FREELINE

Corporate Presentation

9 August 2022

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Freeline

Transforming the lives of patients with systemic debilitating diseases using AAV-mediated gene therapies

Pioneering transformative gene therapies with best-in-class and/or first-in-class potential

High protein expression at low doses enabled by potent, proprietary capsid

Developing novel, high-quality gene therapy candidates, combining cutting-edge protein engineering, analytics and CMC

Leveraging strong foundational science established in hemophilia B and in lysosomal storage diseases with high medical need and value

Targeting diseases where high protein expression at low doses offers best-in-class and/or first-in-class potential and unlocks opportunities beyond the reach of first-generation AAV gene therapy

Three clinical programs with best-in-class and/or first-in-class potential

FLT180a

For treatment of hemophilia B

Demonstrated Factor IX (FIX) activity at protective levels, preventing bleeds and the need for FIX replacement therapy[1]

FLT190

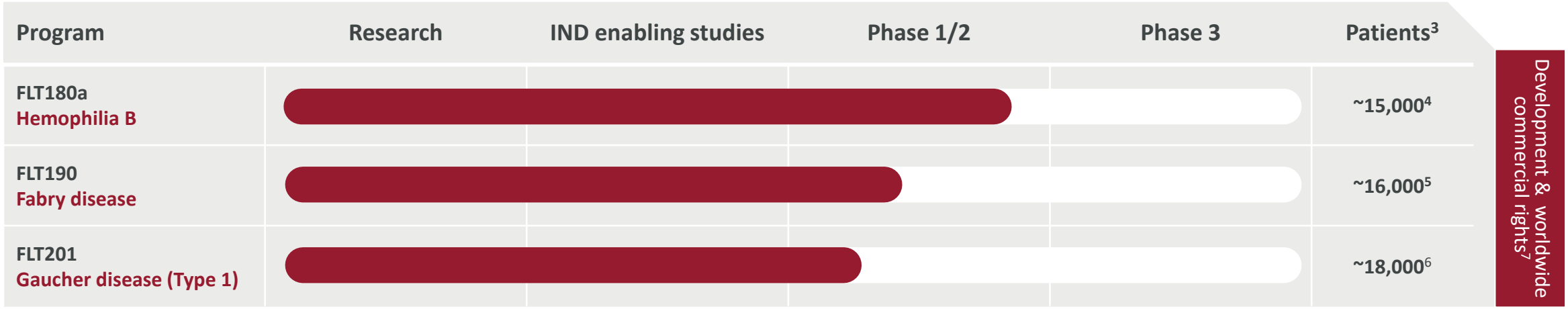
For treatment of Fabry disease

Data from lowest dose cohort show promising and durable efficacy upon which to build

FLT201

For treatment of Gaucher disease[2]

Novel protein engineered treatment shows promising pre-clinical data; first AAV gene therapy program for Gaucher disease

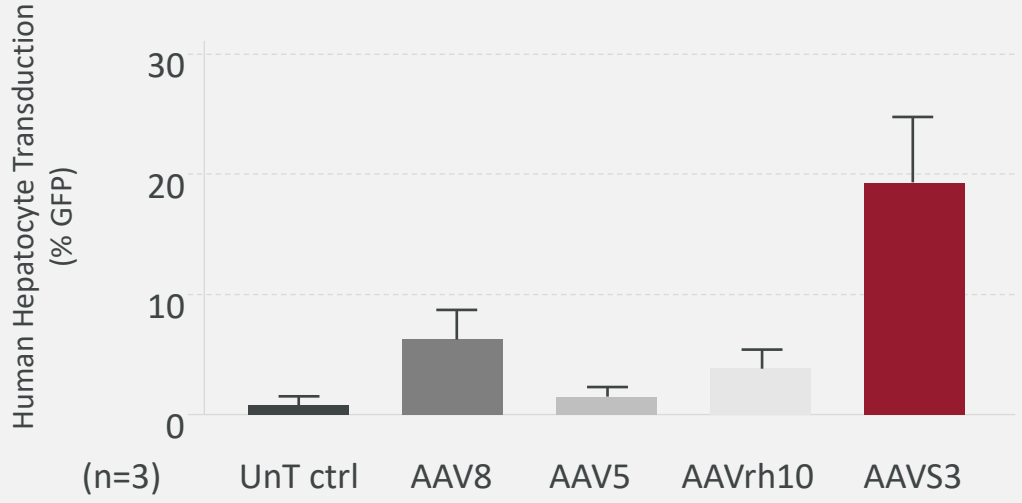


[1] In adult men with severe to moderately severe hemophilia B
[2] Gaucher disease Type 1
[3] These figures represent the total approximate diagnosed population of Hemophilia B patients and the total theoretical genetic prevalence of the other indications. The seroprevalence of antibodies against the AAV capsid renders approximately 30-50% of patients currently not eligible for gene therapy.
[4] Hemophilia epidemiology: World Federation of Hemophilia 2020; Markets: EU4, UK, US, Japan, RoE.
[5] Ann Intern Med. 2003;138:338-346; Markets: EU4, UK, US, Japan.
[6] Hematology. 2017 Mar;22(2):65-73. doi: 10.1080/10245332.2016.1240391; Markets: EU4, UK, US, Israel.
[7] Owned and in-licensed intellectual property rights.

Platform Technology: AAVS3 capsid engineered to more efficiently transduce human hepatocytes

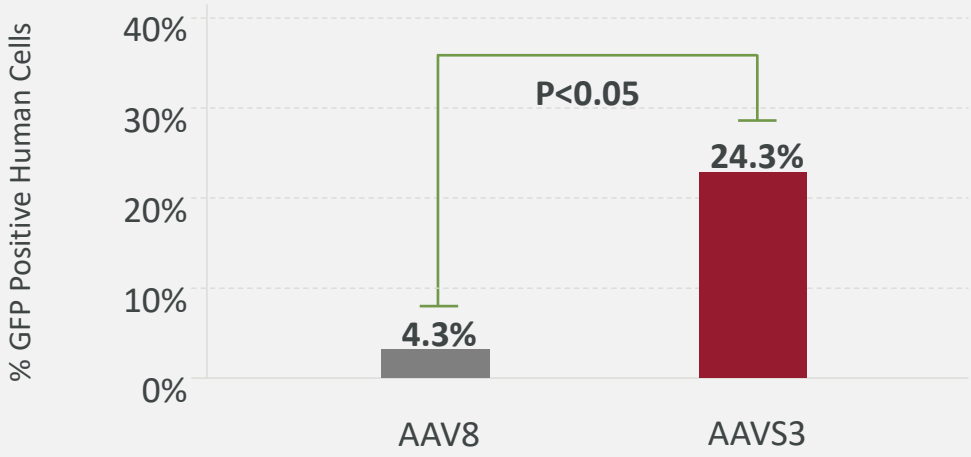
AAVS3 transduction significantly higher compared to other serotypes and untreated control

Transduction efficiency of AAVS3 in vitro compared with other vectors in primary human hepatocytes[1]



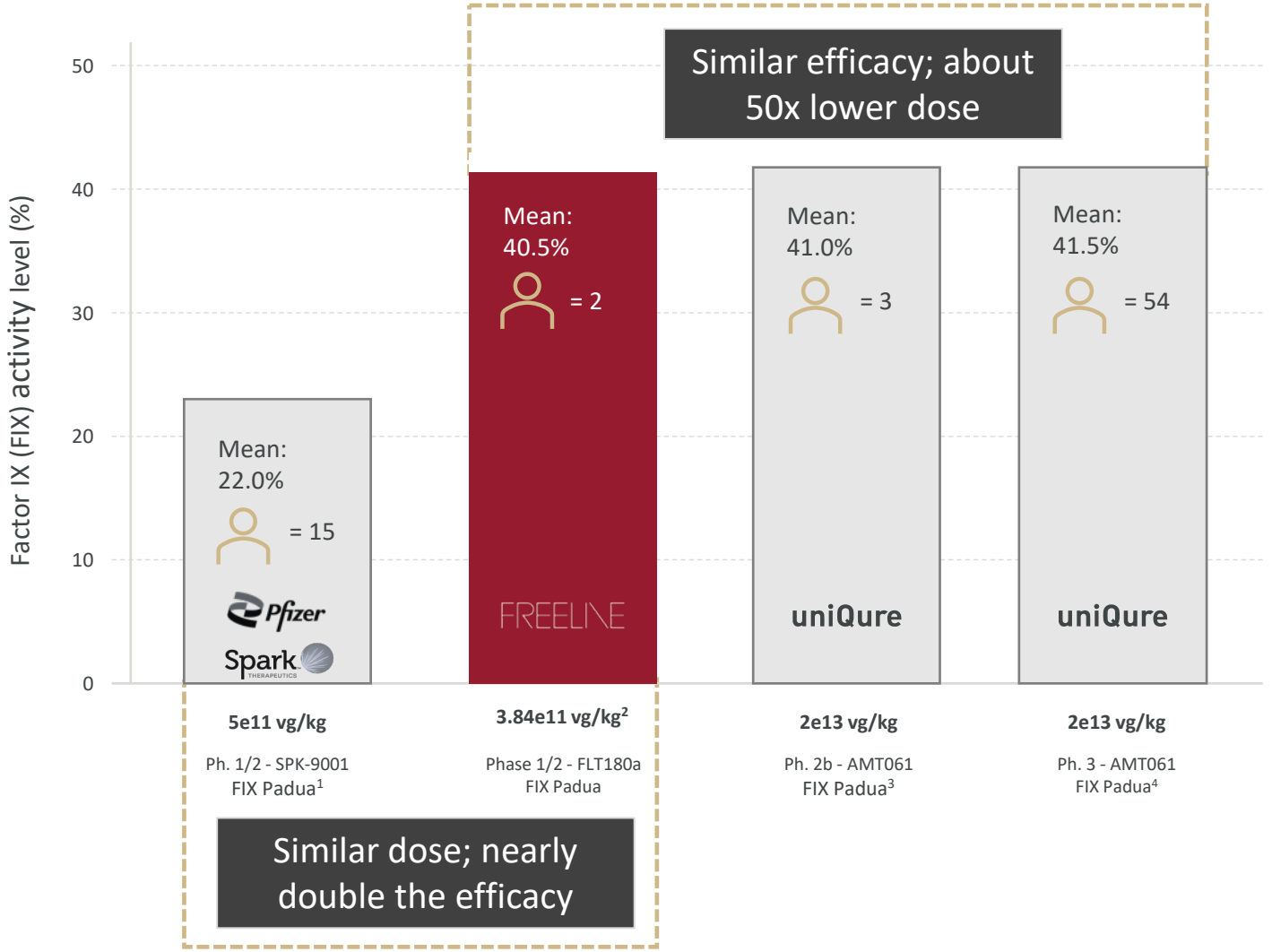
AAVS3 achieved nearly 6-fold higher transduction compared to AAV8

Transduction of human hepatocyte *in vivo* in AAV8 and AAVS3[2]



[1] Percentage of vectors containing GFP, green fluorescent protein, measured in primary human hepatocytes following transduction. AAVS3 pseudo typed vector used.
[2] Number of human hepatocytes expressing GFP following transduction. Measured in a human xenograft mouse model.

