FREELINE

Corporate Presentation

August 2023

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Creating better gene therapies for chronic debilitating diseases

Potential first- and best-in-class lead program

Highly differentiated gene therapy candidate FLT201 for Gaucher disease type 1 in first-in-human clinical trial

Extending innovation into Parkinson's disease

Lead research program leverages same novel GCase variant as FLT201 for GBA1-linked Parkinson's disease

Near-term data readout in Gaucher disease

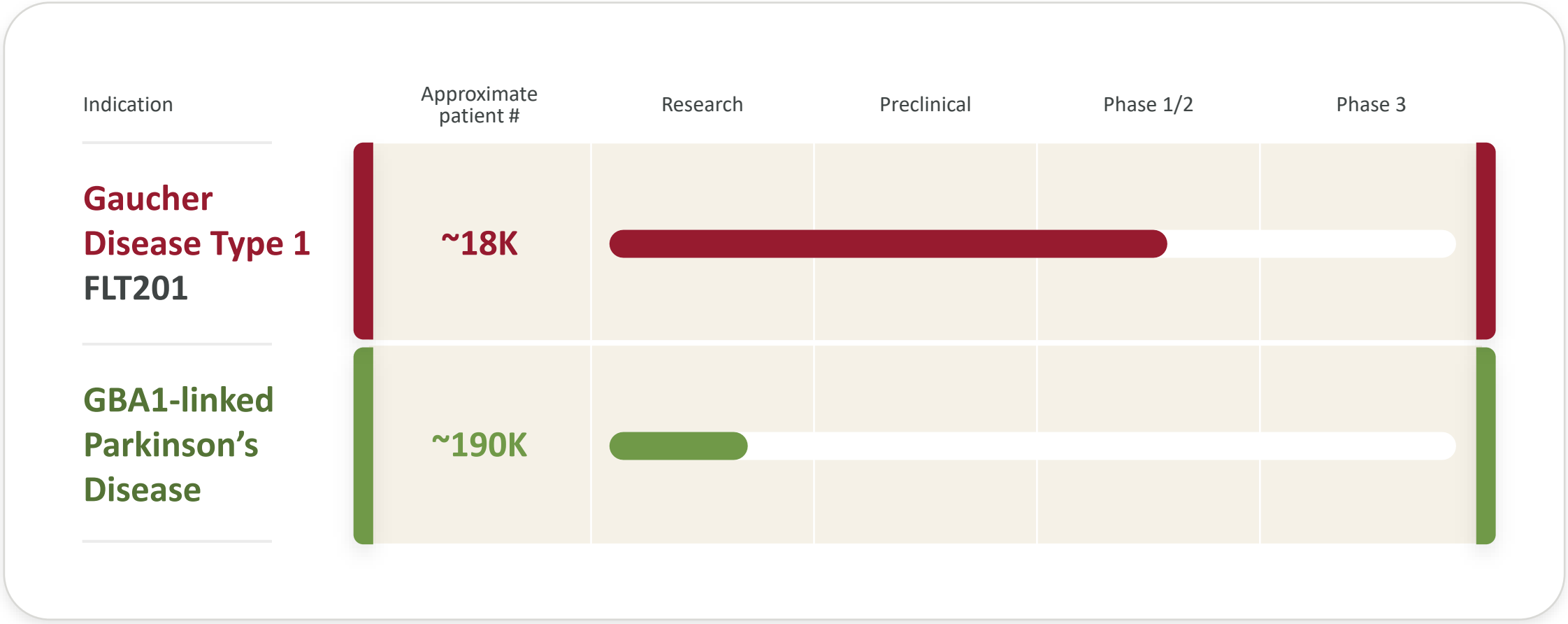
Initial safety and enzyme activity data for FLT201 expected in Q3 2023

Experienced management team

Seasoned leaders with the experience and expertise to drive progress and execution

Our approach is to optimize all components of our product candidates to unlock the true potential of gene therapy

Lead clinical program with first- and best-in-class potential with research extending innovation into larger disease area



Estimated patient numbers for Gaucher disease Type 1 are for US, UK, EU4 and Israel (Hematology. 2017 Mar;22(2):65-73. doi: 10.1080/10245332.2016.1240391; this figure represents the total theoretical genetic prevalence of the indication. The seroprevalence of antibodies against the AAVS3 capsid renders some patients ineligible for AAV gene therapy. We estimate approximately 60% would be eligible for AAVS3 gene therapy. Company estimate of patient numbers for GBA1-linked PD are for US, UK and EU4 .

FLT201 in Gaucher Disease

FLT201: Potential first- and best-in-class gene therapy for Gaucher disease Type 1

HIGHLY DIFFERENTIATED

- Novel transgene encoding a rationally engineered longer-acting GCase variant
- Potential to penetrate deeper tissues that current therapies do not sufficiently reach
- Proprietary AAVS3 capsid delivers high and durable protein expression at low doses

