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Examples include statements that the Phase 1/2 dose confirmation trial for FLT180a is expected to be initiated by the end of 2021 and provide a data readout in 2022, that the Phase 3 pivotal trial is expected to be initiated by the middle of 2023, that a BLA filing for FLT180a is expected to be made by the end of 2024, that the Company will be able to present durability data for up to four years from its Phase 1/2 B-AMAZE clinical trial in 2021, that the Company's immune-management regimen will be successful in preserving Factor IX expression or eliminating the need for Factor IX supplementation, that the Company will be able to progress dose escalation of FLT190 in its current Phase 1/2 clinical trial and provide a data readout in 2021 or at all, that patients treated with FLT190 will continue to demonstrate sustained αGLA activity levels for one year or longer post-treatment, that the Company will be able to initiate first-in-human dose finding studies for FLT201 in 2021, that FLT210 has the potential to deliver stable Factor VIII expression or that such expression will be demonstrated in human clinical trials, that the Company will be able to complete proof-of-concept studies for FLT210 in 2021, or that the Company will be able to develop plans for a manufacturing facility in 2021, as well as any other discussion of the Company's strategies, financing plans, business plans and prospects, capital allocation objectives and manufacturing, research, pipeline and clinical trial plans, including anticipated clinical development milestones for the Company's product candidates. 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In particular, no assurance can be provided as to whether the Company will be able to meet or achieve any near-term value creating milestones for 2021 or. that the achievement of any such milestones, including but not limited to the milestones in its revised clinical development plan for FLT180a, will result in any value creation, whether the Company will be able to initiate a pivotal trial, whether the FDA will provide any feedback on the revised clinical development plan that impacts the timing or design of its clinical trial plans for FLT180a or any of its other product candidates, whether there will be any impact to the Company's regulatory submissions timeline for FLT180a or any of its other product candidates as a result of any feedback from the FDA or otherwise, whether the Company will be able to progress dosing of FLT190, initiate dose-finding studies for FLT201 or complete pre-clinical proof-of-concept studies of the safety, efficacy or durability of FLT210 and whether FLT210 is able to deliver stable Factor VIII expression. The forward-looking statements included in this presentation are made only as of the date hereof. The Company does not undertake, and specifically declines, any obligation to update any such statements or to publicly announce the results of any revisions to any such statements to reflect future events or developments, except as required by law.

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Clinical-stage biotechnology company developing transformative AAV-mediated gene therapies for patients suffering from inherited systemic debilitating diseases



Proprietary capsid enables high protein expression at low doses in humans

Freeline positioned to target diseases perceived as beyond the reach of first-generation AAV gene therapy

Lead product FLT180a for treatment of hemophilia B* demonstrated Factor IX expression levels in normal range enabling potential for functional cure

FLT190 for treatment of Fabry disease completed lowest dose cohort; study positioned for dose escalation; plan to share data by year-end; FLT201 for treatment of Gaucher disease Type 1 shows promising pre-clinical data; targeting entry into the clinic by the end of 2021

Proprietary protein engineering, analytics and CMC platform that deliver novel, high-quality gene therapy product candidates at commercial scale

* Certain adult hemophilia B patients.

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FIX

LSDs

Experienced Leadership Team with CMC, research & development, and commercial expertise in gene therapy and rare diseases

In-house research and manufacturing platform allows us to rationally design & deliver novel AAV gene therapy programs