Clinical data demonstrated greater potency of AAVS3 relative to competitors



The FLT180a dose listed, 3.84e11 vg/kg, is equivalent to 4.5e11 vg/kg under the previous equivalent dosing nomenclature.

[1] Pfizer R&D Day Sep 2020 – up to four-year follow-up data in 15 patients from Phase 1/2 trial.

[2] B-AMAZE long-term follow-up data as of the cut-off date of September 20, 2021 measured using one-stage assay, central laboratory measurement. Two patients dosed at this dose level, with mean value calculated based on following Week 52 FIX activity levels: Patient 1, 45%, Patient 2, 36%.

[3] Miesback et al; Blood 2018 131:1022-1031.

[4] uniQure R&D day June 22, 2021 – 12-month follow-up data in 54 patients from the HOPE-B Phase 3 trial. Uncontaminated central laboratory data.

Company Strategy: Pioneering innovations that transform the lives of patients

1

Leverage highly potent capsid and platform capabilities to deliver best-in-class and first-in-class treatments

Clinical programs with potential to deliver transformative therapies

2

Execute clinical programs to generate data demonstrating the value of Freeline's products and technology

Data anticipated across all clinical programs over the next year

3

Invest in future innovations by leveraging Freeline's unique scientific capabilities in new disease areas

Next generation capsid design and development; novel protein variants engineered with enhanced therapeutic properties

Lean organization with core gene therapy discovery and development capabilities

Experienced and innovative leadership team

Leading industry experts in clinical development

Lean organization of ~180 FTEs

Cash runway into H2 2023

Focused on gene therapy candidates with best-in-class and/or first-in-class potential

Distinct in-house research capabilities and CMC technology

Operational efficiency enhances financial flexibility for future growth and platform investments

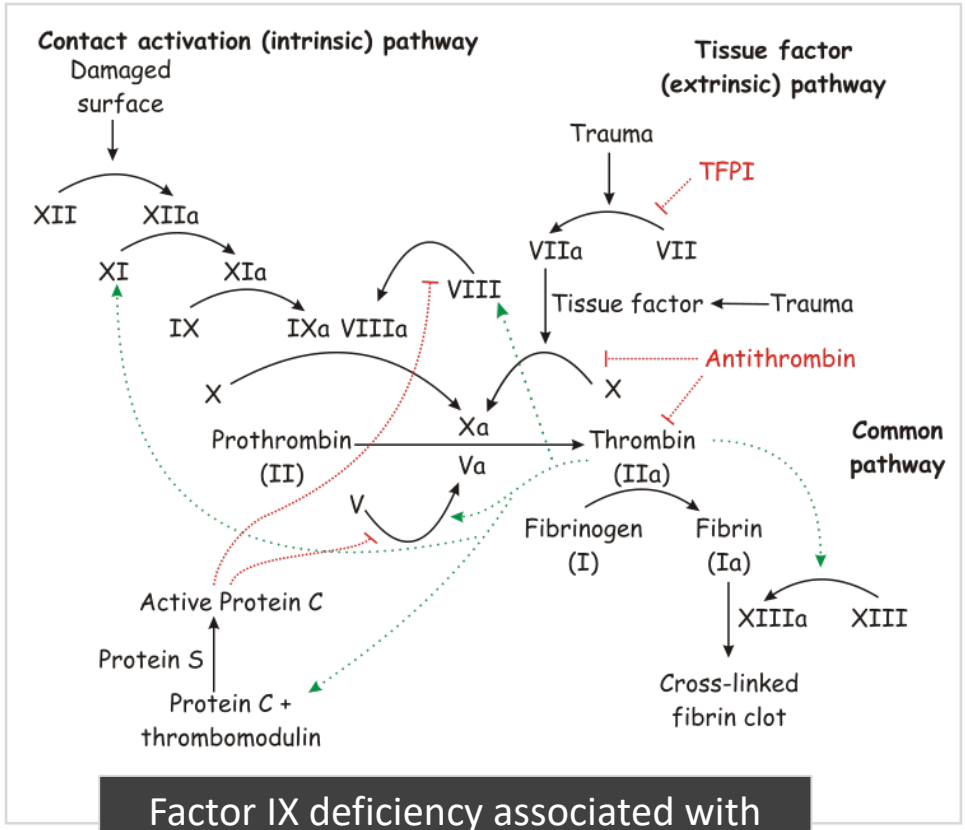
Hemophilia B

Hemophilia B Overview

Disease Characteristics:

- Rare, X-linked, congenital bleeding disorder caused by deficiency of coagulation Factor IX (FIX)
- Depending on the severity of the disease, symptoms can range from frequent, spontaneous bleeding into joints and muscles to abnormal bleeding from minor injuries
- Most patients are male given that hemophilia is an X-linked disorder

Blood Coagulation Cascade



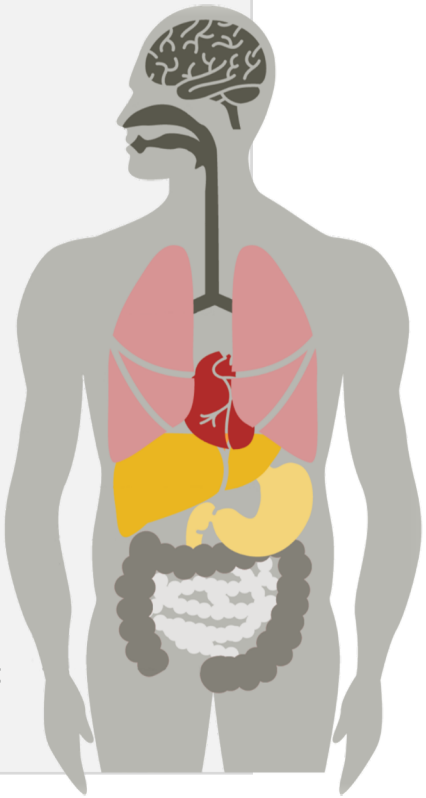
Factor IX deficiency associated with hemophilia B

Clinical Manifestations

Frequent, spontaneous bleeding

Abnormal bleeding from minor injuries

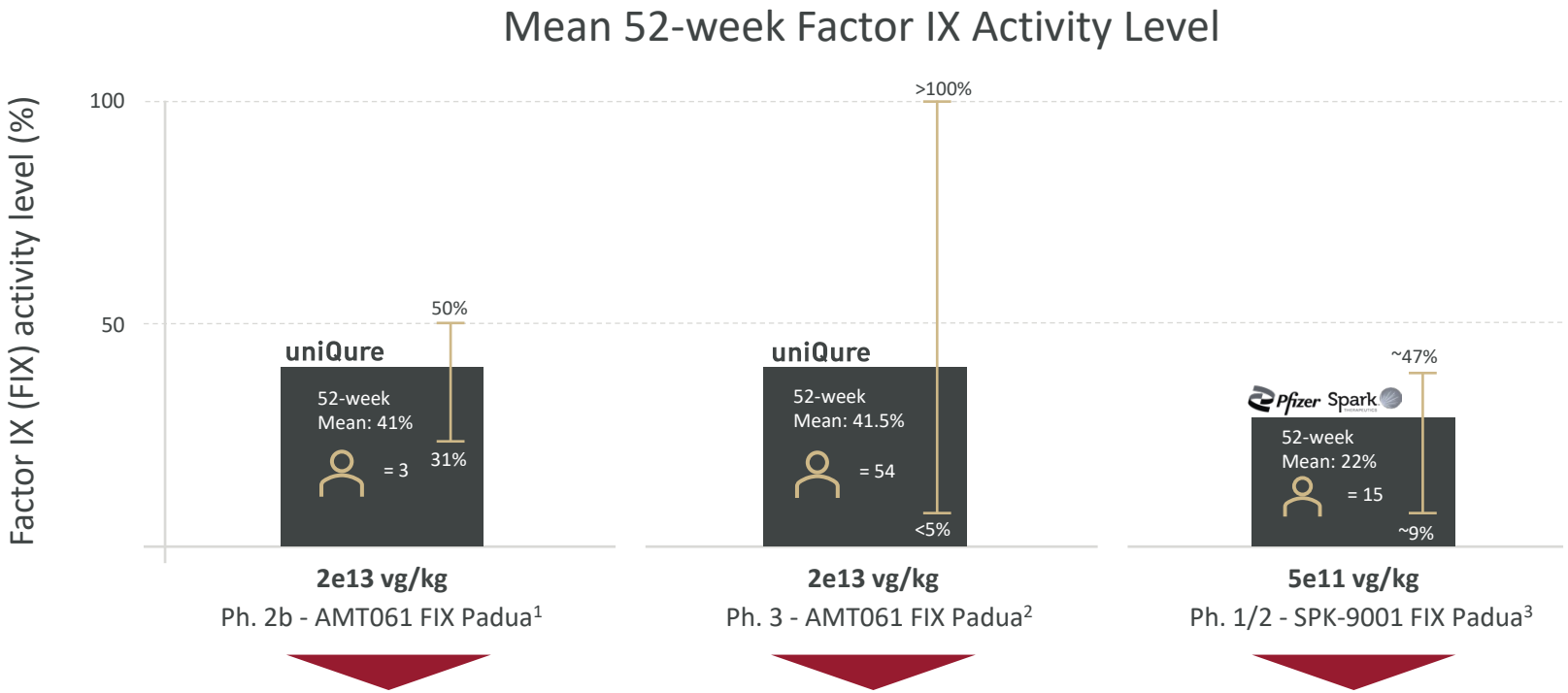
Risk of joint bleed which may result in permanent joint damage



Schulman (2012); World Federation of Haemophilia; Nilsson (1976); Thrombosis and Haemostasis; Orphanet.

Challenge: First-generation capsids do not adequately protect patients from bleeds

FIX activity levels achieved using first-generation capsids are in the mild range with large variability



Treatment with FIX needed for high risk activities, surgery and trauma

44% of patients experienced a bleed

27.8% of patients had bleeds treated with FIX

8 spontaneous bleeds required treatment with FIX

20% of patients experienced a bleed

[1] Miesback et al; Blood 2018 131:1022-1031.

[2] uniQure R&D day June 22, 2021 – 12 month follow-up data in 54 patients from the HOPE-B Phase 3 trial. Uncontaminated central laboratory data.

