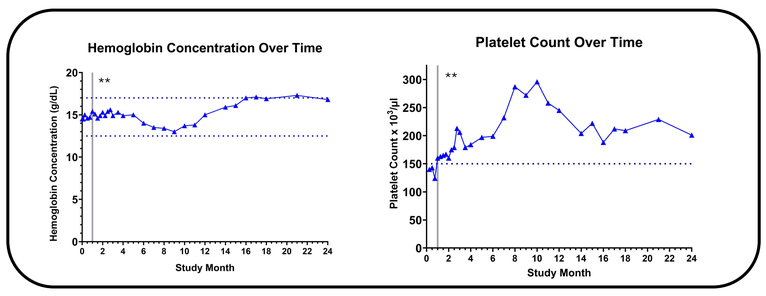


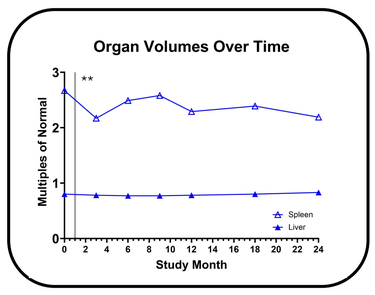
Normal DBS lyso-Gb1 activity: ≤6.8 ng/mL

Pathologic DBS lyso-Gb1 activity: > 12 ng/mL

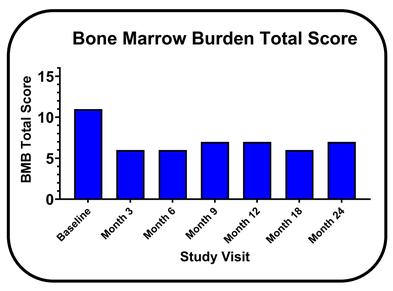
**Grey vertical lines on graphs represent the point at which each participant discontinued background ERT/SRT therapy

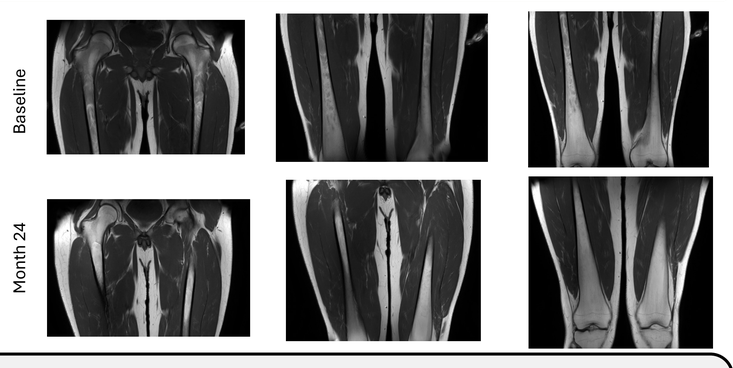
Normalization of platelet levels maintained out to 2 years; improved spleen volumes





Clinically relevant improvements in bone health





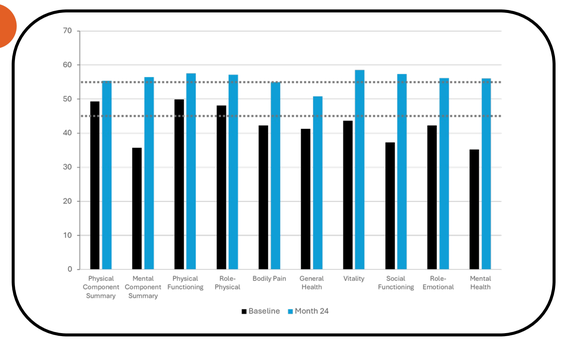
Case discussion

- FLT201 resulted in a rapid rise in GCase expression followed closely by marked reductions in lyso-Gb1, with platelets and bone improvements thereafter
- Clinically relevant reductions in bone marrow infiltration/dark matter can be seen on MRI

