

Results from GALILEO-1, a first-in-human clinical trial of FLT201 gene therapy in patients with Gaucher disease Type 1

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2. Freeline Therapeutics, Stevenage, UK

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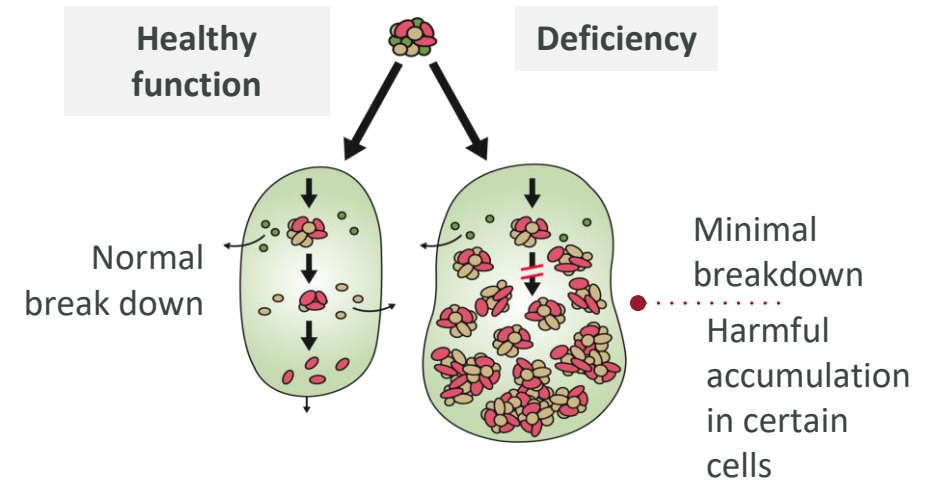
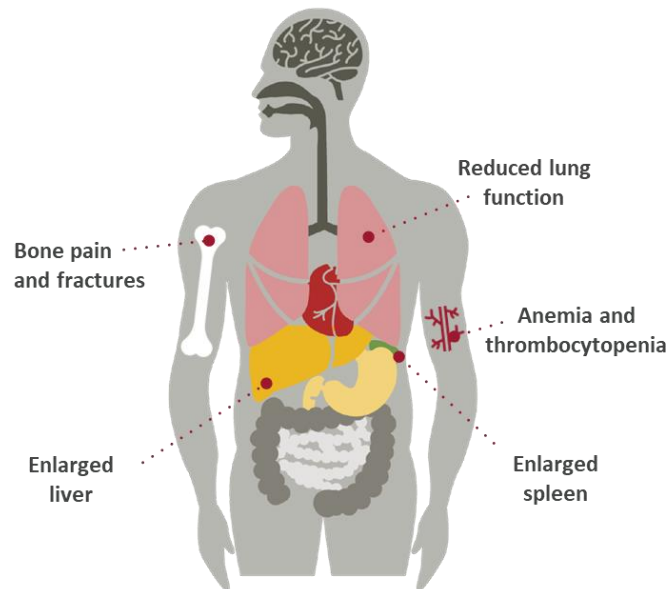


Conflicts of interest

Dr. Goker-Alpan is an investigator on the Freeline FLT201 GALILEO-1 study and has received funding from Freeline for travel and sponsorship of educational Gaucher disease meetings.

Gaucher disease Type 1 is a progressive multisystem disorder

- Rare genetic Lysosomal Storage Disease resulting from deficiency of glucocerebrosidase (GCase) due to mutations in *GBA1*
- GCase deficiency leads to accumulation of glucocerebroside throughout the body, including in macrophages and the reticuloendothelial system



- GD Type 1 is characterized by hepatosplenomegaly, anemia, thrombocytopenia, bone disease and pulmonary involvement without neurological involvement
- Approved therapies include life-long enzyme replacement therapy (IV q2 weeks) and substrate reduction therapy (oral BID-TID)

FLT201: an AAV gene therapy generating continuous GCCase production may address aspects of Gaucher disease that ERT cannot



- 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** in at lysosomal pH conditions
- Produces robust and sustained secretion of GCase into the bloodstream
- No changes in predicted immunogenicity compared to velaglucerase alfa

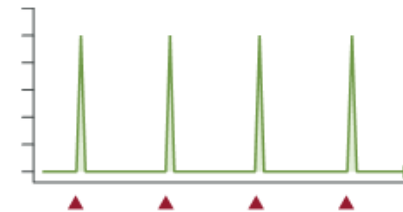


ERT



Every 2 weeks

Transient spikes in GCase in during infusion, limited systemic distribution and short-lived retention in cells