[3] Pfizer R&D Day Sep 2020 – up to four year follow-up data in 15 patients from Phase 1/2 trial.

Opportunity: Best-in-class therapy providing durable FIX activity at levels protecting patients from bleeds and FIX replacement therapy

Market need[1]

Patients
Will wait for a gene therapy that delivers durable FIX activity at protective levels

Physicians
Eliminating bleeds is an important consideration in selecting gene therapy

Payers
Consider the curative and cost-saving potential of gene therapy attractive

Hemophilia B target product profile

- Predictably provide durable FIX activity at protective levels
- Eliminate or significantly reduce the occurrence of bleeds
- Eliminate or significantly reduce the need for FIX replacement therapy

[1] Market research: Interviews, survey and analysis

B-AMAZE Phase 1/2 dose-finding trial design

Features of B-AMAZE

- Targeted normal range of FIX levels
- Adaptive dosing design to facilitate dose finding
- Prophylactic immune management plus reactive as needed for vector-related transaminitis

Duration

- 26 weeks for B-AMAZE
- 15 years for the LTFU trial

Key inclusion

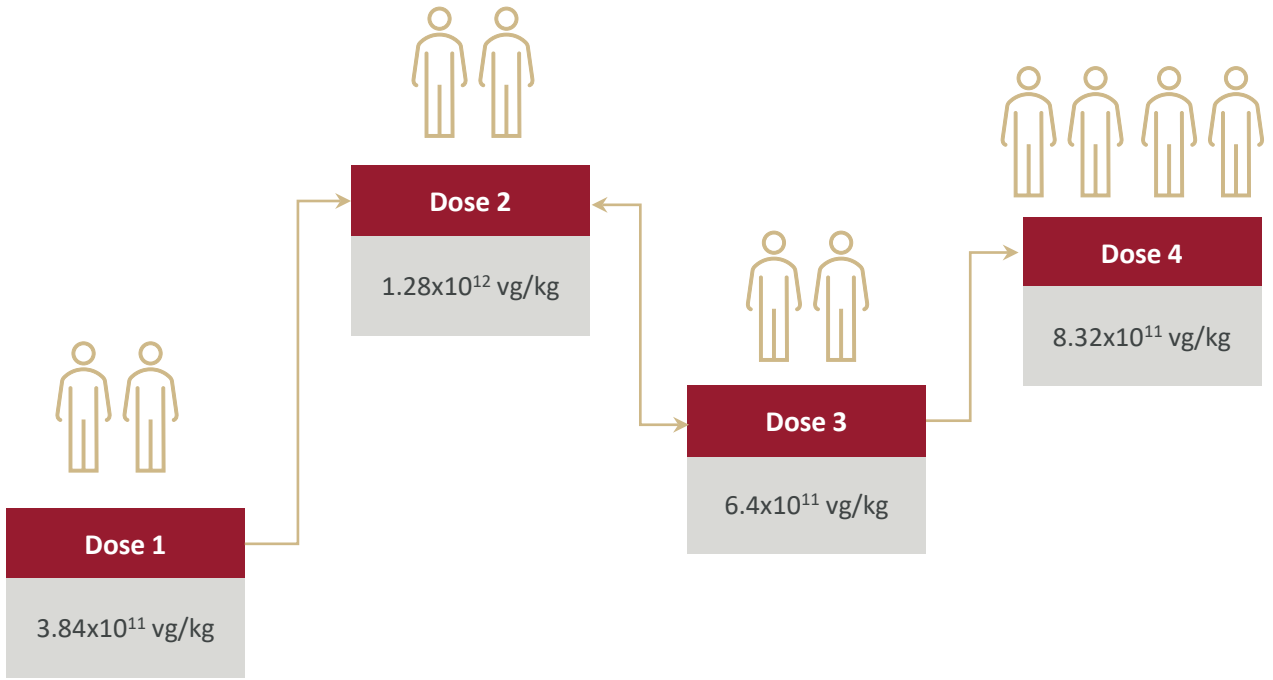
- Adults (aged ≥18 years)
- FIX levels ≤2%

Key exclusion

- Neutralizing antibodies to AAVS3
- Liver disease
- FIX inhibitors

B-AMAZE Week 26 endpoints

- Safety, as assessed by AEs
- FIX activity



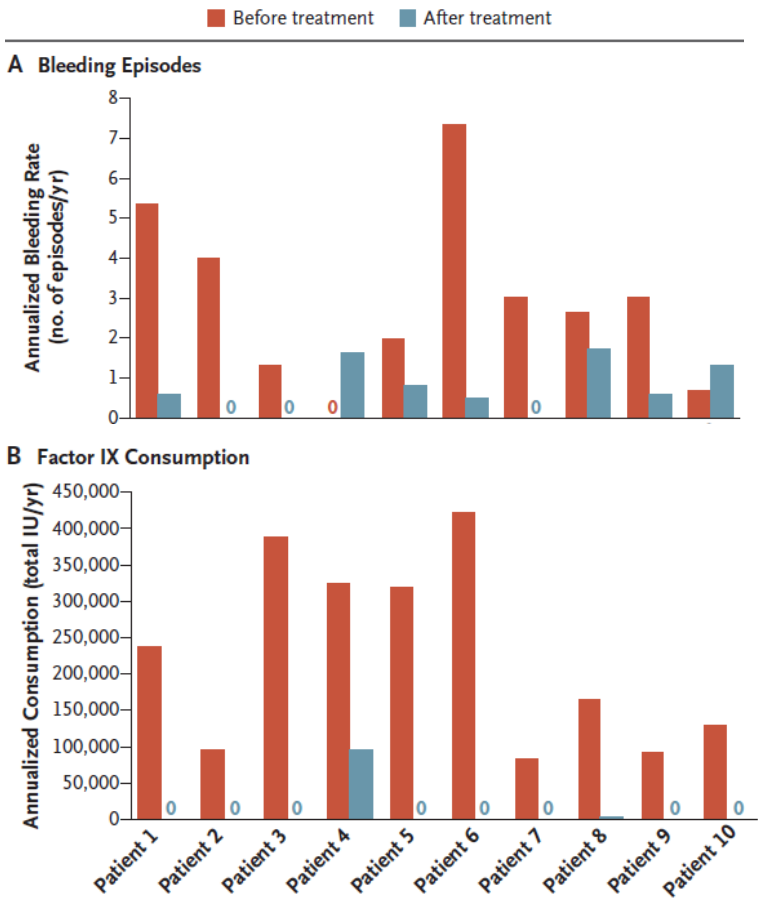
Prophylactic IM (prednisolone +/- tacrolimus) plus reactive as needed

FLT180a (verbrinacogene setparvovec) uses the potent, rationally designed AAVS3 capsid carrying a FIX-R338L 'Padua' variant transgene to enable high FIX expression with relatively low vector doses.

ClinicalTrials.gov identifiers: NCT03369444 for B-AMAZE and NCT03641703 for the LTFU trial.

AAV, adeno-associated virus; AE, adverse event; FIX, Factor IX; IM, immune management; LTFU, long-term follow-up; vg, vector genomes.

FLT180a delivered durable FIX expression, strongly decreasing both bleeding rates and need for FIX replacement in B-AMAZE for up to 3.5 years



Effect of treatment with FLT180a on annualized bleeding rate (A) and total FIX consumption (B)

Reproduced with permission. Copyright Massachusetts Medical Society.

- Dose-dependent increases in FIX for all patients
- 9 of 10 patients had sustained FIX activity at a median follow-up of 27.2 (19.1-42.4) months.
- 5 patients had FIX levels in the normal range (51-78%), 3 had levels ranging from 23% to 43%, and 1[†] was at 260%[†]
- Mean annualized bleeding rate across all patients decreased from 2.93 (0-7.33) events/year at BL to 0.71 (0-1.7) events/year
- Mean annualized FIX consumption per patient decreased from 226,026 (83,263-423,333) IU/yr at BL to 9,723 (0-95,532) IU/year
- Generally well tolerated with a good safety profile[‡]

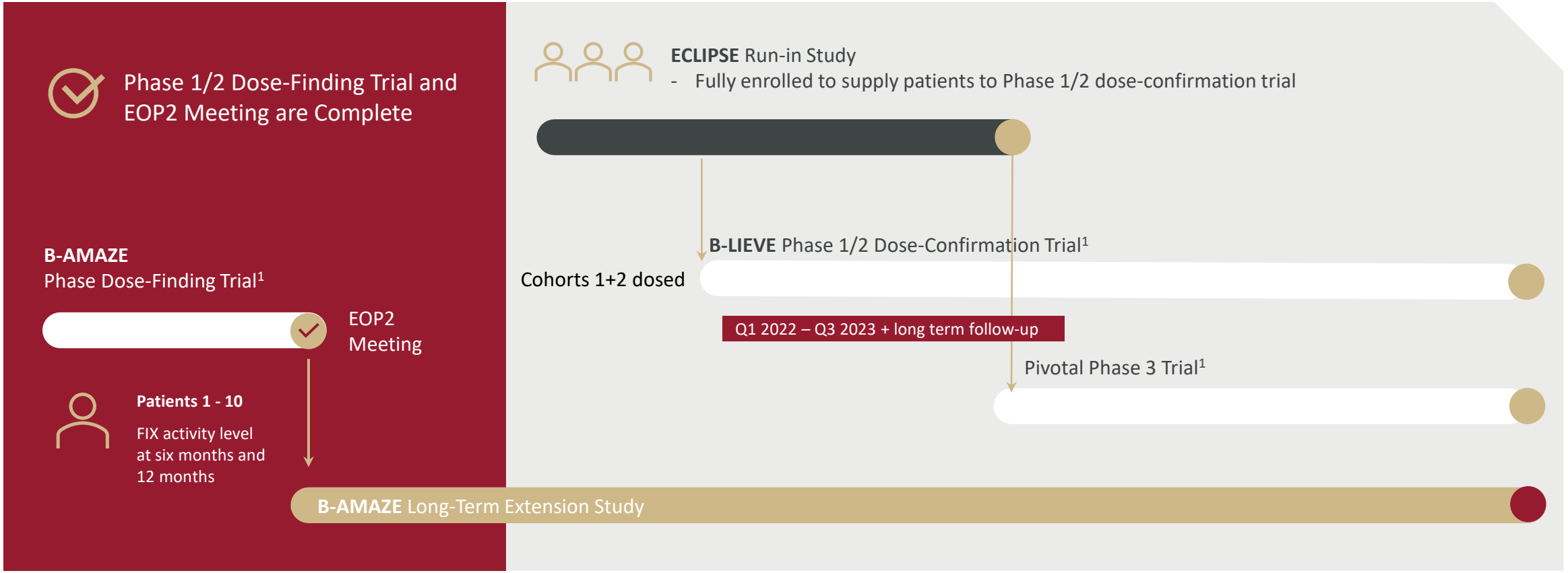
* High dose (1.28e12 vg/kg); † All at last follow-up; ‡ With transient transaminitis being the most common FLT180a-related AE; no patient discontinued infusion or withdrew from the study; no infusion reactions occurred, and no inhibitors to FIX were detected; AEs related to immune management were consistent with the known safety profiles of corticosteroids and tacrolimus; BL baseline, AE adverse event

In the B-AMAZE trial, patients had received one of four doses of FLT180a (3.84e11, 6.4e11, 8.32e11 or 1.28e12 vg/kg) together with a prophylactic immune management regimen. The cutoff date for the published follow-up data was September 20, 2021. The follow-up continues.