Vector design

Optimise vector design and thereby enhance candidate properties

Protein engineering

Design and develop novel protein molecules with favourable properties

Assay development

Develop assays to support candidate selection and advancement to clinical trials

Rapid candidate screening

High-throughput screening to enable rapid identification of lead candidates

Manufacturing technology & Development

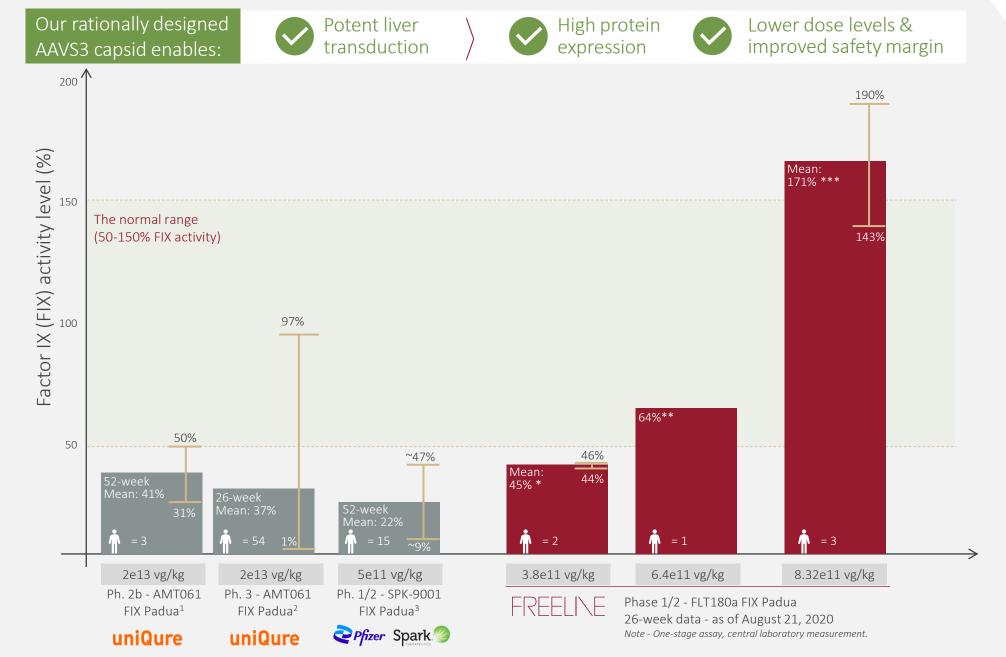
Create technology that enables high safety and potency and speed to GMP

Cutting edge analytics

Provides unique insight into AAV vectors and guides systematic platform development

- ✓ Identify and design novel targets/candidates with high potential to address unmet patient need
- Proprietary modular manufacturing technology enables development high quality products rapidly
- De-risked capsid with significant clinical data validating potency and durability in humans

Hemophilia B data validates AAVS3 capsid and platform



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The FLT180a doses listed, 3.8e11, 6.4e11 and 8.32e11 vg/kg are equivalent to 4.5e11, 7.5e11 and 9.75e11 vg/kg respectively under the previous equivalent dosing nomenclature.

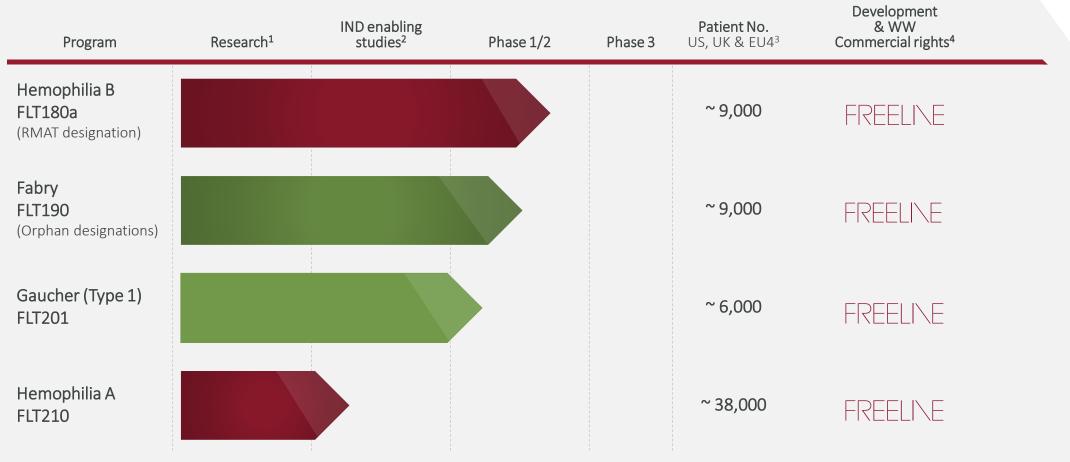
- *3.8e11 vg/kg dose: Mean value calculated based on following FIX levels: patient 1, 44%, patient 2, 46%.
- **6.4e11 vg/kg dose: Two patients dosed at this level. Value of patient 5, 64%. Patient 4, experienced loss of expression due to transaminitis and is not represented on this chart. At Week 26, Patient 4 FIX expression was 7%, which would result in a mean FIX activity level of 36% for this dose cohort.
- ***8.32e11 vg/kg dose: Four patients dosed at this level, with mean value calculated for three of them based on following FIX levels: patient 8, 180%, patient 9, 190%, patient 10, 143%.