After 10 years on ERT up to

60%

still experience symptoms¹

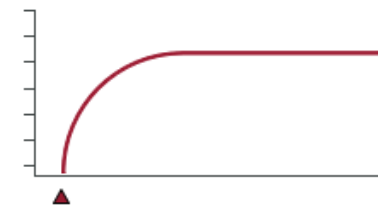


FLT201



Single dose

Steady, constant GCase expression in plasma and within all cell types tested²



Near complete prevention of substrate accumulation²

Liver, spleen, bone marrow, lung

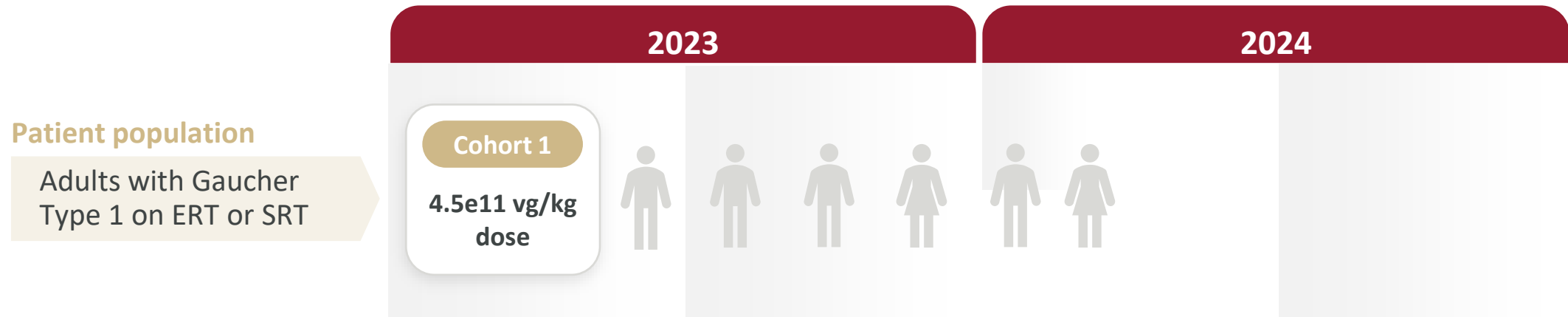
in non-clinical studies

GBA = glucosylceramidase beta; LSP = liver-specific promoter; PolyA = polyadenylation signal sequence; velaglucerase alfa = enzyme replacement therapy

2. Internal Freeline data from non-clinical Gaucher models

Ongoing GALILEO-1 Phase 1 dose-finding study

First-in-human, open-label, international, multicenter study



- 6 patients dosed: 2 females and 4 males; age range 24 – 58 years; 4 on SRT and 2 on ERT
- Patients come off prior therapy upon evidence of GCase expression
- Prophylactic immune regimen begins 3 weeks post-infusion - oral prednisone and oral tacrolimus
- Primary objective = safety
- Secondary objectives = transgene expression and efficacy
- Patients enter long-term follow-up study for a total of 5 years

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

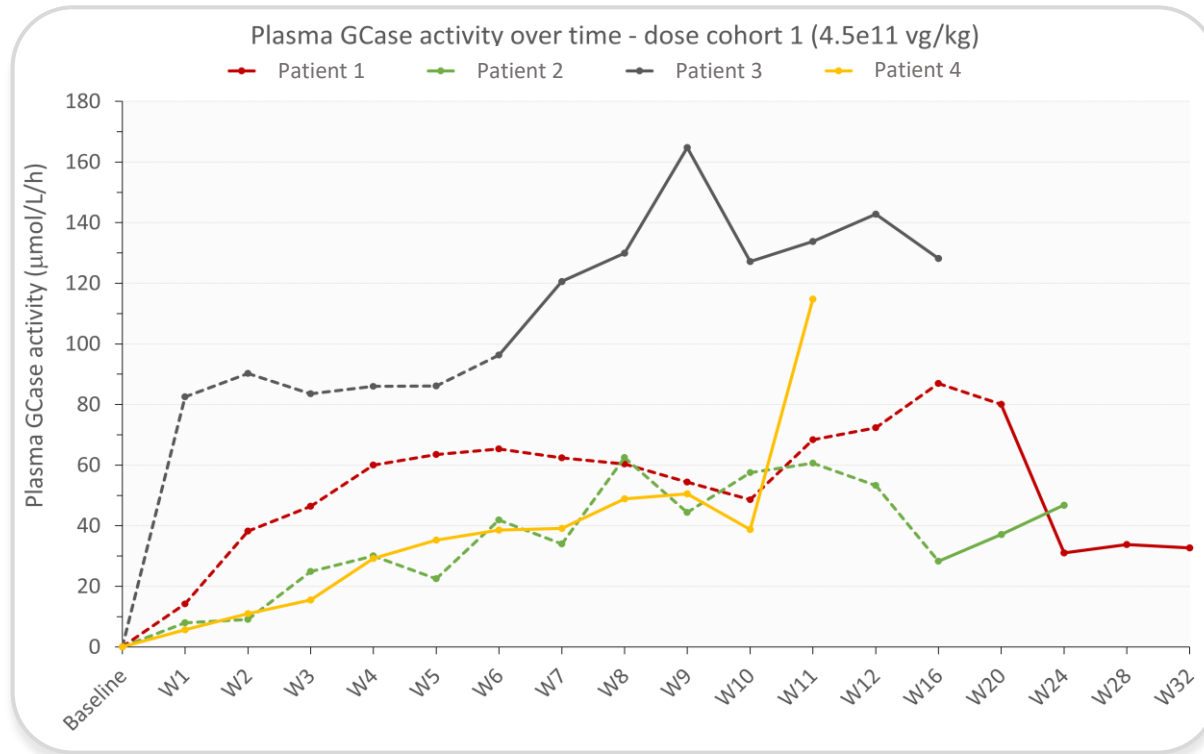
Safety

- Infusions well tolerated; no reactions
- No serious adverse events
- No severe adverse events or dose-limiting toxicities
- Any modest ALT elevations managed with immune therapy with no impact on efficacy
- Non-serious adverse events all mild or moderate in severity
- AEs related to immune management consistent with known profile of prednisone and tacrolimus