Chowdary P et al. *n engl j med* 387;3 nejm.org July 21, 2022

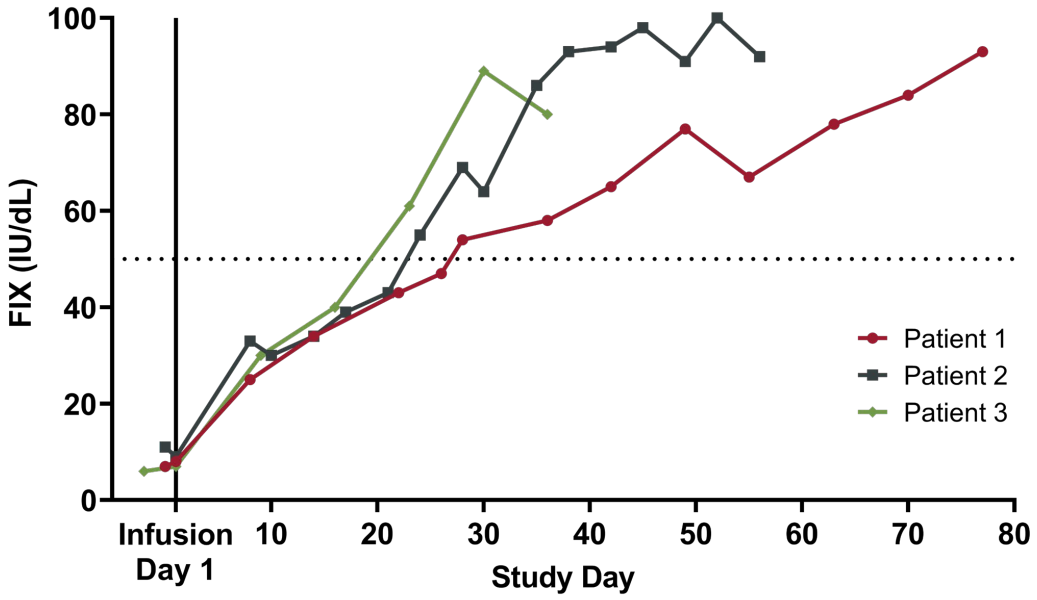
FLT180a clinical development plan

B-LIEVE: Phase 1/2 trial to confirm the dose and immune management regimen for use in a pivotal Phase 3 trial



[1] To measure safety, efficacy and durability.

FLT180a generated protective FIX levels with no bleeding or need for FIX replacement in first cohort of B-LIEVE trial



Young G et al. poster #PB0213, July 10, 2022, International Society on Thrombosis and Haemostasis (ISTH) Congress, London, July 9-13, 2022

- FLT180a dose of 7.7e11 vg/kg plus proactive immune management*
- Rapid increase of FIX levels, reaching normal range (93, 92 and 80 IU/dL) for the three patients through days 77, 56 and 36, respectively†
- Patients stopped FIX prophylaxis and did not require FIX replacement or experience bleeding
- FLT180a treatment and prophylactic immune management regimen were well tolerated with a good safety profile‡

- Early cohort 2 results showed similar initial response to same treatment
- After data cutoff for cohort 1†, two patients experienced a decrease in FIX expression together with mild and transient transaminitis
- All patients continued to have FIX expression levels above baseline, and no patient had experienced a bleed or required FIX supplementation

Freeline press release, July 10, 2022

* Starting 3 weeks after dosing: 4 weeks of tacrolimus 0.2 mg/kg/day and 4 weeks of oral prednisolone (1 mg/kg/day) followed by a 12-week slow taper

† Data cutoff date of May 23, 2022

‡ No serious adverse events or infusion reactions were observed, and there was no evidence of FIX inhibitors. All adverse events (AEs) were mild, and most were transient. AEs related to immune management were consistent with the known profiles of corticosteroids and tacrolimus

Anticipated FLT180a milestones

FLT180a – Hemophilia B Phase 1/2 B-LIEVE dose-confirmation trial

2022		2023	
H1	H2	H1	H2
Completed dosing of the first cohort	Report updated safety and efficacy data	Follow-up	
Reported initial safety and efficacy data	Conclude evaluation of strategic options, including partnership that would enable the continuation through Phase 3		
Completed dosing of the second cohort			

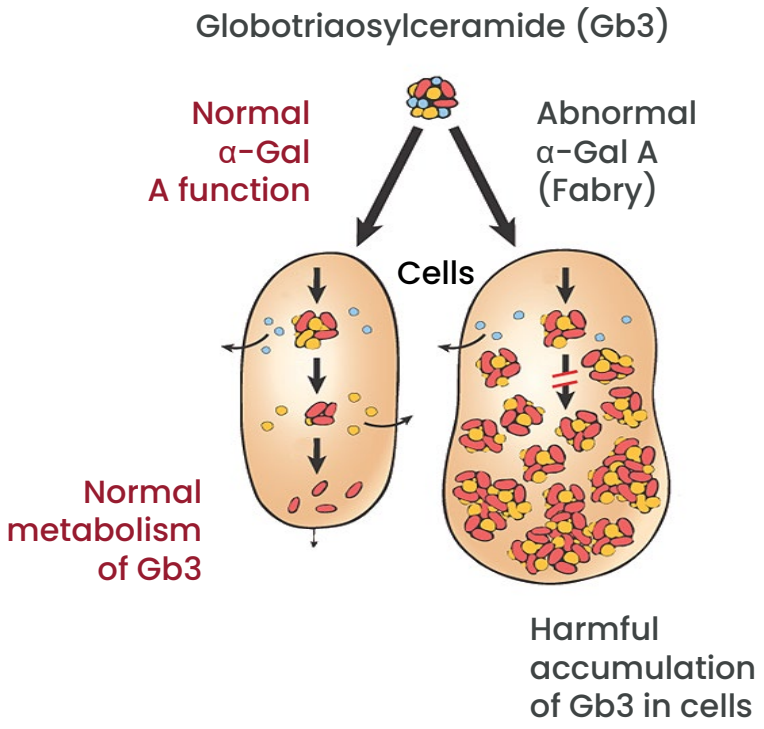
Fabry Disease

Fabry Disease Overview

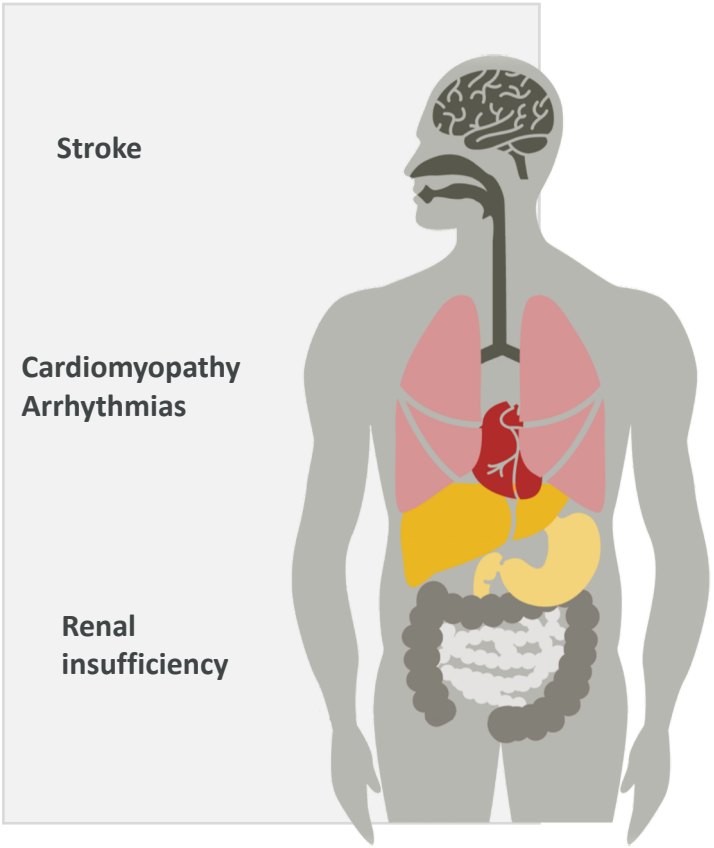
Disease Characteristics:

- Rare X-linked lysosomal storage disorder (LSD) resulting from deficient activity, or absence, of α Galactosidase A (α-Gal A)
- Deficiency of α-Gal A levels result in accumulation of substrates such as Gb3 and lyso-Gb3
- Characterized by progressive multi-systemic damage including the kidney, heart and vasculature

Fabry Disease Mechanism



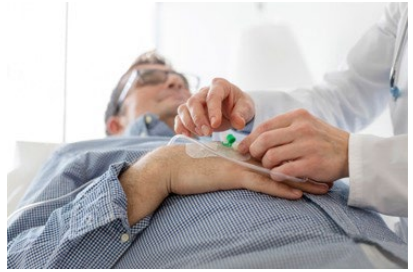
Clinical Manifestations



NORD; National Fabry disease Foundation; Fabrydisease.org; Tsukimura et al 2018; GeneReviews; Waldek et al 2009; Mehta et al 2006.

Challenge: No curative therapy exists and high unmet medical need remains for Fabry disease patients receiving ERT

Fabry disease patient perspectives[1]



ERT treatment burden

"Travelling to and from the hospital, the time spent for infusions, and trying to keep my spirit up and adjusting to treatment is a significant challenge."

Need for greater efficacy

"My son who is 35 was having bi-weekly infusions with not much positive results."

Exhaustion

"The pain doesn't just affect me but so does the fatigue. Sometimes the pain literally wipes me out."

Limitations of ERT

- Lifelong, intravenous infusions every 2 weeks placing significant burden on patients and healthcare systems
- Despite treatment with ERT, patients continue to experience debilitating symptoms and disease progression resulting in a shortened lifespan

Average life expectancy[2]	General population	Fabry disease population
US Males	74.7 years	58.2 years

- ERT is seen as expensive and burdensome by physicians

ERT= Enzyme Replacement Therapy

[1] Market research - interviews, survey and analysis

[2] Waldek S, Patel MR, Banikazemi M, Lemay R, Lee P. Life expectancy and cause of death in males and females with Fabry disease: findings from the Fabry Registry. Genet Med. 2009 Nov;11(11):790-6.