Patient 7, not represented on chart, achieved FIX expression of 53% at Week 26, which would result in a mean FIX activity level at of 142% for this dose cohort. Patient 7 remains in normal range of FIX expression.

- 1. Miesback et al; Blood 2018 131:1022-1031.
- 2. uniQure's late-breaking ASH abstract; first data from the Phase 3 HOPE-B Gene Therapy Trial.
- 3. Pfizer R&D Day Sep 2020 up to four year follow-up data in 15 patients from Phase 1/2 trial.

Robust pipeline in place: Aim to have third program in the clinic by end of 2021

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- 1. In the research stage, we conduct *in vitro* and *in vivo* preclinical studies to evaluate different product candidates to select those with the best tolerability and potency profiles.
- 2. In the IND enabling studies stage, we conduct preclinical in vivo studies in disease-specific mouse models and good laboratory practice, or GLP, toxicity studies in non-human primates and generate the CMC information and analytical data required for an investigational new drug, or IND, submission to the FDA for a clinical trial authorization, or CTA, submission to the EMA.
- 3 These figures represent the total approximate diagnosed population for each indication. The seroprevalence of antibodies against the AAV capsid renders approximately 30-50% of patients currently not eligible for gene therapy.
- 4. Owned and in-licensed intellectual property rights.

Hemophilia epidemiology: World Federation of Hemophilia 2018.

Fabry Disease epidemiology: Metchler et al 2012; Spada et al 2016; Fabry Register; Fabry Outcome Survey; Waldek et al 2009; Deegan et al 2006.

Gaucher Disease epidemiology: Nalysnyk et al 2016; Weinreb et al 2008 & 2013; Charrow et al 2000; National Gaucher Foundation; Orphanet; NIH Technology Assessment Panel on Gaucher; Poorthuis 1999; Stirnemann et al 2012; Puopetova 2010; Mehta et al 2006.





Verbrinacogene setparvovec (FLT180a): Potential to provide a functional cure by normalizing FIX activity

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FREELINE Key learnings from the Phase 1/2 B-AMAZE dose-finding clinical trial

- Demonstrated that the dose with potential to achieve FIX activity in the normal range is expected to be between 6.4e11 vg/kg and 8.32e11 vg/kg (7.5e11 vg/kg and 9.75e11 vg/kg, respectively, under the previous equivalent dosing nomenclature)*
- Stable and durable response up to 3 years post-treatment to date
- No bleeds requiring supplemental FIX**
- Favorable safety profile
- Short course of prophylactic tacrolimus combined with prophylactic prednisone and close monitoring expected to preserve expression and eliminate the need for FIX supplementation