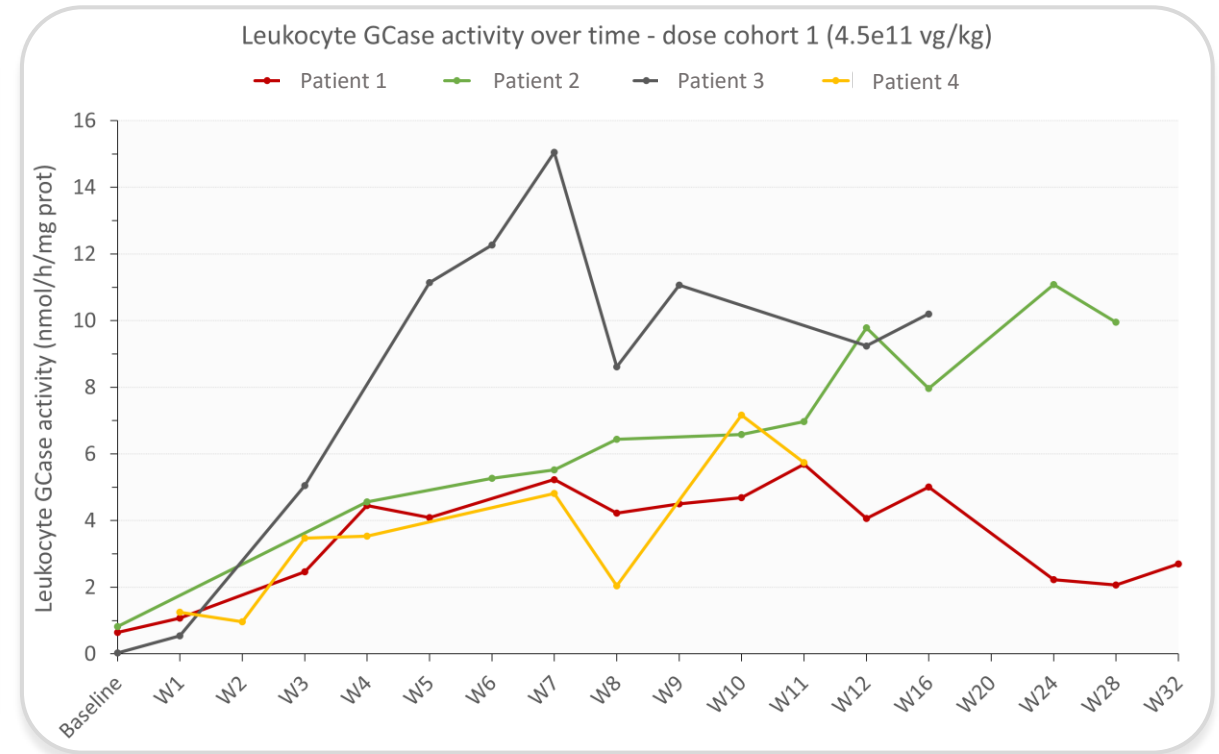
FLT201 generates robust and continuous GCase expression with clear uptake into cells

Dose cohort 1 (4.5e11 vg/kg)