Opportunity: Patients need a therapy that delivers sustained levels of α-Gal A eliminating the need for ERT

Competitor landscape

- Short half-life ERT therapies do not deliver sustained protein levels and patients continue to experience debilitating symptoms and disease progression

Urgent market need[1]

Patients
Attracted to freedom from bi-weekly infusions provided by gene therapy

Physicians
Will prescribe gene therapy with long-lasting efficacy results that are comparable to or better than ERT

Payers
Recognize potential for cost savings compared to chronic lifelong ERT

Fabry disease target product profile

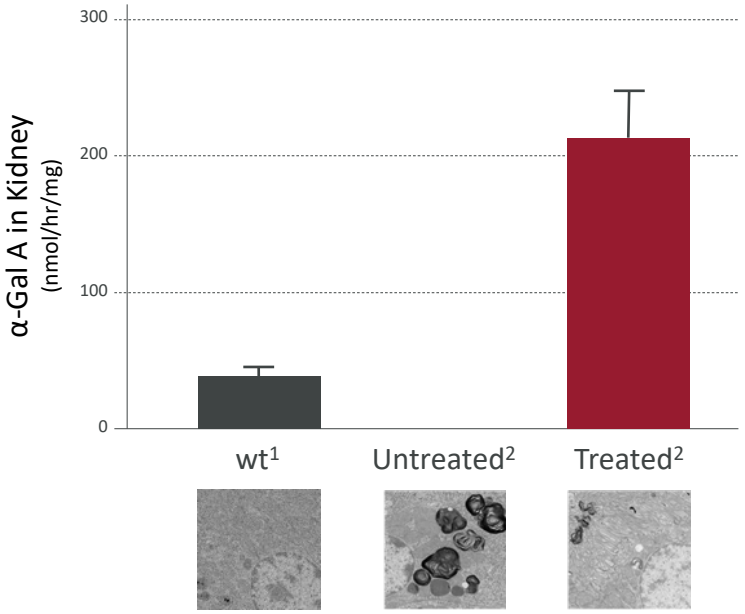
- Durable increased α-Gal A activity levels above the normal range
- Sustained reduction in lyso-Gb3
- Eliminate the need for ERT

[1] Market research - interviews, survey and analysis

FLT190 treatment for Fabry disease: Potential efficacy demonstrated in Fabry mouse model

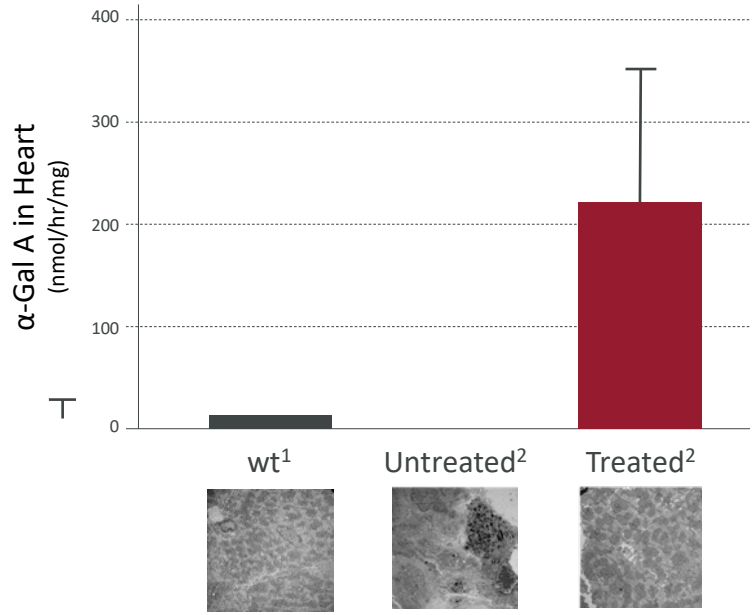
Meaningful increase in α-Gal A expression leading to reduction in pathologic substrate in key tissues

Kidney
α-Gal A activity levels



Electron microscopy x5000

Heart
α-Gal A activity levels



Electron microscopy x5000

WORLD symposia 2019: Jey Jeyakumar et al. Liver-directed gene therapy corrects Fabry disease in mice.

FLT190 vector genome pseudo-typed with AAV8 in GLA knockout ("GLA KO") mice; Dose: 2e12 vg/kg. Error bars: mean ± SD.

Time point: 16-week disease development prior to treatment; analysis 14 weeks post-treatment. Gb3/Lyso-Gb3 data (n=4, 2 males and 2 females).

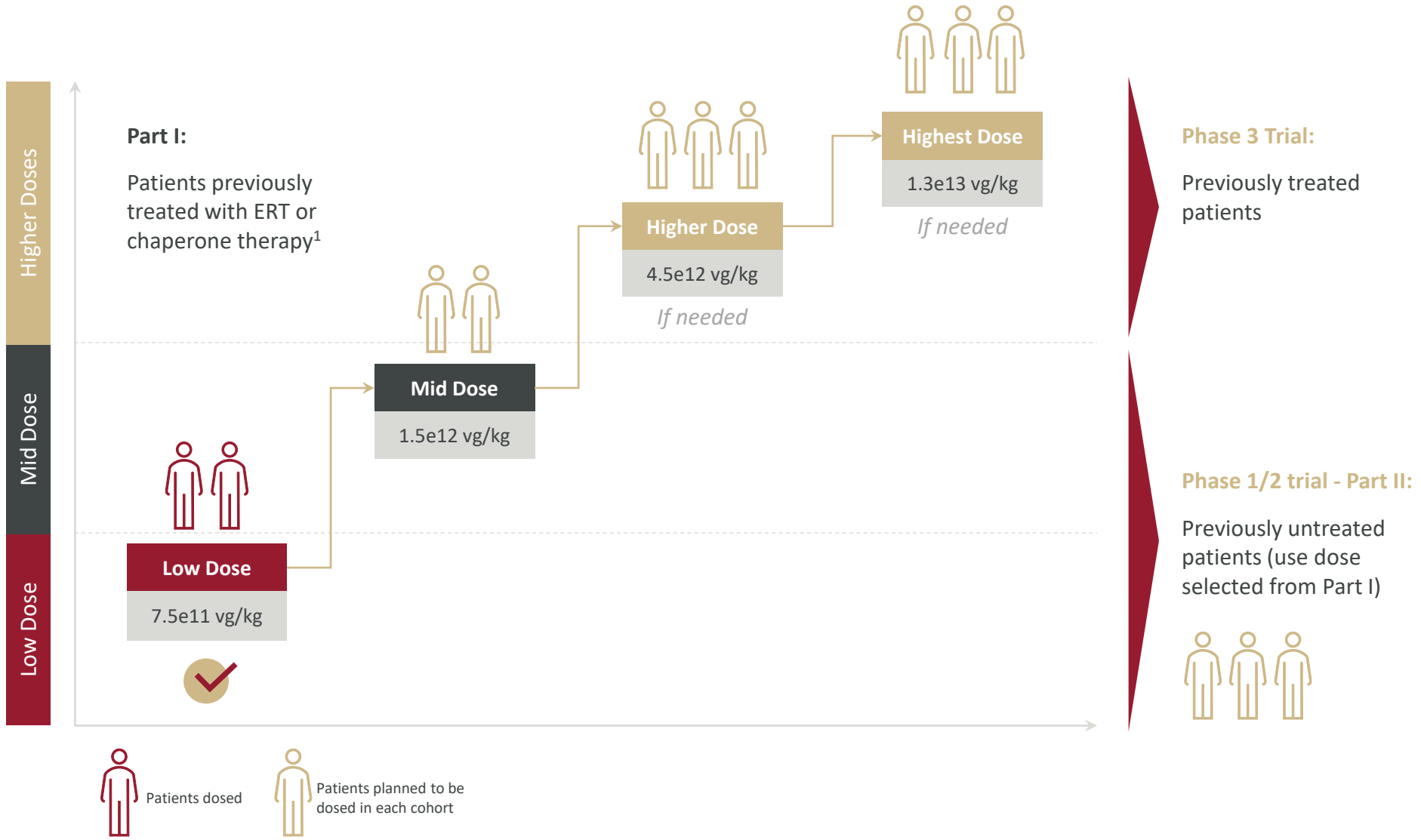
[1] Untreated wild-type (non-GLA KO) mice.

[2] GLA KO mice.

Fabry mouse model: Ohshima T, Murray GJ, Swaim WD, Longenecker G, Quirk JM, Cardarelli CO, Sugimoto Y, Pastan I, Gottesman MM, Brady RO, Kulkarni AB. (1997). alpha-Galactosidase A deficient mice: a model of Fabry disease. PNAS: 18;94(6):2540-4.

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

Adaptive trial:
To establish a dose of FLT190 that delivers sustained increased α-Gal A activity to levels that reduce substrate accumulation

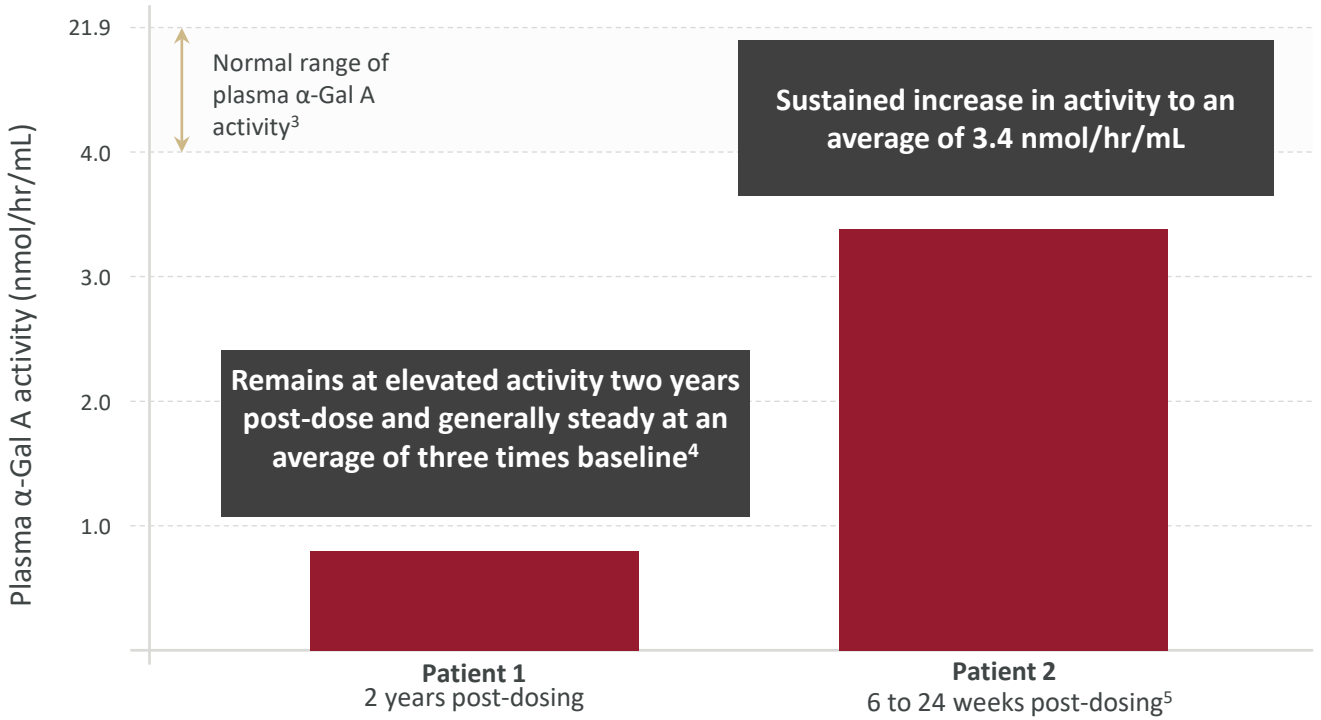


ERT= Enzyme Replacement Therapy.
✓ Marks cohort with patients dosed

Durable α-Gal A activity over 2 years in Patient 1 and near-normal levels in Patient 2