SIGNIFICANT MARKET OPPORTUNITY

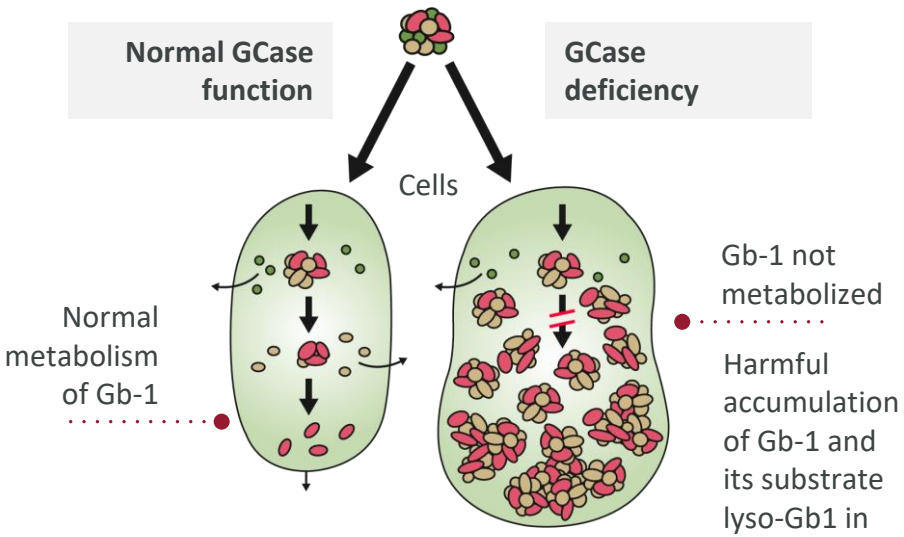
- Most common type of Gaucher disease
- ~18k patients in US, UK, EU4 and Israel

ENCOURAGING DATA & NEAR-TERM CATALYST

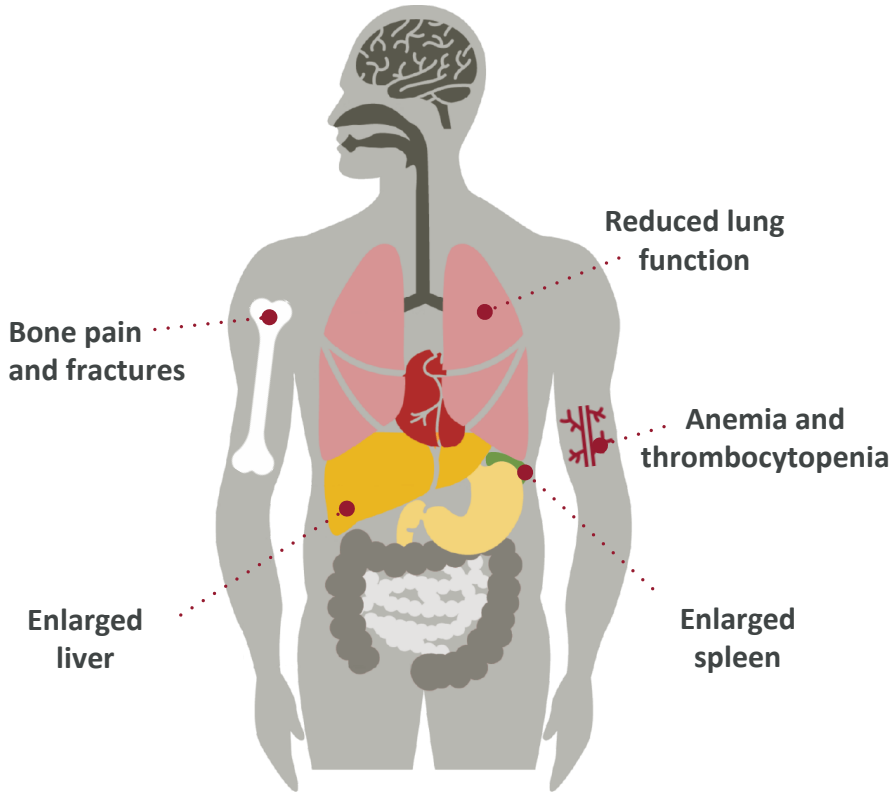
- Robust preclinical data showing GCase uptake and substrate clearance in all disease-affected tissues
- Dosing underway in Phase 1/2 GALILEO-1 trial
- Initial data, including safety and enzyme activity, from first cohort expected in Q3 2023

Gaucher disease type 1 is a debilitating, chronic and progressive disorder with life-altering symptoms

Deficiency of GCase enzyme needed to metabolize Gb-1



Affects multiple organs, leading to wide range of symptoms and shortening life span[1]