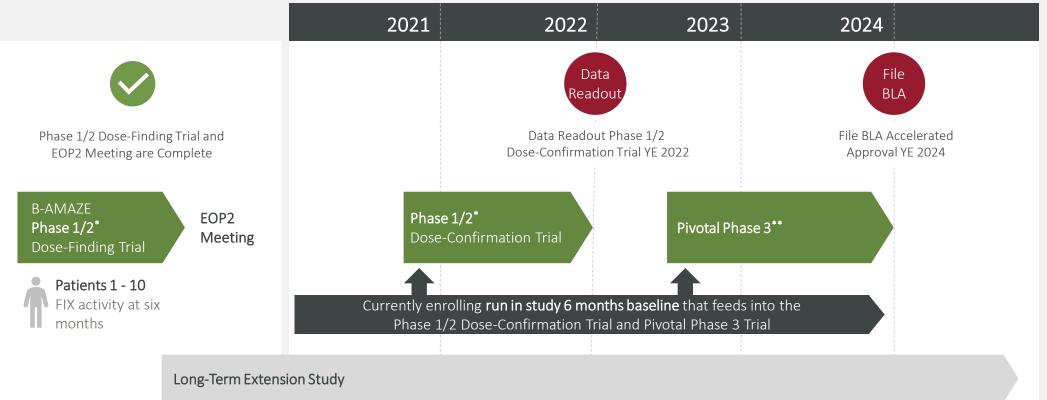
^{*}The Company's B-AMAZE trial dose escalated 10 patients across four dose levels. For future data updates, Freeline expects results will be reported using a new dose level nomenclature in the assay for the commercial-scale process in which the former doses of 4.5e.11, 7.5e.11, 9.75e.11, and 1.5e.12 vg/kg correspond to 3.8e.11, 6.4e.11, 8.32e.11, and 1.28e.12 vg/kg, respectively.

^{**}One patient in the 6.4e11 vg/kg dose cohort (7.5e11 vg/kg under the previous equivalent dosing nomenclature) lost expression and resumed FIX prophylaxis.

FLT180a clinical development plan to accelerated approval

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- Six-month Phase 1/2 trial to confirm the dose and immune management regimen for use in a pivotal Phase 3 study
- File accelerated approval using the surrogate endpoint of FIX activity levels combined with demonstration of a positive correlation between 26-week FIX activity levels and 52-week Annualized Bleeding Rate



^{*}To evaluate safety and durability.

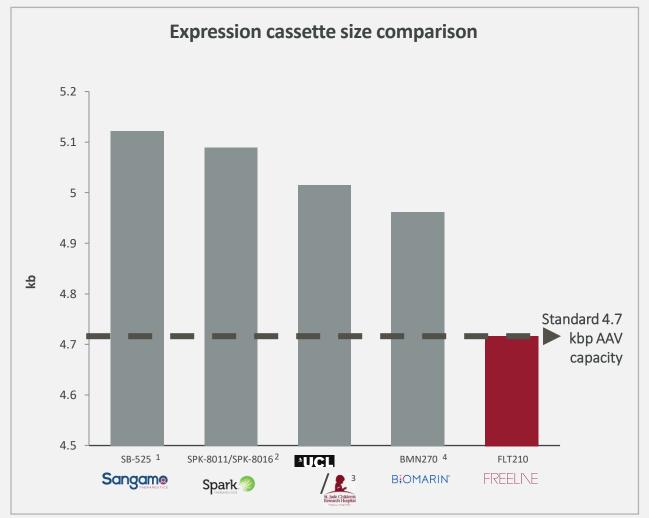
^{**}To evaluate safety, durability and efficacy.





FLT210 contains the only Factor VIII construct that fits within the carrying capacity of an AAV capsid

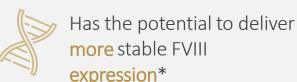
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Key attributes of FLT210

- Smallest disclosed liver specific promoter in development
- Shortened FVIII gene to reduce expression cassette size
- Allows expression cassette to fit within the natural capacity of AAV capsid





*Can only be demonstrated in human trials, which have not yet been conducted.

Note: Hem A candidate nomination reached. Toxicology, CMC and disease animal model confirmation work ongoing.

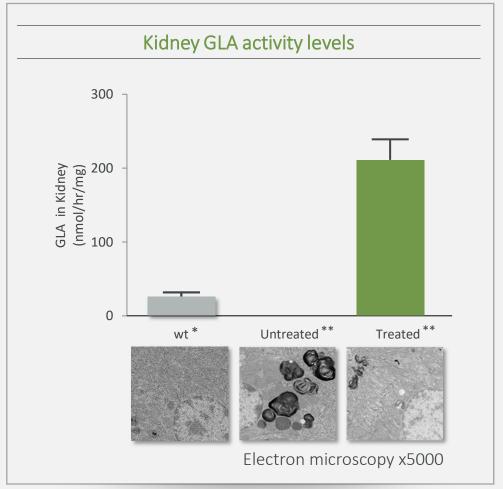
Sources of construct sizes:

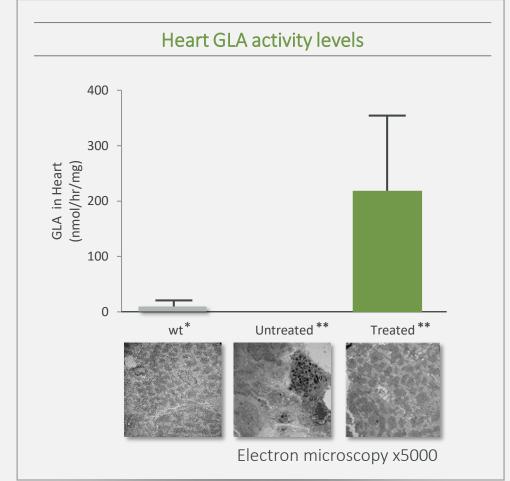
- 1. As presented at ASGCT (2016) and WFH (2020).
- 2. As documented in patent (international patent number: WO/2016/025764).
- 3. McIntosh J, Lenting PJ, Rosales C, et al. Therapeutic levels of FVIII following a single peripheral vein administration of rAAV vector encoding a novel human factor VIII variant. Blood. 2013;121(17):3335-3344.
- 4. Bunting S, Zhang L, Xie L, et al. Gene Therapy with BMN 270 Results in Therapeutic Levels of FVIII in Mice and Primates and Normalization of Bleeding in Hemophilic Mice. Mol Ther. 2018;26(2):496-509.



FLT190 demonstrates increased GLA expression and reduction in pathologic substrate in key tissues in Fabry mouse model

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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.

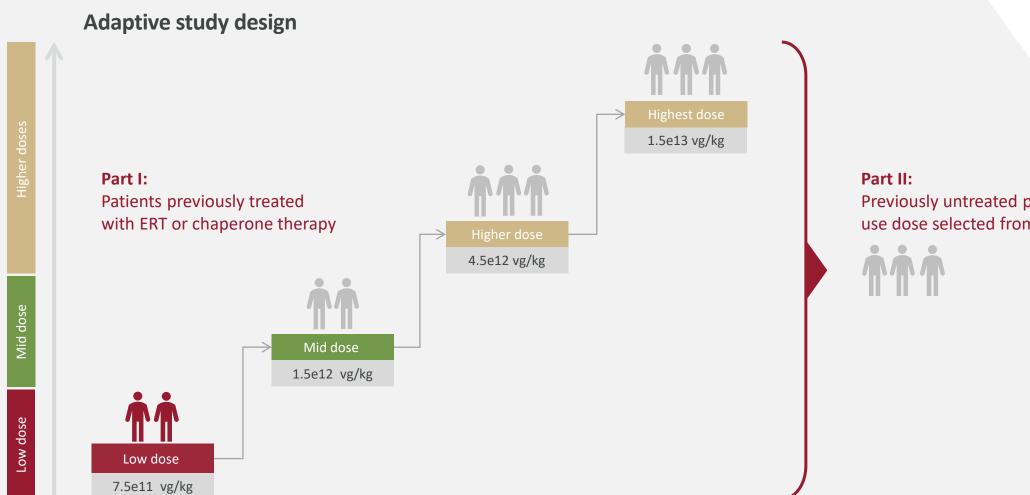
Time point: 16-week disease development prior to treatment; analysis 14 weeks post-treatment. Gb3/Lyso-Gb3 data (n=4, 2 males and 2 females).

*Untreated wild-type (non-GLA KO) mice.