~40% increase in total dose with ~400% increase in activity[1]

Average Plasma α-Gal A[2] Activity Following Treatment with 7.5e11 vg/kg of FLT190



Patient 2

- No rise in ALT/AST levels; received optimized immune management regimen
- Treatment well-tolerated with no SAEs
- Transient troponin-T elevation has returned to baseline consistent with mild myocarditis

Patient 1

- Experienced no enduring clinical sequelae of the mild transient myocarditis episode previously reported in 2019

[1] As of the data cut-off date of Dec 22, 2021.
[2] α-Gal A: Plasma α-galactosidase A, the missing enzyme in Fabry disease.
[3] Current assay normal range: 4.0-21.9 nmol/hr/mL.
[4] Patient 1 had a subtherapeutic response with mean trough plasma α-Gal A of 0.8 nmol/hr/mL.
[5] The total vector genome (vg) dose Patient 2 received was approximately 40% higher than Patient 1 due to differences in their weights

Anticipated FLT190 milestones

FLT190 – Fabry disease Phase 1/2 MARVEL-1 dose-finding trial

2022		2023	
H1	H2	H1	H2
Reported updated safety and efficacy data from the first cohort	Dose in second cohort	Dose additional patient(s)	
Accelerated escalation to the second cohort of 1.5e12vg/kg	Provide a program update	Report updated safety and efficacy data	

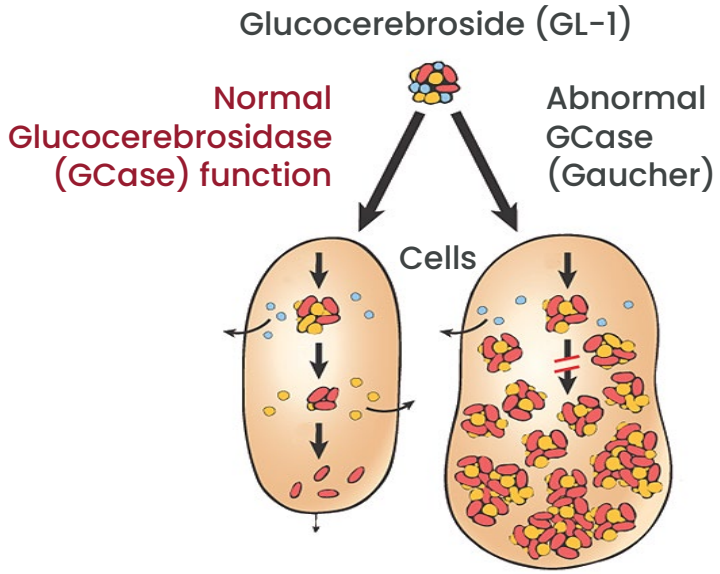
Gaucher Disease (Type 1)

Gaucher disease (Type 1) Overview

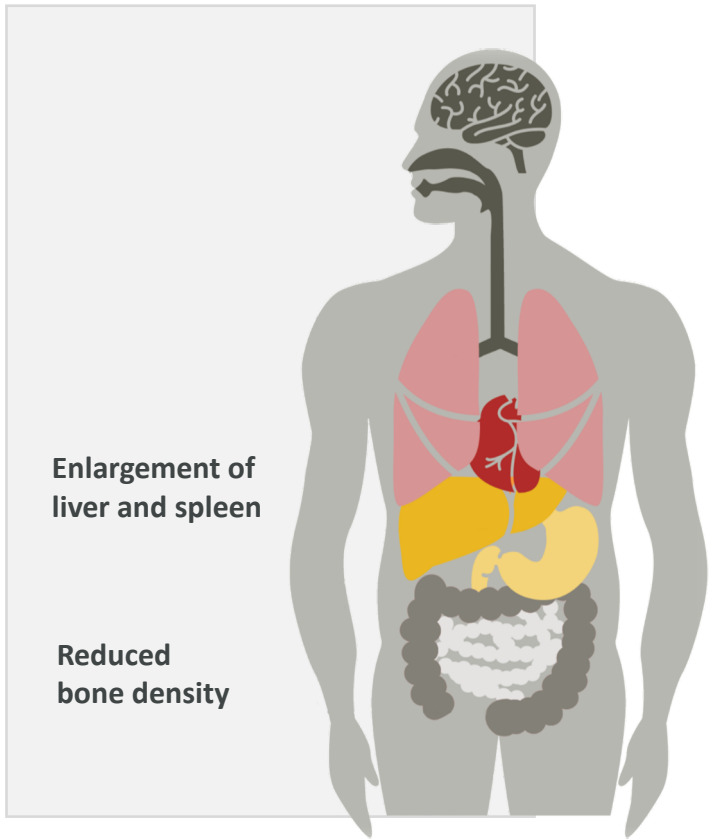
Disease Characteristics:

- Rare genetic LSD resulting from deficiency of glucocerebrosidase (GCase)
- Leads to accumulation of glucocerebroside (GL-1)
- Characterized by bone disease, hepatosplenomegaly, anaemia and thrombocytopenia with absence of primary CNS disease

Gaucher Disease Mechanism



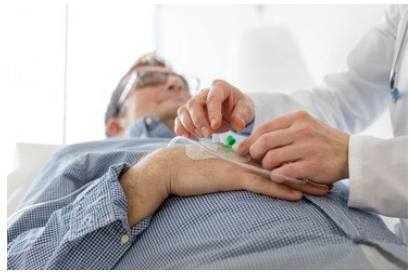
Clinical Manifestations

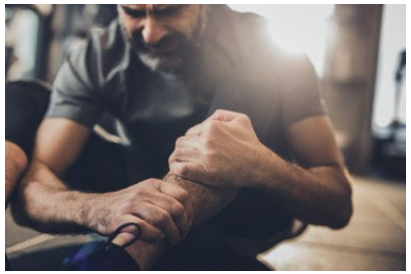


National Gaucher Foundation; Orphanet, Medscape; GeneReviews; Weinreb et al 2008; Mignot et al 2003.

Challenge: No curative therapy exists for Gaucher disease (Type 1) patients receiving lifelong ERT or SRT

Gaucher disease patient perspectives[1]





ERT treatment burden

"… It would be a lot easier if I didn't have to do the infusions every two weeks…it takes two or three hours…"

"… The main reason for considering a gene therapy would be to be free of the infusions. It would be brilliant, absolutely brilliant…"

Limitations of ERT and SRT

- Lifelong intravenous infusions every two weeks placing significant burden on patients and healthcare systems
- Daily oral administration for SRT makes it difficult for patients to adhere to treatment
- SRT and ERT are viewed as expensive by physicians
- No curative therapy exists; patients continue to experience disease progression

ERT= Enzyme Replacement Therapy; SRT = Substrate Reduction Therapy

[1] Market research - interviews, survey and analysis

Opportunity: Freeline has most advanced AAV gene therapy program for Gaucher disease (Type 1)

Competitor landscape

- Limited competition in the Gaucher gene therapy market
- Short-half life therapies do not deliver sustained protein levels. Gene therapy offers the potential of chronically sustained normal GCase levels
- *Ex vivo* lentiviral gene therapy is more burdensome and invasive for the patient compared to AAV approaches. Manufacturing scale-up is also highly complex

Urgent market need[1]

Patients
Attracted to freedom from bi-weekly infusions provided by gene therapy

Physicians
Will prescribe durable gene therapy with efficacy comparable to or better than ERT

Payers
Are attracted to the potential cost savings associated with the displacement of chronic ERT

Gaucher disease target product profile

- Durable increased GCase activity levels
- Sustained reduction in lyso-GL-1
- Eliminate the need for ERT / SRT

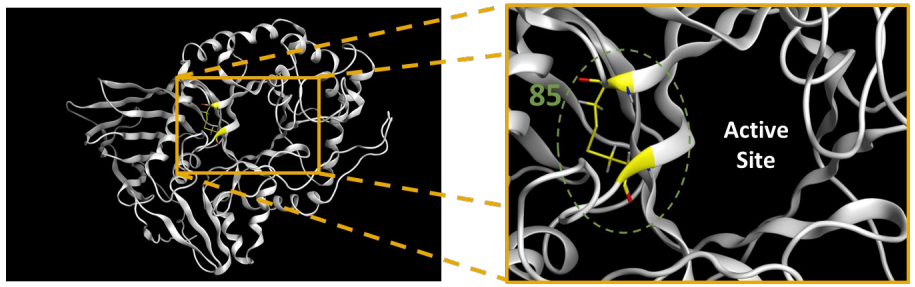
[1] Market research - interviews, survey and analysis

FLT201 produces a more stable GCase variant that achieves higher expression levels