[1]Weinreb, et al., 2008

Existing therapies poorly address certain aspects of disease

LENGTHY INFUSION EVERY TWO WEEKS

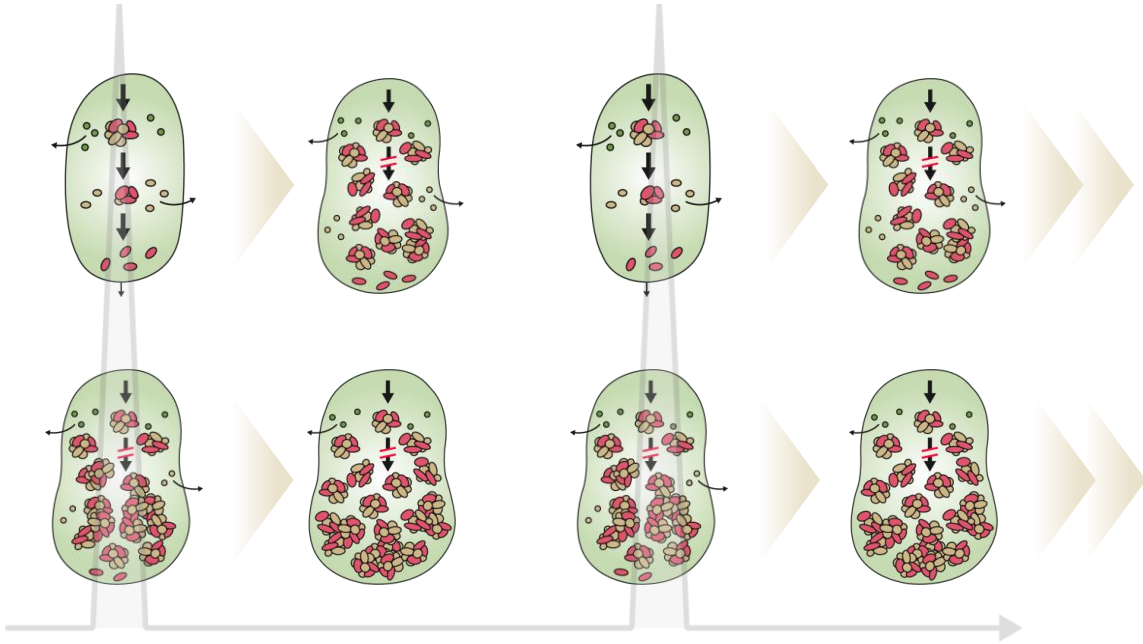
ERT

Enzyme replacement therapy current standard of care

PEAKS AND TROUGHS in enzyme levels between infusions allow harmful substrates to build back up

Easier to reach organs: liver, spleen

Harder to reach organs: bone, lung



DOES NOT ADEQUATELY PENETRATE deeper organs, including bone and lung

Despite treatment, many patients continue to have disease progression and debilitating symptoms

After 10+ years on ERT up to **60%** still experience symptoms[1]

bone pain

enlarged liver

enlarged spleen

low blood counts

43%
still have bone pain†

56%
still have severely enlarged livers †

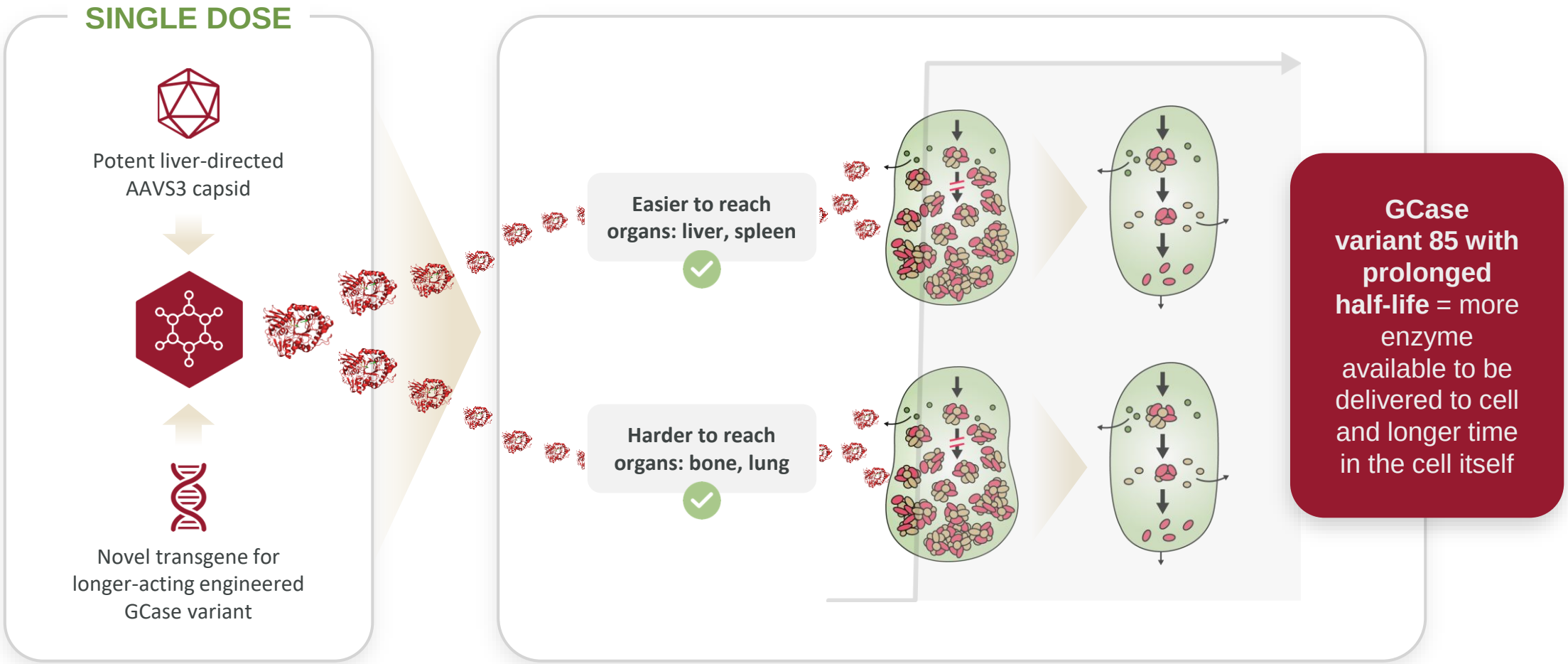
61%
still have severely enlarged spleens †

43%
still have severely low platelet counts †

68%
have pulmonary dysfunction at baseline with most likely not having any normalization with ERT[2]

[1] Weinreb et al., 2013; 2 Kerem, et al., 1996 and Goitein, et al 2001; † in those with these symptoms before ERT

FLT201 has potential to deliver continuous level of enzyme and penetrate deeper tissues that ERT does not reach



Our scientists engineered GCase variant with substantially longer half-life than wildtype

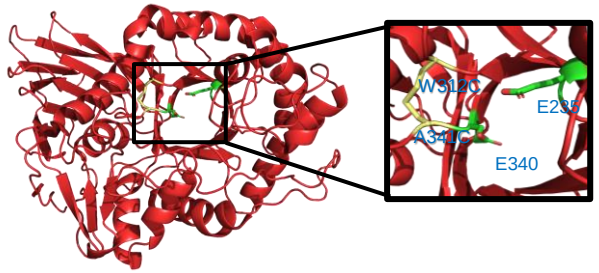
Key features of GCase variant

- 20-fold increase in half-life in lysosomal pH compared with wildtype (wt)
- Specific activity unchanged compared to wt GCase
- 6-10 fold increase in half-life compared to wt, enabling increased steady-state plasma levels *in vivo*