Plasma GCase activity over time

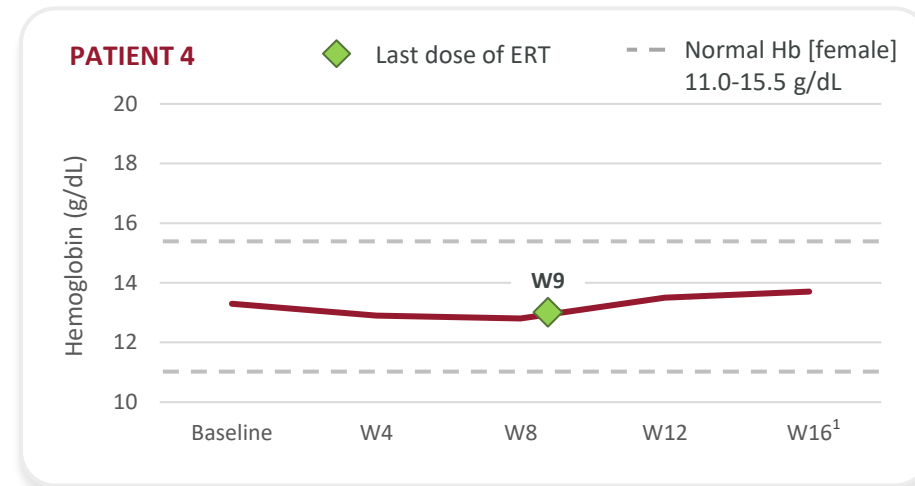
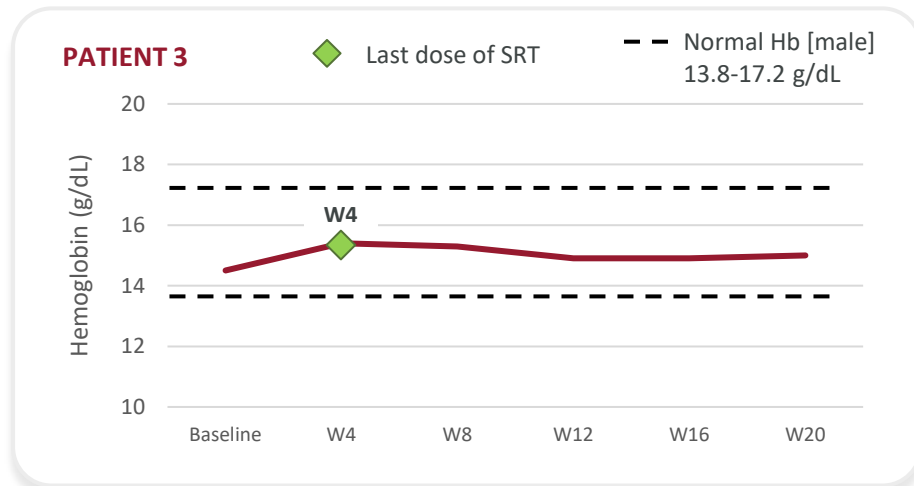
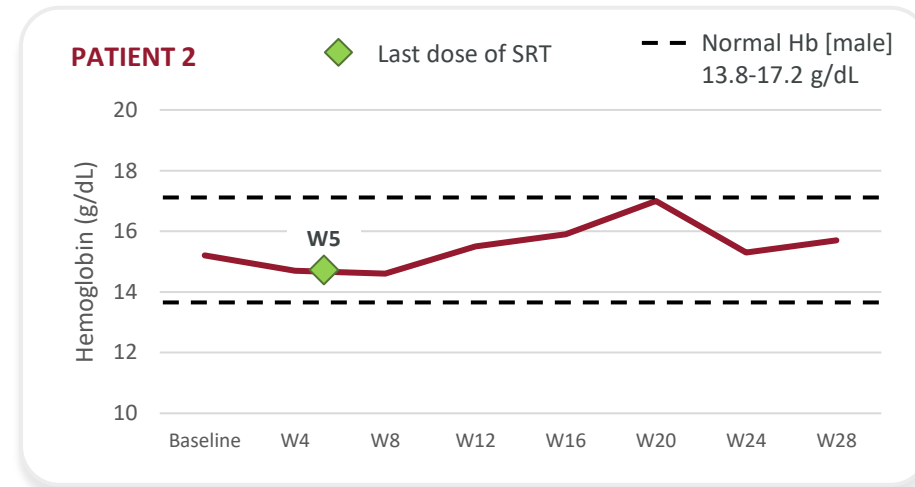
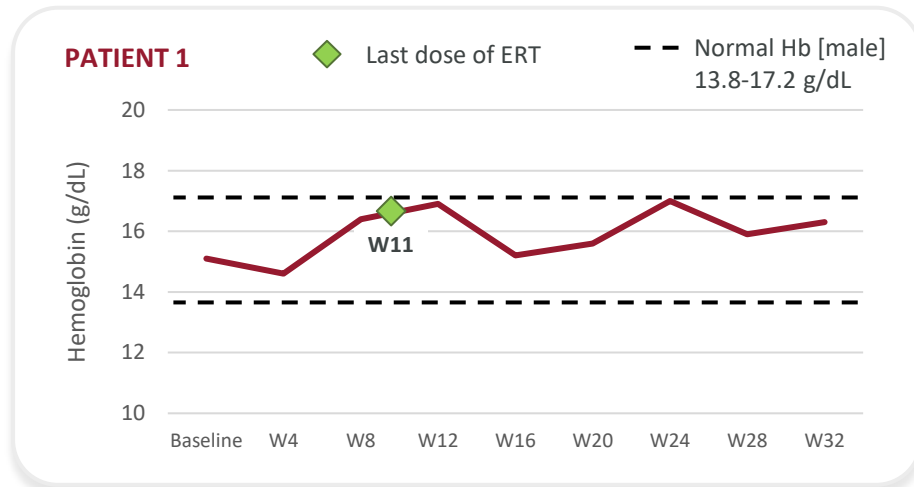