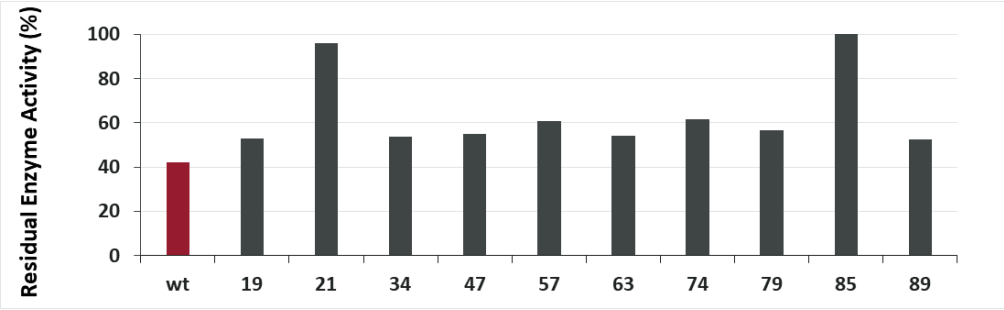
Key features of GCase variant

- > 20-fold increase in half-life in lysosomal pH compared with wild type (wt)
- Compared to wt, 6-10 fold increase in half-life in serum, resulting in a 20-fold increase in potency of the vector
- Unchanged kinetics or the anticipated antibody response

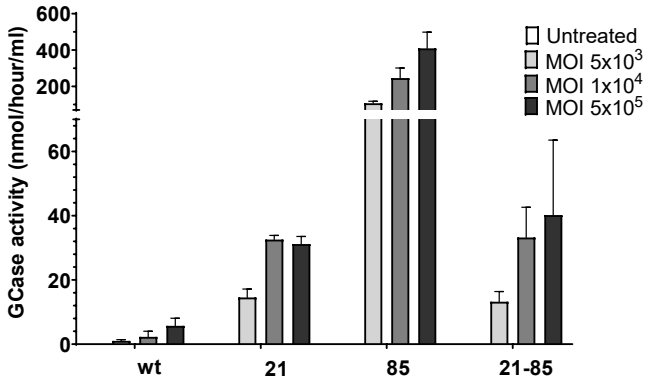
Structure of GCase variant:
GCase variant 85



In vitro stability: 10 of 86 GCase protein variants showed improved stability compared with wt



Variant 85 showed the highest level of GCase activity when transduced using AAVS3 in Huh7 cells: >80-fold increase in activity vs. wt GCase

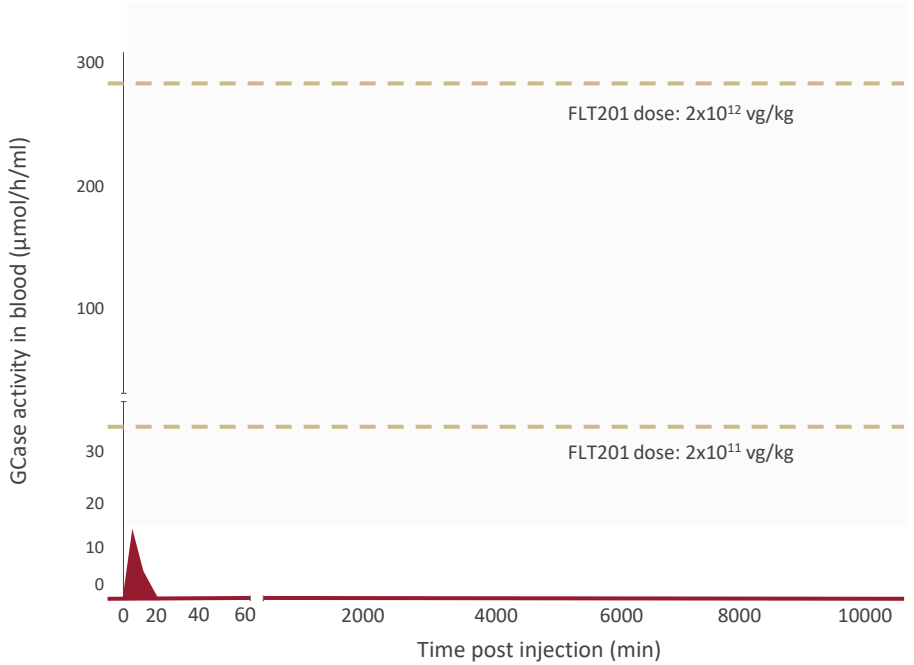


FLT201 produces more stable protein; higher uptake in Gaucher mice

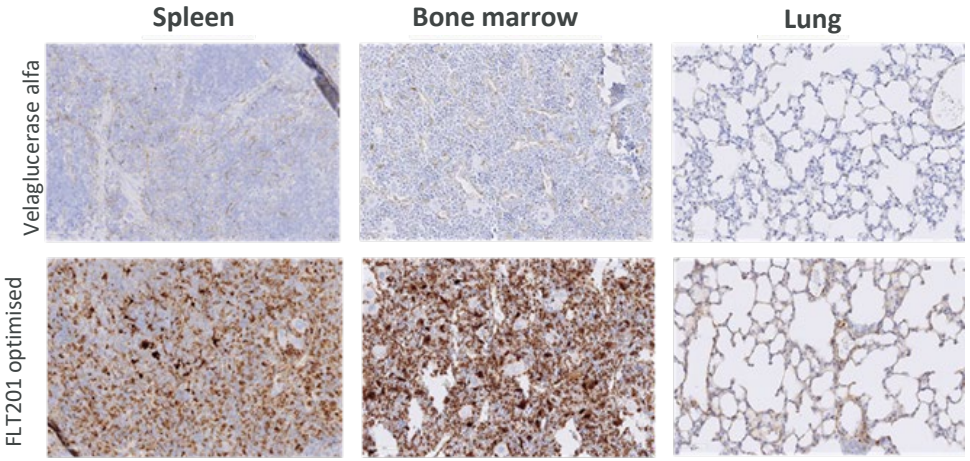
Higher GCase expression at low doses and increased uptake in key tissues

- Novel GCase variant produced by FLT201 is more stable in plasma than wild-type protein
- Greater than 20-fold increase in potency vs. vector expressing wild-type protein and better uptake in key tissues in Gaucher mice
- Enhanced potential for substrate clearance in key tissues in Gaucher mice

Increased protein stability sustains higher GCase levels compared with velaglucerase alpha[1]



Enhanced and sustained GCase uptake observed in key tissues as compared with velaglucerase alpha



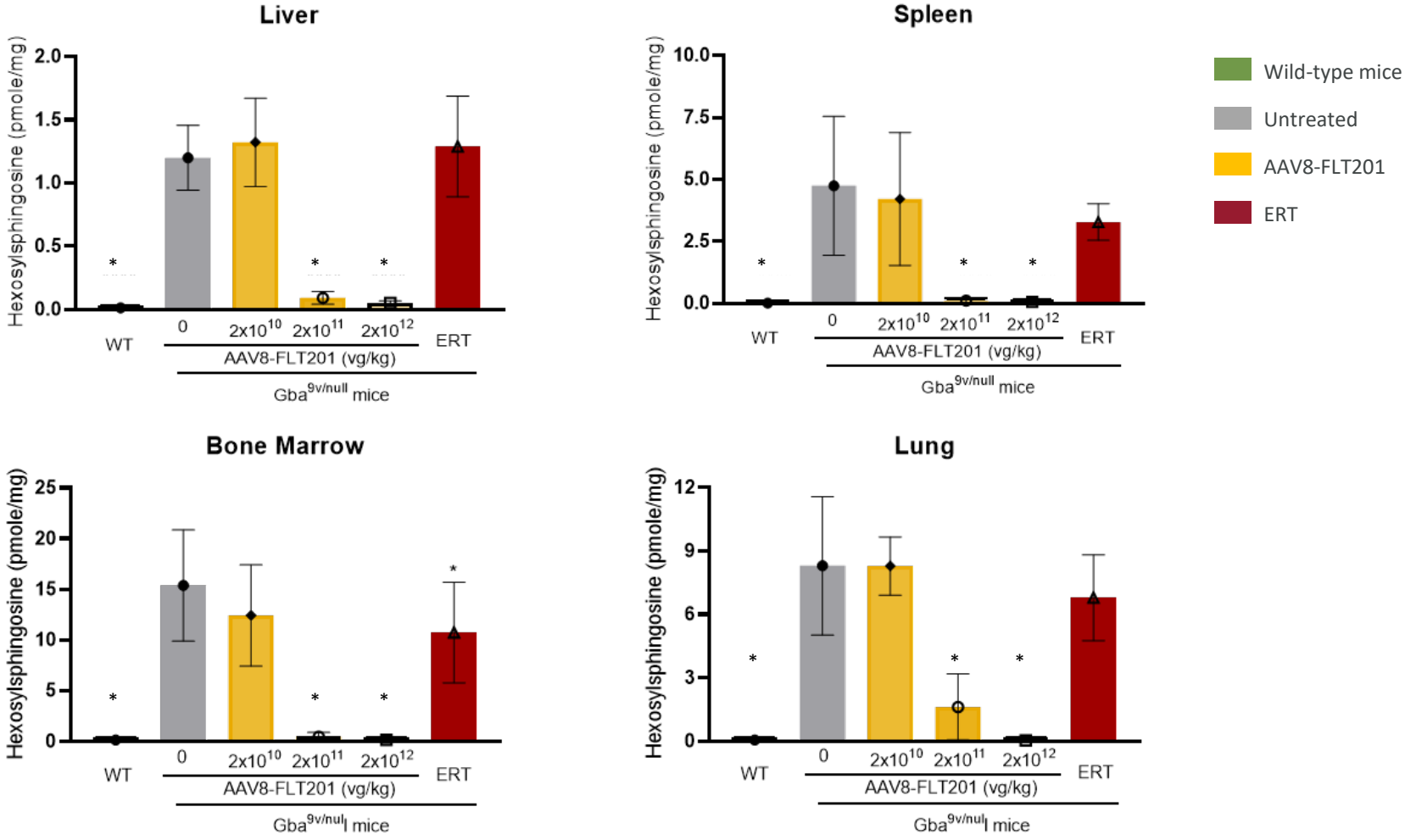
Anti-GCase – DAB, Haematoxylin counterstain, AAV8

[1] Velaglucerase alfa is an Enzyme Replacement Therapy (ERT) for Gaucher disease.
[2] FLT201 vector genome pseudo-typed with AAV8 in Gaucher mice

FLT201 clears substrate in key tissues in Gaucher mice

GCase tissue penetration and enzymatic activity leads to substrate level reduction across key tissues

- Dose-dependent reductions of lyso-GB1 observed in all tissues analyzed, including bone marrow and lung