GCase variant 85 structure

Two internal amino acid substitutions

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

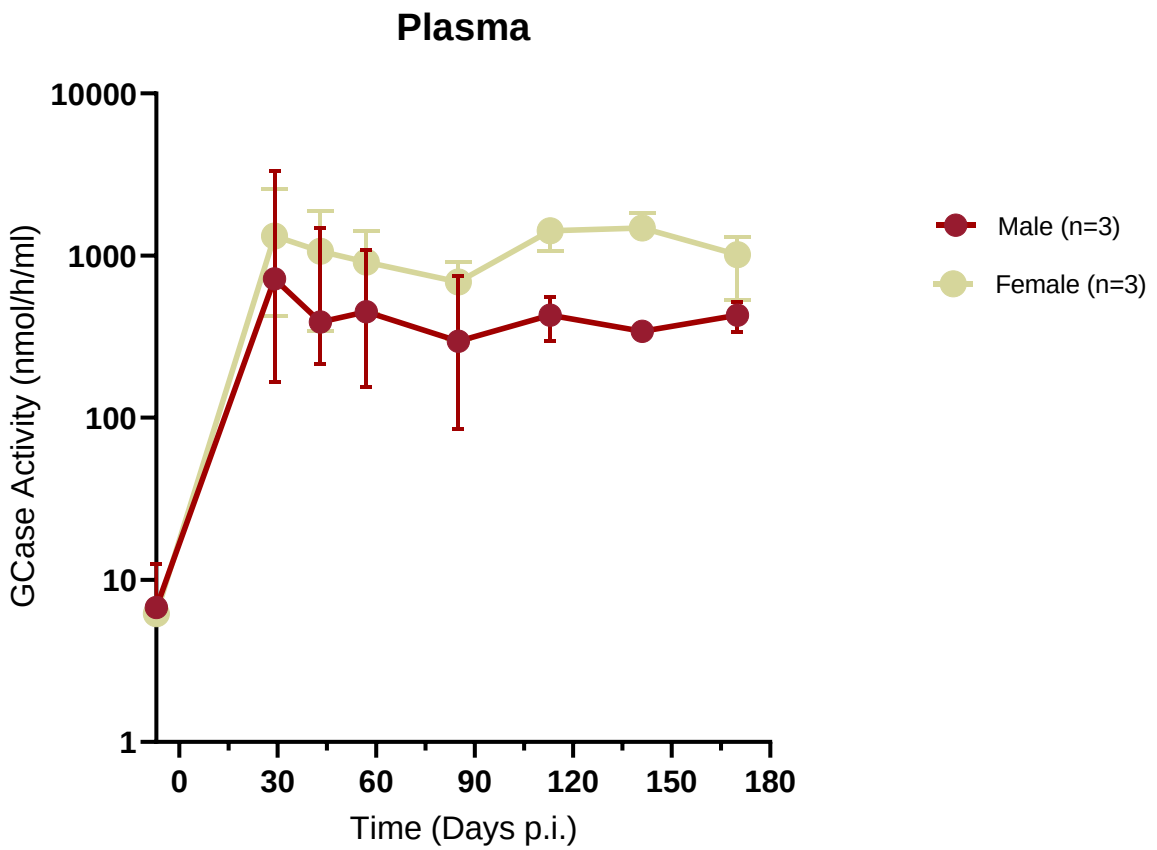


Biophysical properties of variant 85 and wildtype GCase

	Lysosomal pH	Human serum
	HALF-LIFE (MINUTES)	
WT GCase	388	24
Variant 85	>8,639	143
Improvement	**>21X**	**6X**

WORLD*Symposium* 2021: Fabrizio Comper et al. Generation of β-Glucocerebrosidase Variants with Increased Half-life in Human Plasma for Liver Directed AAV Gene Therapy Aimed at the Treatment of Type 1 Gaucher Disease