Leukocyte GCase activity over time



Maintenance of hemoglobin observed after withdrawal of ERT or SRT

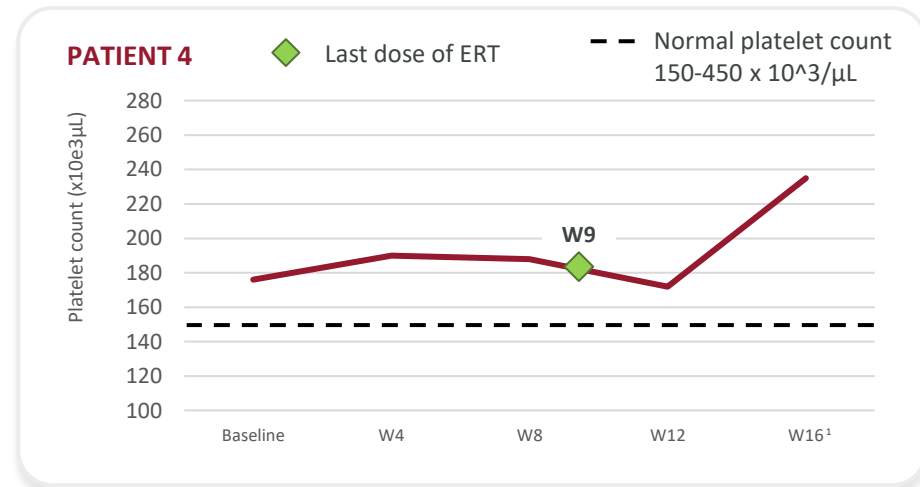
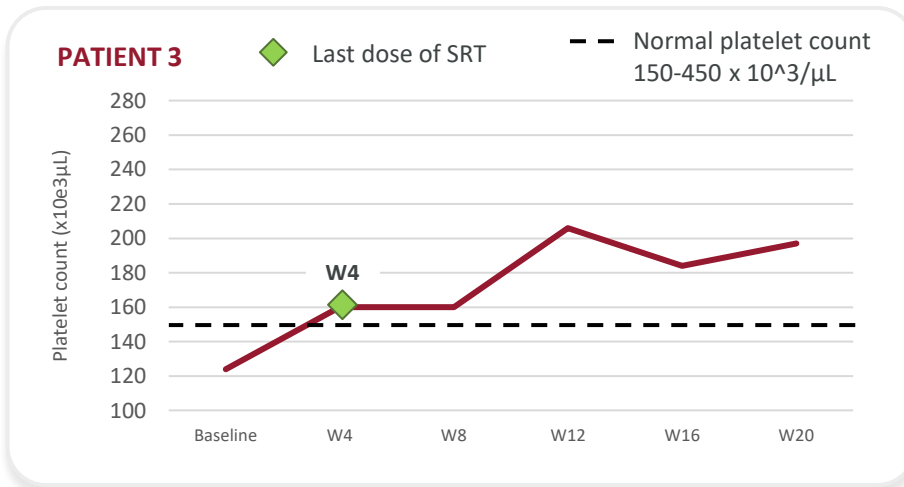
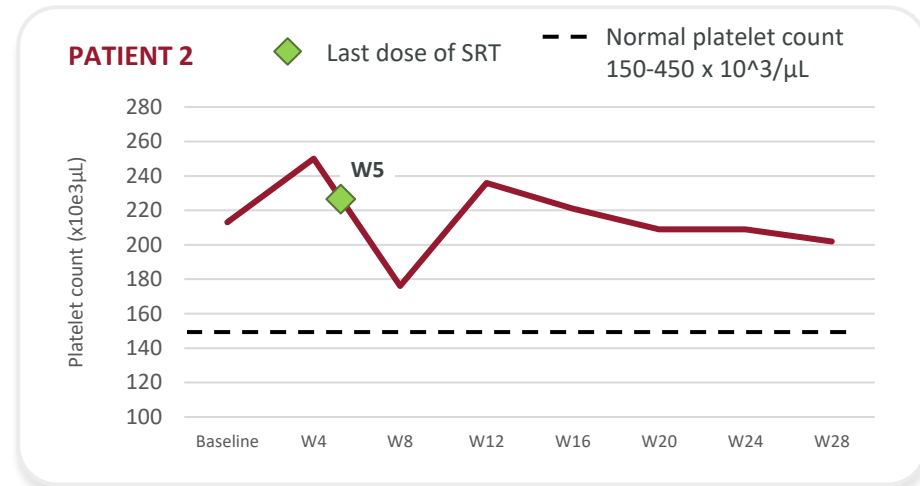
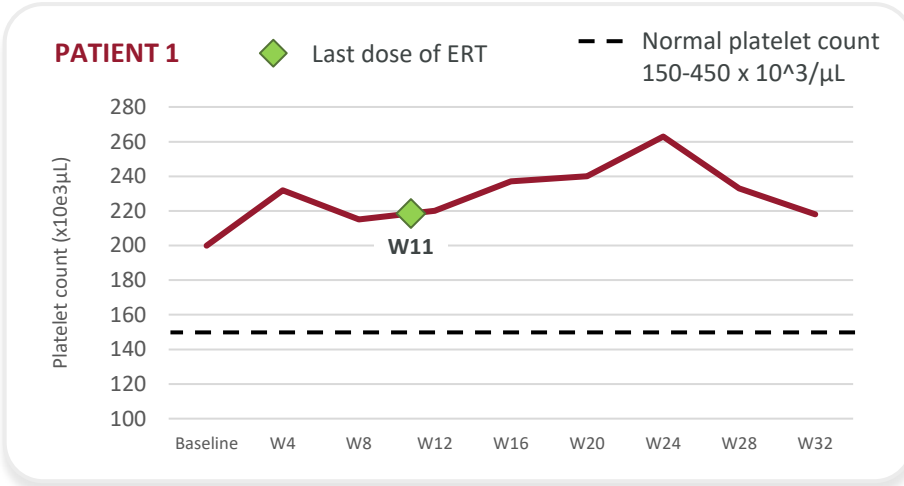
Hemoglobin concentration over time