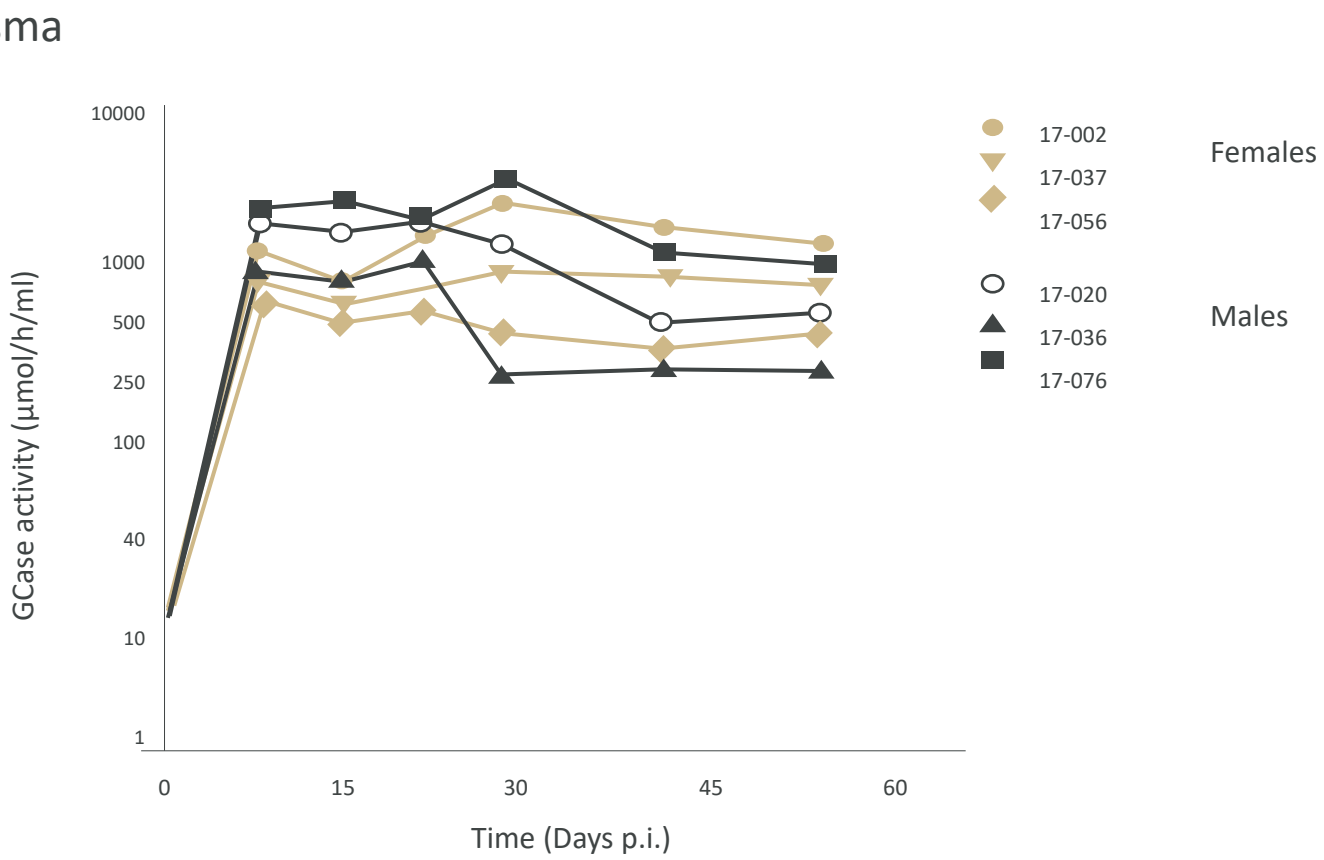
Data from trial conducted in collaboration with Professor Ying Sun (Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA) and presented at the 17th Annual WORLDSymposium.
Velaglucerase alpha - an ERT used for Gaucher disease.
AAV8-FLT201 = AAV8 pseudo-typed FLT201 genome.
ERT = Velaglucerase alfa 60 U/kg biweekly (equivalent of the standard of care in humans).

WT = wild-type mice.
Evaluated 12 weeks post-injection.
[1] Lack of GCase enzyme in humans leads to the accumulation of lyso-GB1 and Gaucher disease.
*p ≤ 0.0001.

FLT201 demonstrates high levels of GCase expression in non-human primates

Achieves 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 two months (trial ongoing)

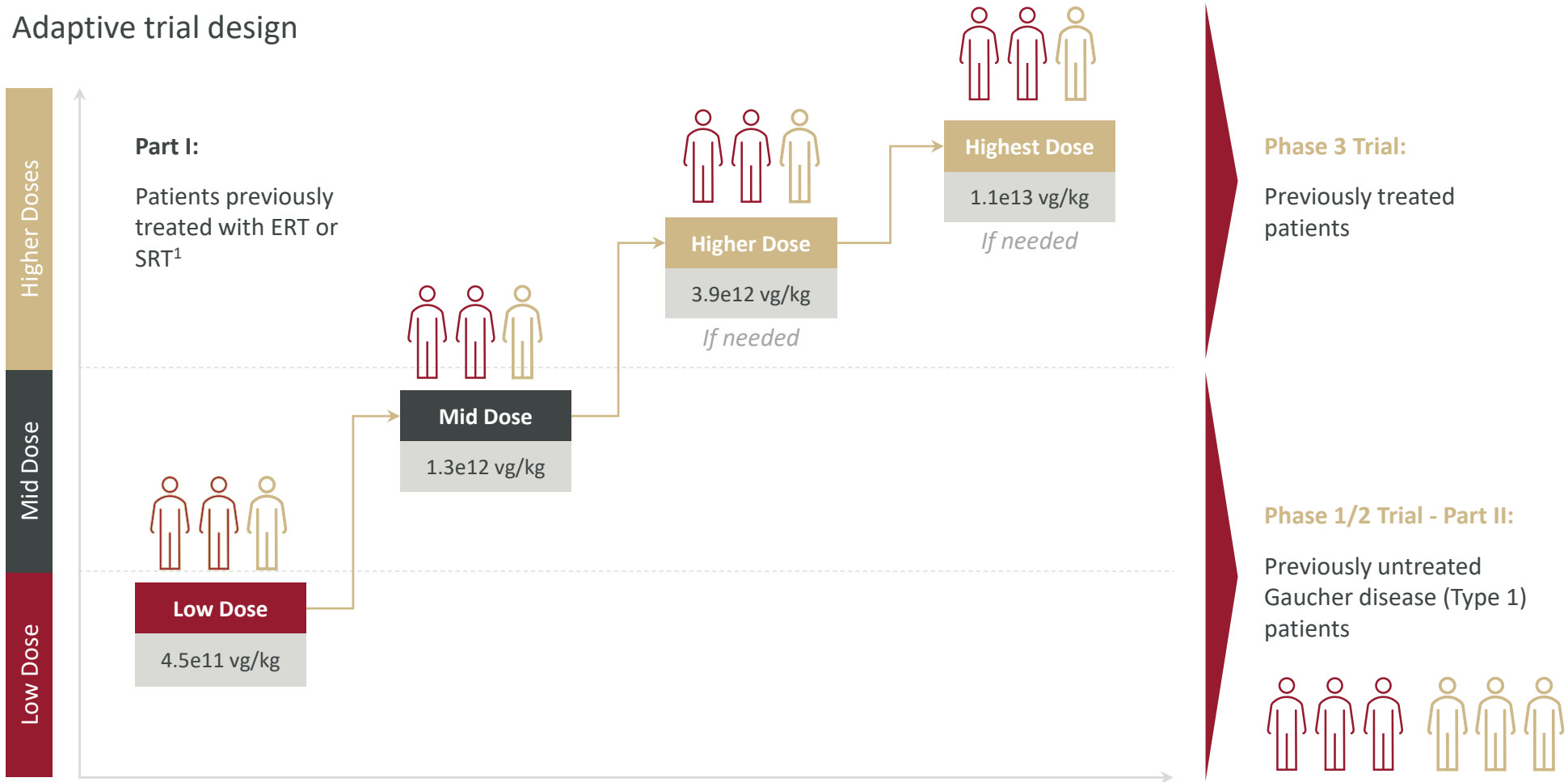


Dose: FLT201 $2x10^{12}$ vg/kg (long-term observational trial)

Phase 1/2 dose-finding trial design

Trial to evaluate safety and tolerability of FLT201 and establish a dose that delivers sustained increased GCase to levels that reduce substrate accumulation and improve clinical parameters

Adaptive trial design



GCase = glucocerebrosidase

The trial protocol allows for testing up to four doses in Part I of the clinical trial. However, depending on dose response in the initial cohorts, we may not ultimately need to escalate to the later doses.

The Data Monitoring Committee (DMC) 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.

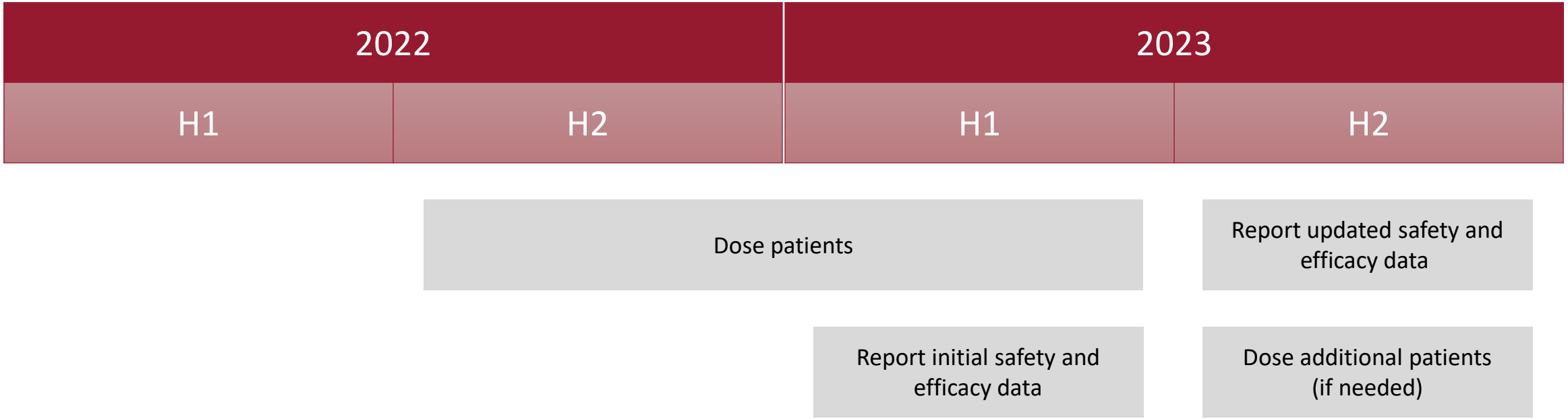
[1] ERT = Enzyme Replacement Therapy; SRT = Substrate Reduction Therapy

This symbol equates to one patient planned for dosing.

If appropriate, we may decide to expand the number patients dosed in a given cohort. This symbol represents an additional potential patient for dosing.

Anticipated FLT201 milestones

FLT201 – Gaucher disease (Type 1) Phase 1/2 dose-finding trial



FREELINE

Thank you

9 August 2022