FLT201 showed high GCase expression in non-human primates

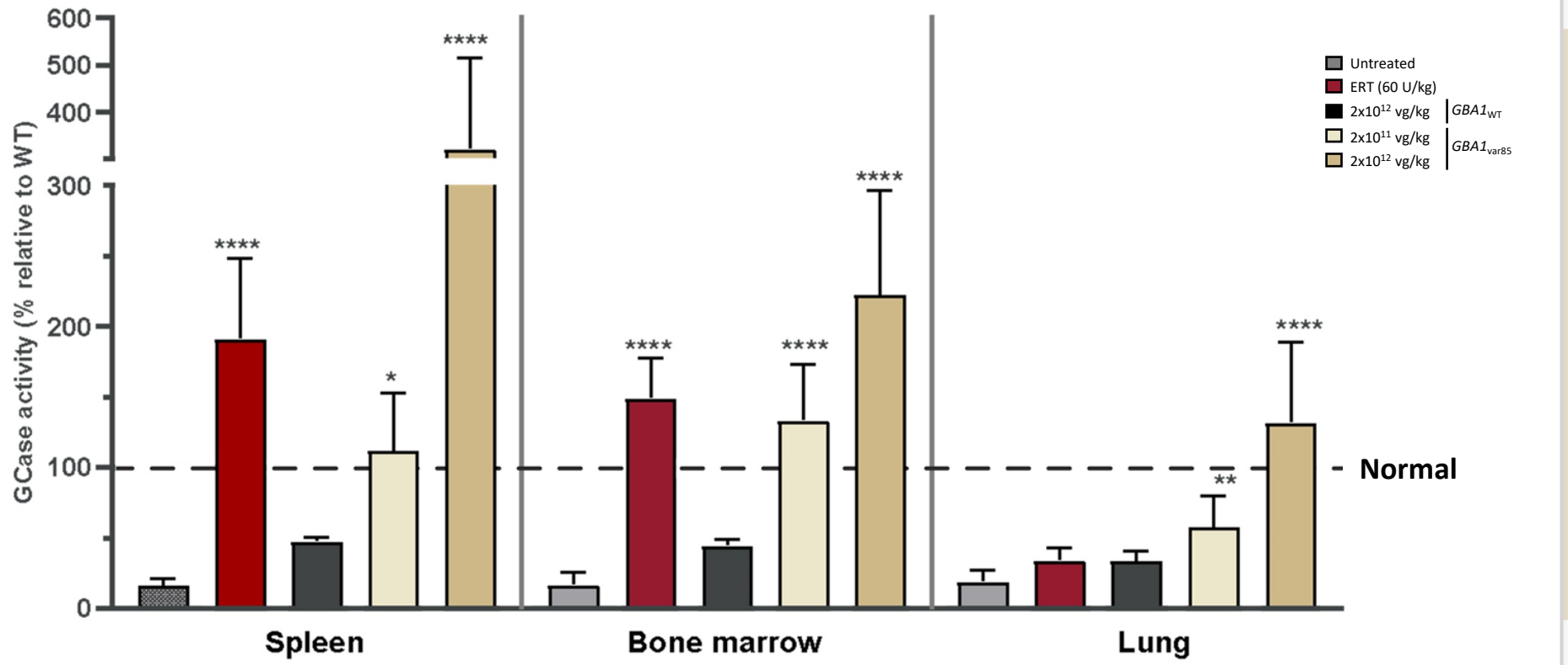


Achieved steady increases in GCase plasma levels

- A single injection of FLT201 was well tolerated
- Resulted in a rapid increase of GCase in plasma that was sustained for at least six months (trial ongoing)

Dose: FLT201 $2x10^{12}$ vg/kg (long-term observational trial)

FLT201 led to increased uptake in key tissues in Gaucher mice



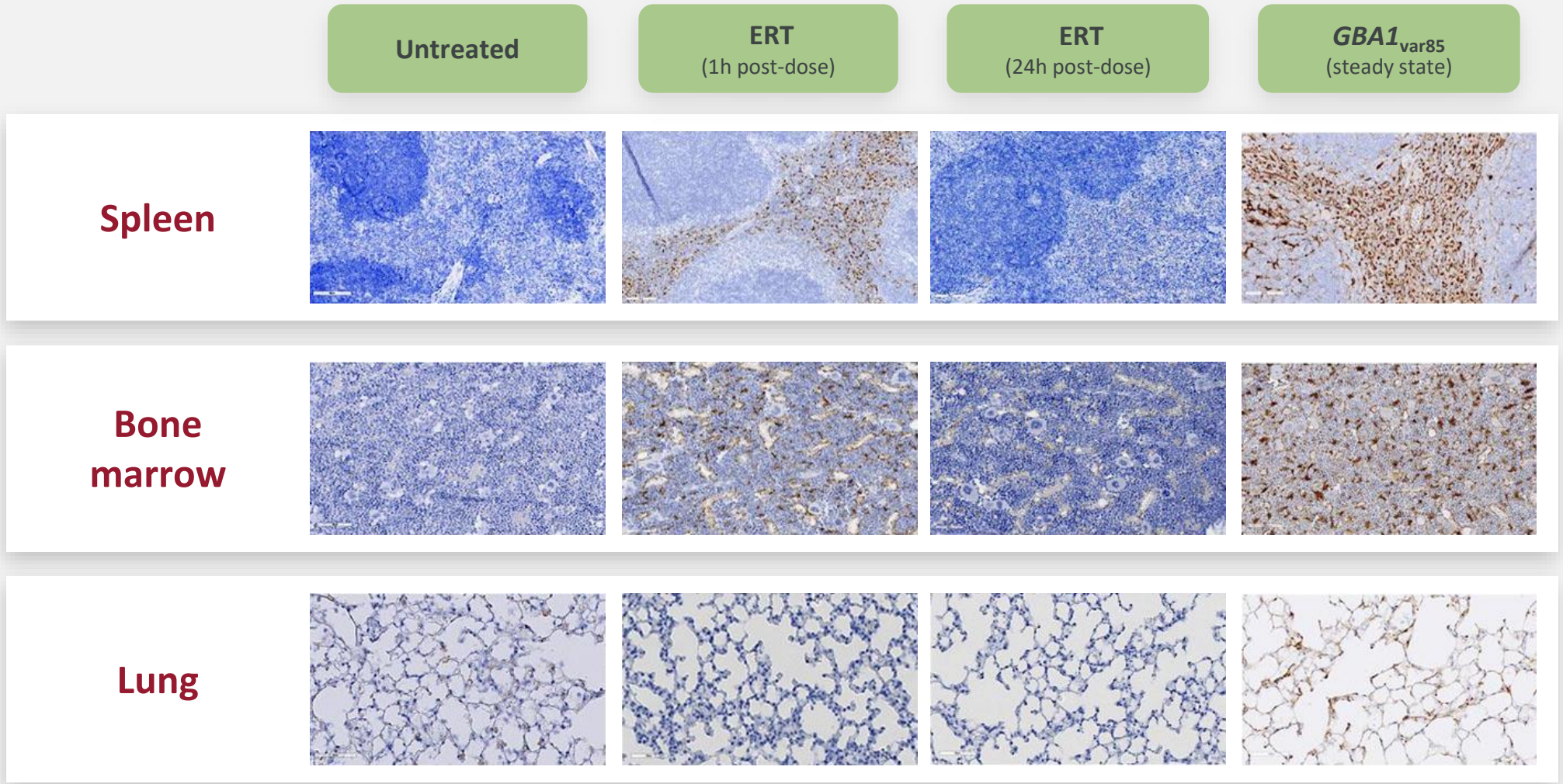
- Dose-dependent increases in GCase to above normal levels in key tissues
- Greater GCase uptake in key tissues than with ERT or with short half-life wildtype gene therapy