¹ W14 represented; closest patient measurement at W16

Improvement or maintenance of platelets observed after withdrawal of ERT and SRT

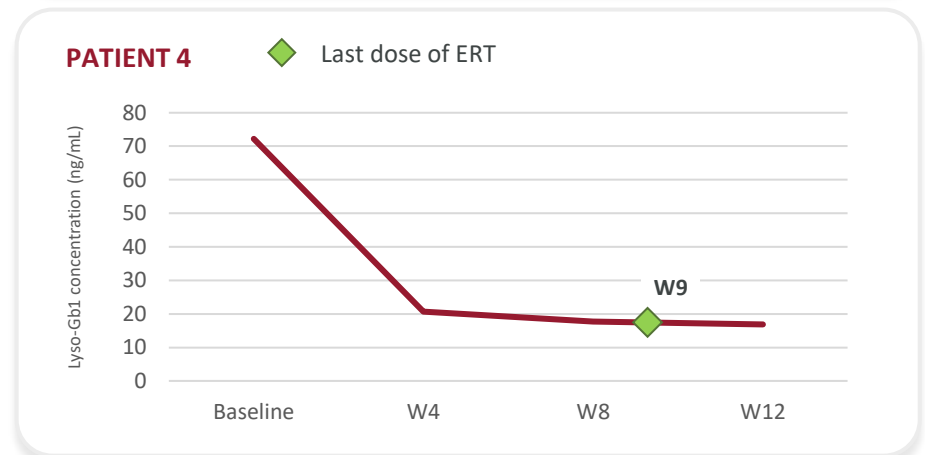
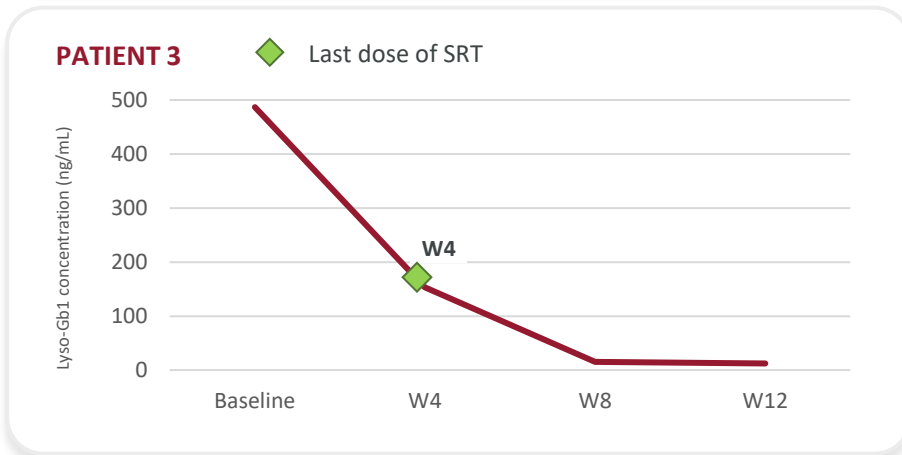
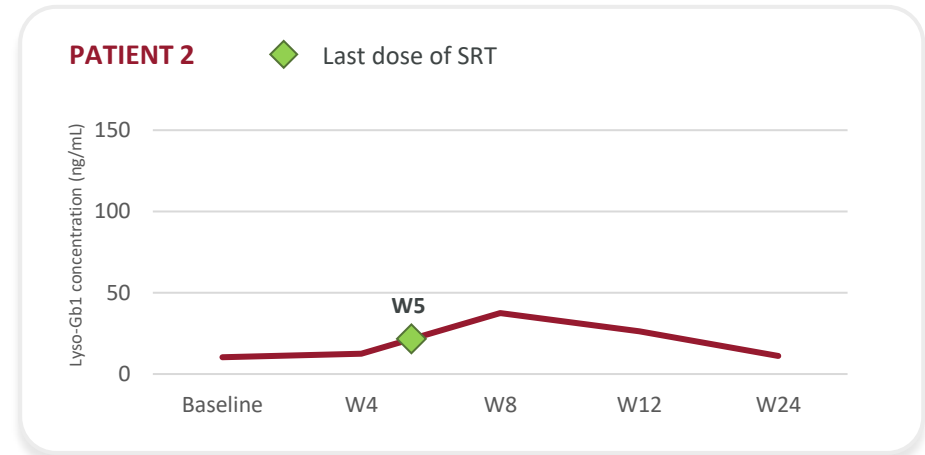
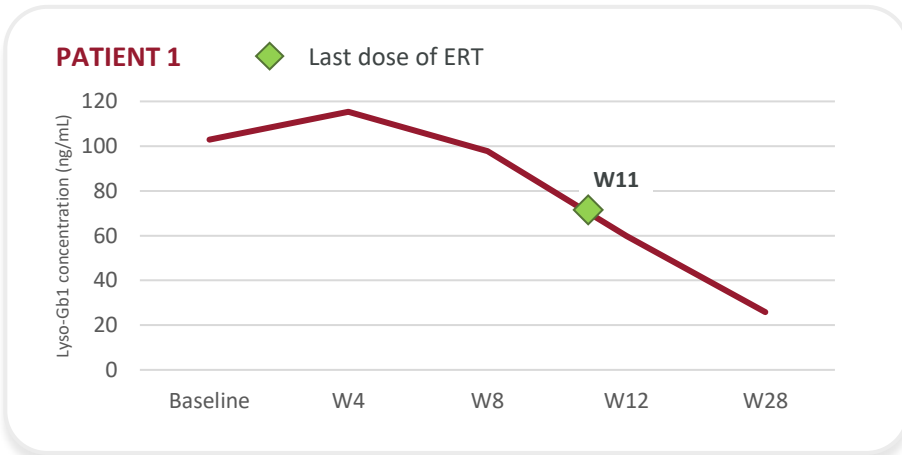
Platelet count over time