SF-36

- A Minimally Important Difference (MID) generally refers to the smallest change in score that a person perceives as meaningful; SF-36 User's Manual proposes MID values of 2 to 4 across component and scale groups in terms of T-score points[3]
- Validated MID in the SF-36 scale has not been published to date for the Gaucher population; ranges for various chronic diseases have been reported with an MID ranging from 1-6 based on the population
- All patients either remained in or improved to the "normal" range after receiving FLT201, with one patient having a notable improvement in all components
- Overall, meaningful improvements were seen in general health, vitality, and bodily pain after receiving FLT201

1



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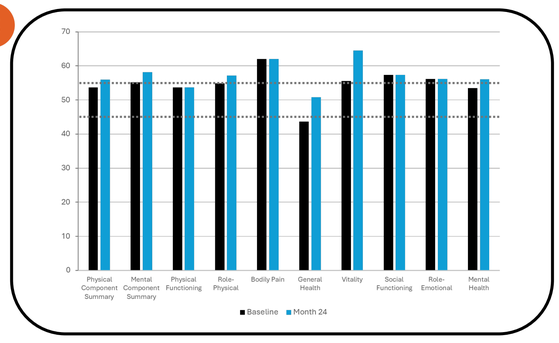

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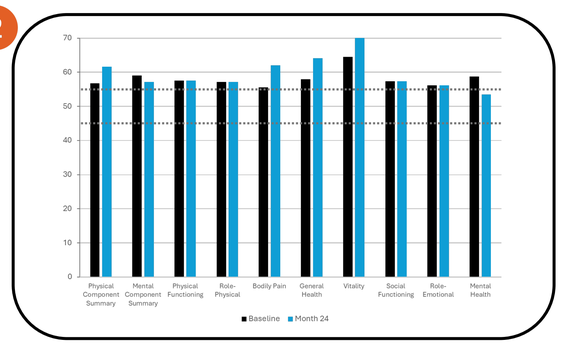

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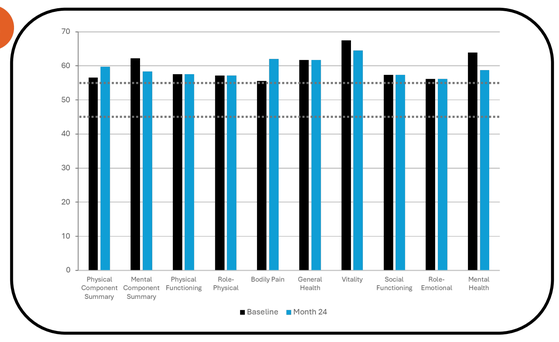

The dashed horizontal lines indicate the upper and lower bounds of *T* scores considered to be in the average range for individual respondents from the 2009 US general population[3]

SF-36 component	MID	SF-36 component	MID
Physical Component Summary	2	General Health	2
Mental Component Summary	3	Vitality	2
Physical Functioning	3	Social Functioning	3
Role-Physical	3	Role-Emotional	4
Bodily Pain	3	Mental Health	3

Please see **Poster #315** for clinical outcomes after FLT201 dosing

Acknowledgements

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References

1. Kiss F et al. *Int J Environ Res Public Health*. 2022;20(1):771. 2. Cella D at al. *J Rheumatol* 2005;32(5):811-819. **3.** Maruish ME (Ed.). (2011). *User's manual for the SF-36v2 Health Survey* (3rd ed.). Lincoln, RI: QualityMetric Incorporated. **4.** Cozma C et al. *Int J Mol Sci.* 2020. 27(13):4577.

Abbreviations: AAV: adeno associated virus; BPI: brief pain inventory; DBS: dried blood spot; ERT: enzyme replacement therapy; FTB: forced treatment break; GCase: Glucocerebrosidase; GD1: Gaucher disease type 1 ; Lyso-Gb1: glucosylsphingosine; MCID: Minimal Clinically Important Difference; MN: Multiples of normal; QoL: quality of life; SF36: 36-Item Short Form Health Survey; SRT: substrate reduction therapy; vg: vector genome.

Data cut off as of November 20, 2025

GALILEO-1 / GALILEO-2 studies are sponsored by Spur Therapeutics