Data represented as mean ± SD. n= 9 to 16 per treatment group. * P≤0.05, ** P≤0.001, P≤0.001, **** P ≤ 0.0001, one-way ANOVA.

American Society of Gene & Cell Therapy 2021 Annual Meeting: Romuald Corbau et al. FLT201, a Novel Investigational AAV-Mediated Gene Therapy Candidate for Gaucher Disease Type 1
WORLD*Symposium* 2021: Romuald Corbau et al. FLT201: An AAV-Mediated Gene Therapy for Type 1 Gaucher Disease Designed to Target Difficult to Reach Tissues

ERT=Velaglucerase alfa

Enhanced and sustained GCase uptake observed in key tissues compared to ERT



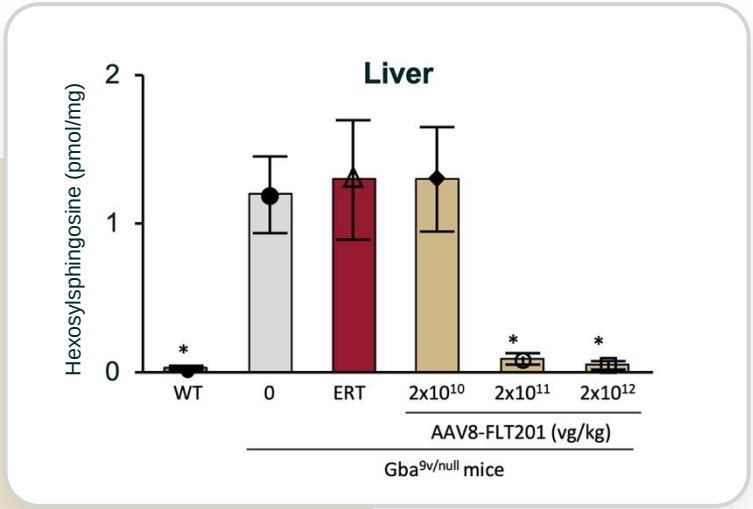
Anti-GCase – DAB, Haematoxylin counterstain, AAV8

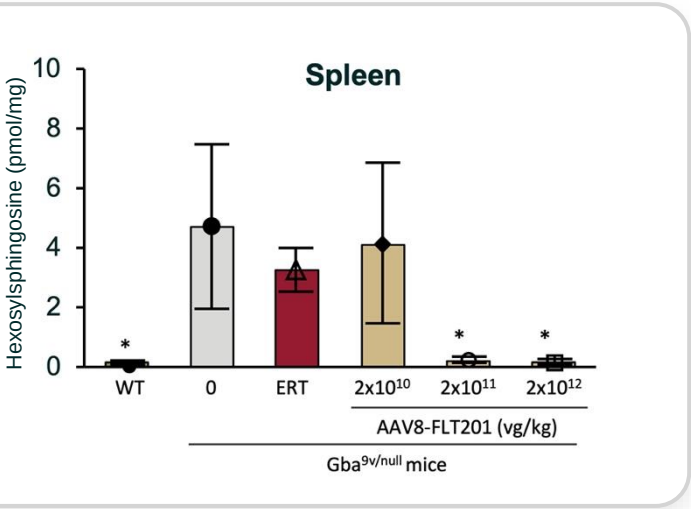
ERT=Velaglucerase alfa

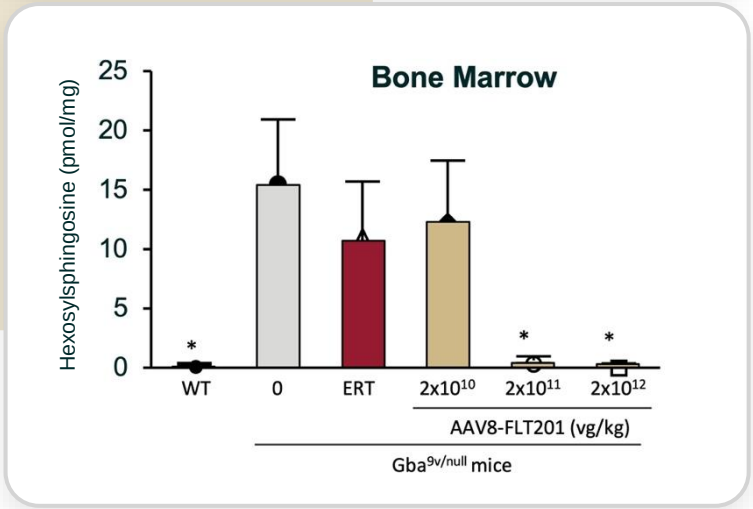
FLT201 cleared harmful substrate in key tissues in Gaucher mice