¹ W14 represented; closest patient measurement at W16

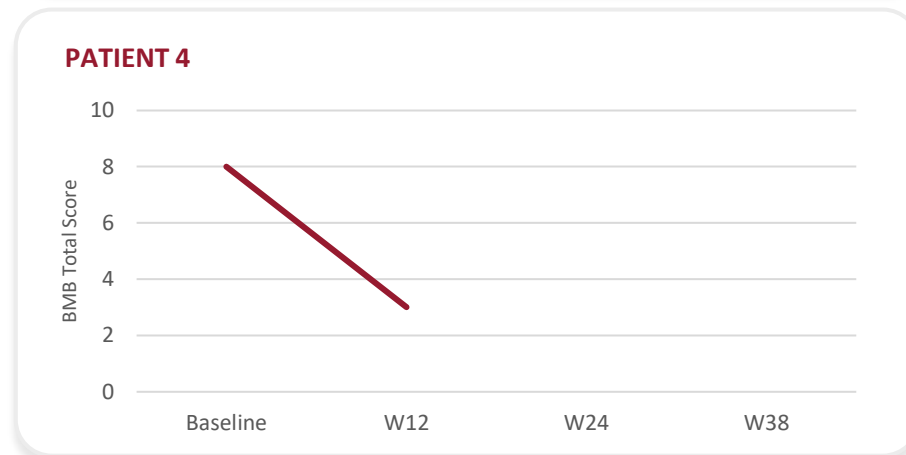
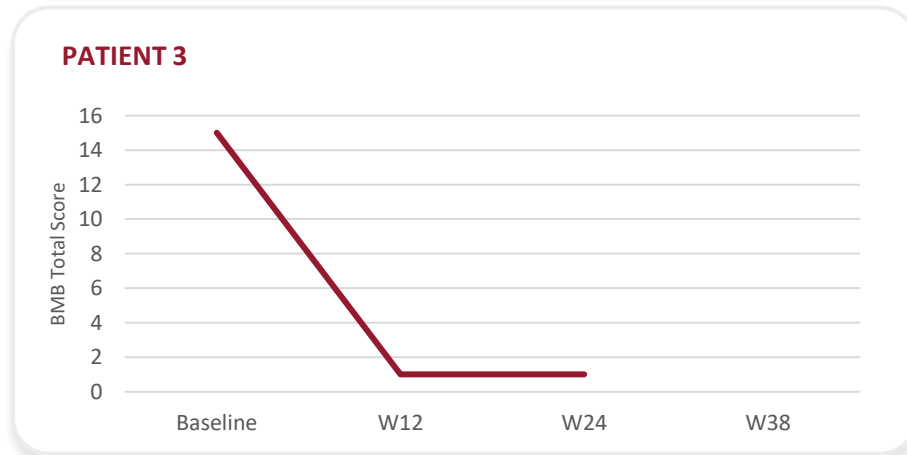
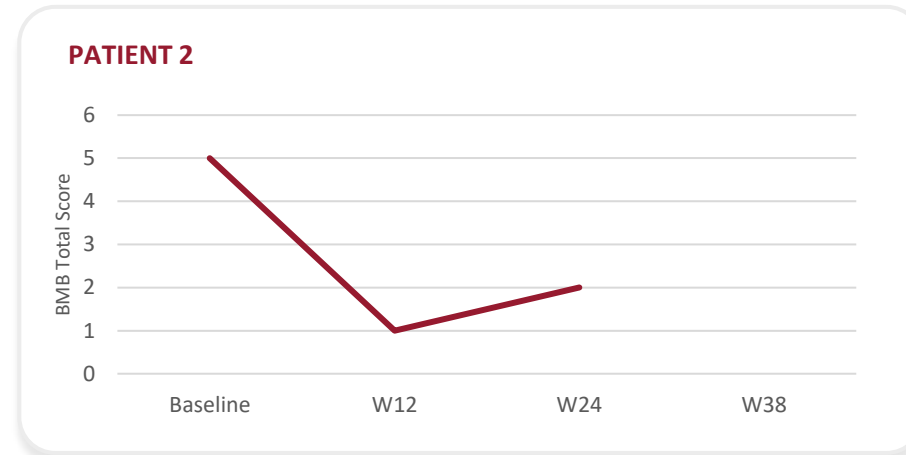
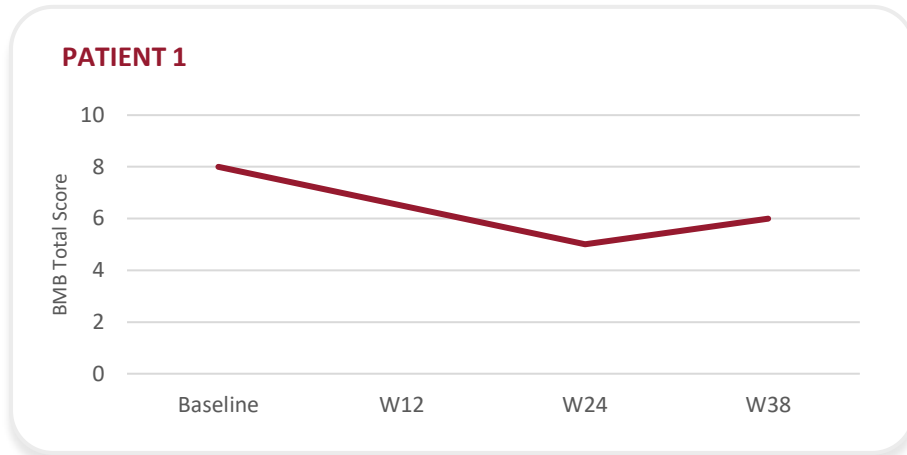
Substantial reductions in lyso-Gb1 as early as week 4 in patients with elevated baseline levels