**GLA KO mice.

FLT190 phase 1/2 dose-finding study poised for dose escalation





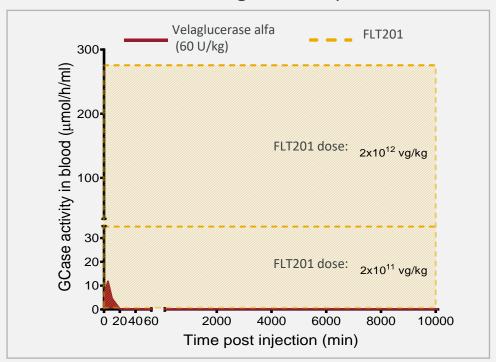
Previously untreated patients; use dose selected from Part I

Low doses of FLT201 in Gaucher mice result in higher expression and increased uptake in tissues affected by Gaucher Type 1 disease

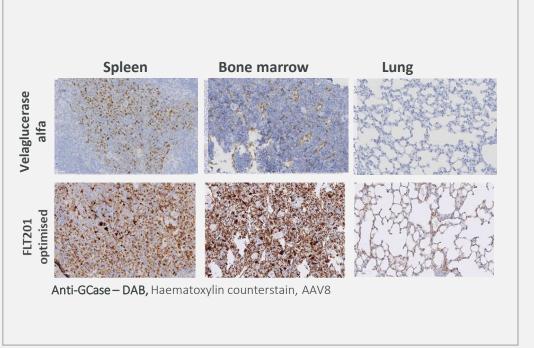
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- Novel GCase variant produced by FLT201 is more stable in plasma than wild-type protein
- This leads to a greater than 20-fold increase in potency vs. wild-type protein and better substrate clearance in key tissues in Gaucher mice

Increased protein stability compared with velaglucerase alpha



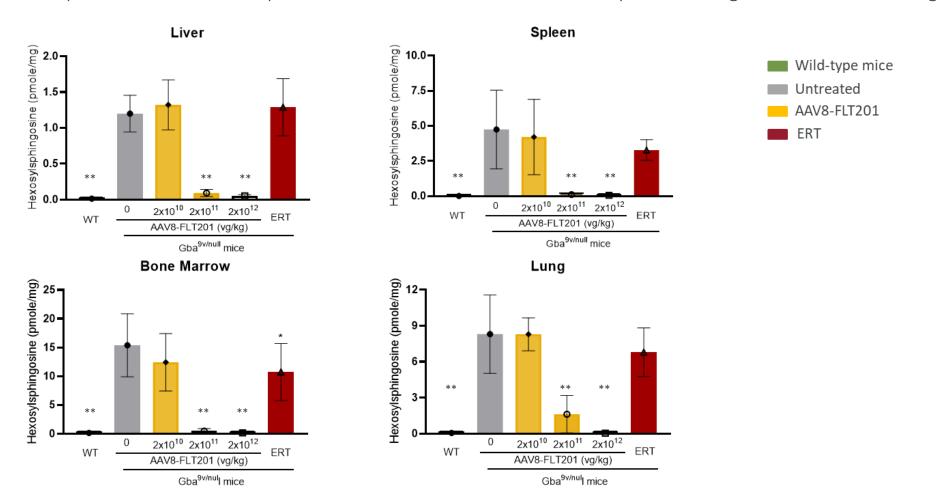
Enhanced and sustained GCase uptake observed in key tissues as compared with velaglucerase alpha



Velaglucerase alfa is an Enzyme Replacement Therapy for Gaucher disease.

Gba-deficient mice data demonstrates GCase tissue penetration by FLT201, enzymatic activity & substrate clearance

- Restoration of GCase activity after FLT201 injection was observed in Gba-deficient mice in difficult-to-reach tissues as shown by decreased levels of lyso-GB1 substrate*
- Dose-dependent reductions of lyso-GB1 were observed in all tissues analyzed including bone marrow and lung



FREELI\E

Data from study 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.

*Lack of GCase enzyme in humans leads to the accumulation of lyso-GB1 and Gaucher disease.

** $p \le 0.0001$.



Multiple potential near-term value-creating milestones targeted for 2021

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2021 Objectives

- Hemophilia B Initiate clinical trial sites for the Phase 1/2 dose confirmation trial
- Hemophilia B Present durability data up to 4 years from Phase 1/2 B-AMAZE dose-finding clinical trial
- Fabry Progress dose escalation in Part I of Phase 1/2 dose-finding clinical trial and share data
- Gaucher Initiate Phase 1/2 dose-finding clinical trial
- Hemophilia A Complete preclinical proof-of-concept studies of the safety, efficacy and durability of FLT210
- Platform Further develop plans for Freeline manufacturing facility