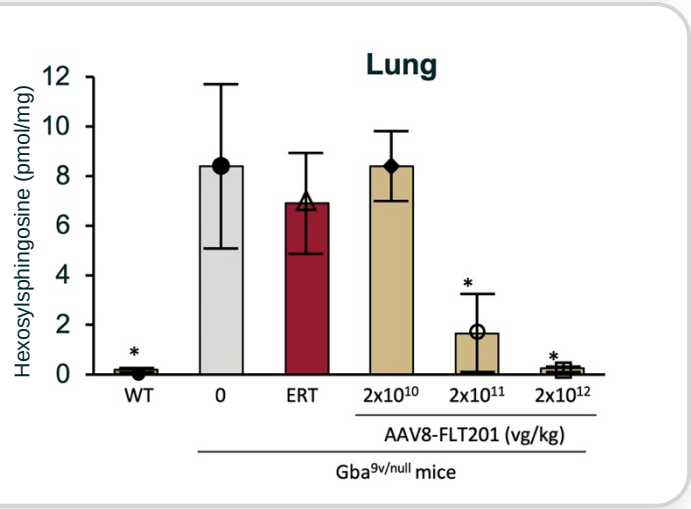
Robust substrate elimination

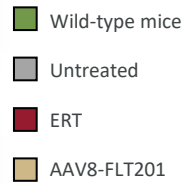
Dose-dependent reductions of lyso-Gb1 observed in all tissues analyzed, including bone marrow and lung









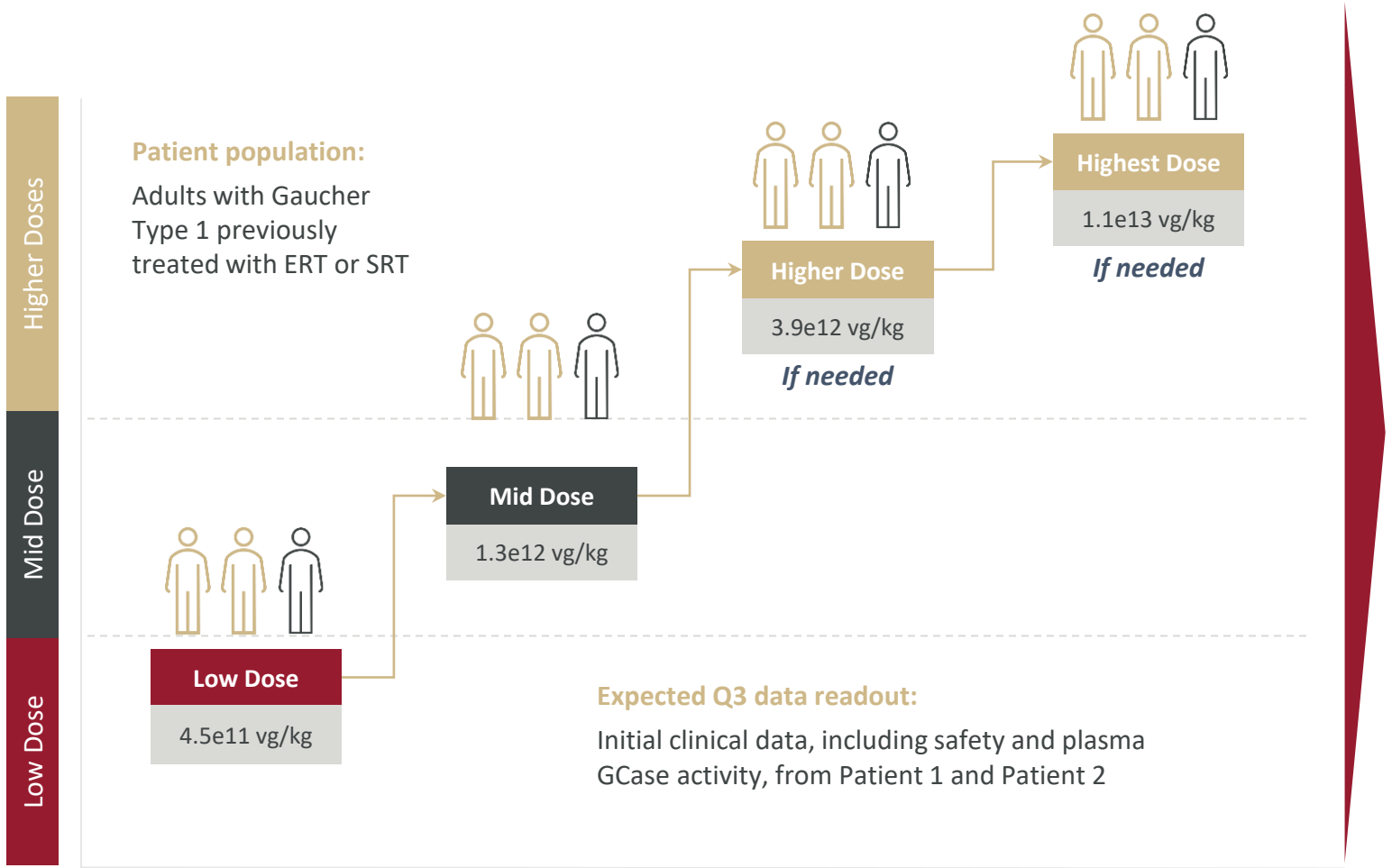


WORLD*Symposium* 2021: Romuald Corbau et al. FLT201: An AAV-Mediated Gene Therapy for Type 1 Gaucher Disease Designed to Target Difficult to Reach Tissues
AAV8-FLT201 = AAV8 pseudo-typed FLT201 genome. ERT = Velaglucerase alfa 60 U/kg biweekly (equivalent of the standard of care in humans). WT = wild-type mice. Evaluated 12 weeks post-injection. *p ≤ 0.0001.