Dried blood spot lyso-Gb1 concentration over time



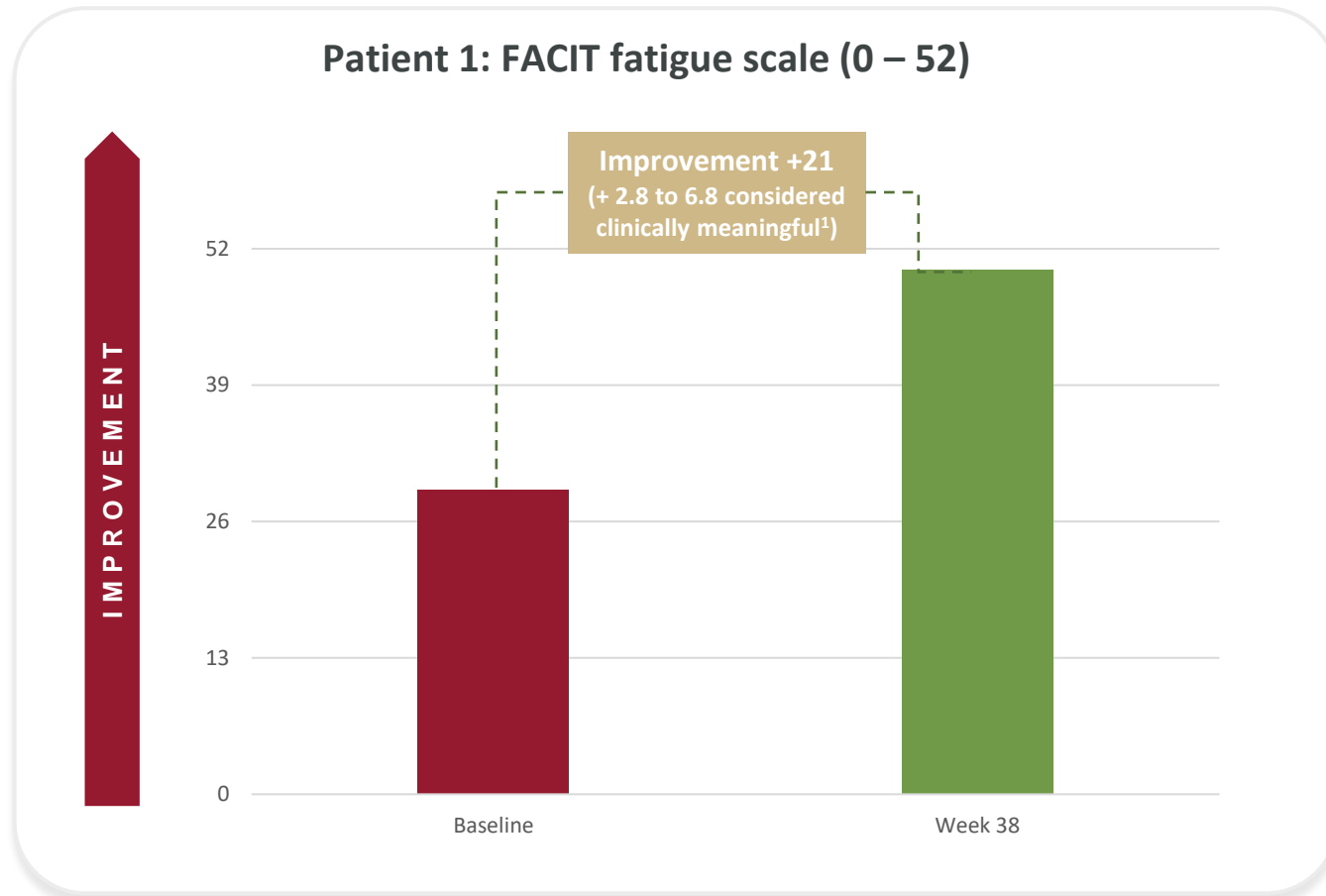
Late breaking: Emerging data demonstrate beneficial effect on Bone Marrow Burden (BMB)

BMB score by MRI over time



Improvements even in patients with severe BMB* indicates clearance of substrate in tissues difficult to reach with current standard of care

Late breaking: Clinically meaningful improvement in fatigue



Patient reported significant improvements in fatigue and ability to perform daily activities

- Has energy
- Able to do usual activities
- No longer feels tired, washed out or weak all over
- No longer has trouble starting or finishing things due to tiredness
- No longer frustrated by being too tired to do the things they want to do
- No longer has to limit social activity due to tiredness

FACIT = Functional Assessment of Chronic Illness Therapy

Data cut off April 8, 2024: patients with available W38 data

¹Greenbaum 2020; clinically meaningful in cancer, lupus, HUS, RA

Promising initial data from GALILEO-1 on FLT201 gene therapy for patients with Gaucher disease Type 1

- FLT201 is an investigational AAV gene therapy being studied in adults with Gaucher disease Type 1
- Continuous presence of GCase85, which is more stable than recombinant human GCase, ensures constant tissue access to the needed enzyme
- Early clinical data shows a favorable safety profile with robust GCase expression in plasma and continuous GCase activity in the cell
- Early lyso-Gb1 data and reduction in BMB and fatigue suggest potential for meaningful improvements in clinical outcomes over existing standard of care with a single infusion of FLT201

Acknowledgements

The Gaucher disease community

- Patients, families and friends
- Gaucher Community Alliance
- International Gaucher Alliance
- Gaucher Association UK

Study investigators

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