GALILEO-1 Phase 1/2 dose-finding trial design

First-in-human, open-label, multicenter study; dosing completed in cohort 1

Establish a dose that delivers sustained increases in GCase activity to reduce substrate accumulation and improve clinical parameters



Planned to be dosed in each cohort

Flexibility to expand number of patients dosed

Trial protocol allows for testing up to four doses. Depending on dose response in the initial cohorts, we may not ultimately need to escalate to the later doses. The Data Monitoring Committee may recommend the next dose level at the next planned dose level, at same, higher or lower dose level based on emerging safety/tolerability, PK, PD and efficacy data. A 4-week stagger between patients is built into the protocol, with the exception of the US where there is an 8-week stagger prior to dosing a subsequent patient.

GBA1-linked Parkinson's Disease

Our longer-acting GCase variant may provide opportunity for best-in-class gene therapy for GBA1-linked PD

EXTEND OUR INNOVATION

- Leverages engineered longer-acting GCase variant with aim of achieving better brain distribution and coverage than wildtype
- Builds on our gene therapy expertise to optimize construct and delivery

HIGH UNMET NEED

- No disease-modifying therapies exist for PD
- GBA1-linked PD associated with earlier onset and more severe disease
- ~5-15% of PD patients have GBA1 mutations; most common genetic risk factor

EARLY DATA SUPPORT MOVE INTO PD

- Demonstrated superior in vitro activity and expression levels of our longer-acting GCase variant compared to wildtype

PD is a severe and progressive neurodegenerative disease with no approved disease-modifying therapies

Characterized by build-up of alpha-synuclein aggregates (Lewy bodies) and death of dopaminergic neurons

Symptoms worsen and treatment becomes less effective over time

No approved disease-modifying therapies

GBA1 mutations are most common genetic risk factor in Parkinson's disease

5-30x

greater risk of developing PD in people with GBA1 mutations[1]

- Associated with earlier onset and more severe disease
- Contributes to formation of Lewy bodies and death of dopaminergic neurons via multiple mechanisms
- Evidence of reduced GCase activity even in patients without a known GBA mutation

[1]Cells 2022, 11(8), 1261; https://doi.org/10.3390/cells11081261

GBA1-linked PD is a substantial and well-defined patient subset

PD is second most common neurodegenerative disease

~1.9M

diagnosed PD patients in US, UK and EU4*

5-15%

have GBA1 mutations†

~190,000

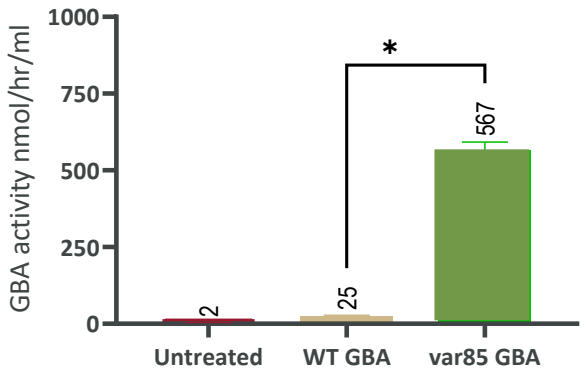
estimated GBA1-linked PD population

* Source: GlobalData; (Benito-León et al., 2003; Bergareche et al., 2004; Wickremaratchi et al., 2009; Blin et al., 2015; Pupillo et al., 2016; Uda et al., 2016; Heinzel et al., 2018; Mantri et al., 2019; United States Census Bureau, 2019)

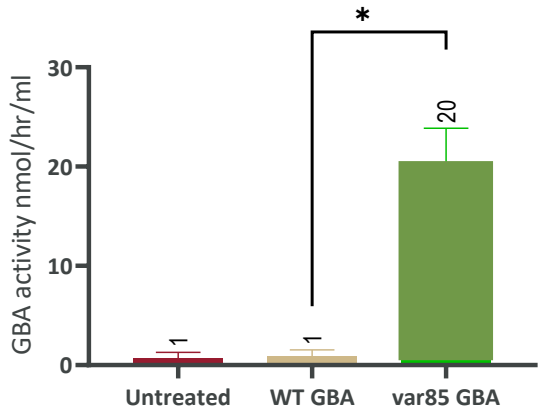
† Cells 2022, 11(8), 1261; https://doi.org/10.3390/cells11081261

Our GCase variant has demonstrated up to 20-fold greater activity levels compared to wildtype in preclinical studies

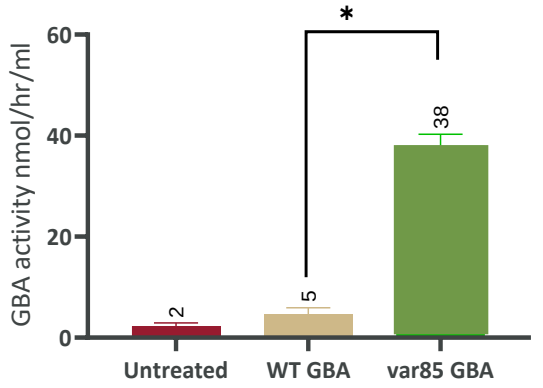
Brain epithelial cell line
(H4)



Neuroblastoma cell line
(NB1643)



Neuronal cell line
(SH-SY5Y)



AAV9 *in vitro* transduction & activity in supernatants; N=3; + SEM, t-test vs. Var85 , *P≤0.05

Freeline: Pioneering gene therapy

FLT201 is a potential first-and best-in-class gene therapy for Gaucher disease Type 1

First-in-human clinical data for FLT201 expected in Q3 2023 provides near-term catalyst

Extending impact of our innovation into GBA1-linked Parkinson's disease

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Thank you