Poster 127

Design of GALILEO-1, a Phase 1/2 safety and efficacy study of FLT201 in adult patients with Gaucher disease Type 1

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Disclosure information

Derralynn A. Hughes

I have the following financial relationships to disclose:

Advisory Board: Freeline, Sanofi, Takeda, Amicus, Idorsia

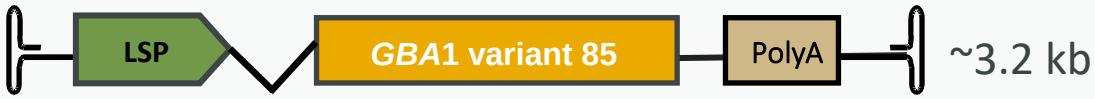
Consulting Fees: Freeline, Sanofi, Takeda, Amicus, Idorsia, Protalix, Sangamo

Honoraria: Freeline, Sanofi, Takeda, Amicus, Idorsia

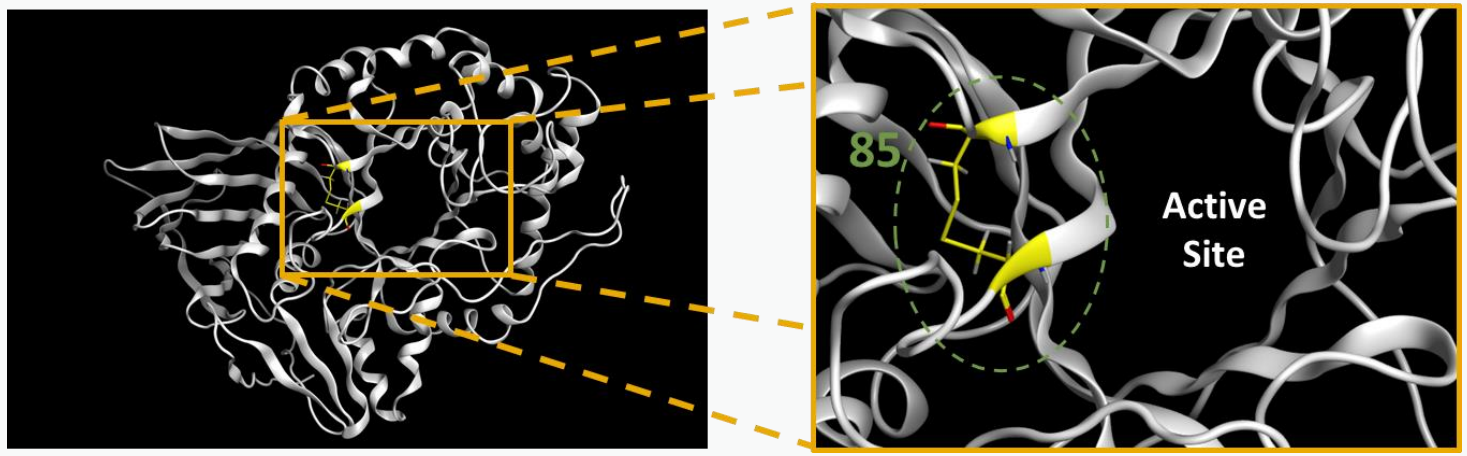
I will discuss the following investigational use in my presentation: investigational use of FLT201 for the treatment of patients with Gaucher disease Type 1

FLT201 is an adeno-associated virus (AAV) gene therapy in development for the treatment of patients with Gaucher disease Type 1

- A novel human liver-tropic AAV capsid (AAVS3)
- Codes for a novel variant of glucocerebrosidase ($GCase_{var85}$)
- Produces robust and sustained secretion of GCase into the bloodstream in mice
- $GCase_{var85}$ shows increased stability at lysosomal and physiological pH in human serum
- Similar catalytic properties to wild-type GCase and velaglucerase alfa



Model of $GCase_{var85}$



$GCase_{var85}$ contains two novel amino acid substitutions to the mature human GCase, resulting in:

- 6-fold increase in GCase half-life in human serum
- 20-fold increase in GCase half-life at lysosomal pH conditions

GBA = glucosylceramidase beta; GCase = β-Glucocerebrosidase; $GCase_{var85}$ = β-Glucocerebrosidase variant 85; LSP = liver-specific promoter; PolyA = polyadenylation signal sequence.

Comper F, 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. Poster presented at: The World Symposium 17th Annual Research Meeting; February 8-11, 2021.

GALILEO-1 is the first AAV gene therapy study in patients with Gaucher disease Type 1

Study Design

- First-in-human, open-label, international, multicentre Phase 1/2 clinical trial
- Patients with Gaucher disease Type 1 will receive a single intravenous infusion of FLT201
- Novel prophylactic immune management regimen to prevent vector-related transaminitis

Objectives

- Evaluate the safety and tolerability of FLT201
- Investigate the relationship of FLT201 dose to production of endogenous GCase
- Determine potential to improve clinical phenotype by reduction in GCase substrate glucosylsphingosine

Patient population

- Adult (≥18 years of age) men and women with Gaucher disease Type 1
- Deficient GCase enzyme activity ≤30% of normal in leukocytes at diagnosis
- Previously treated with ERT/SRT (Part I); previously untreated (Part II)
- Negative result for neutralising antibodies to AAVS3 at screening

Enrolment

- Up to approximately 12 patients in Part 1; up to 6 patients in Part 2

Follow-up period

- 38 weeks in GALILEO-1; ≥5 years post dosing in LTFU study (GALILEO-2)

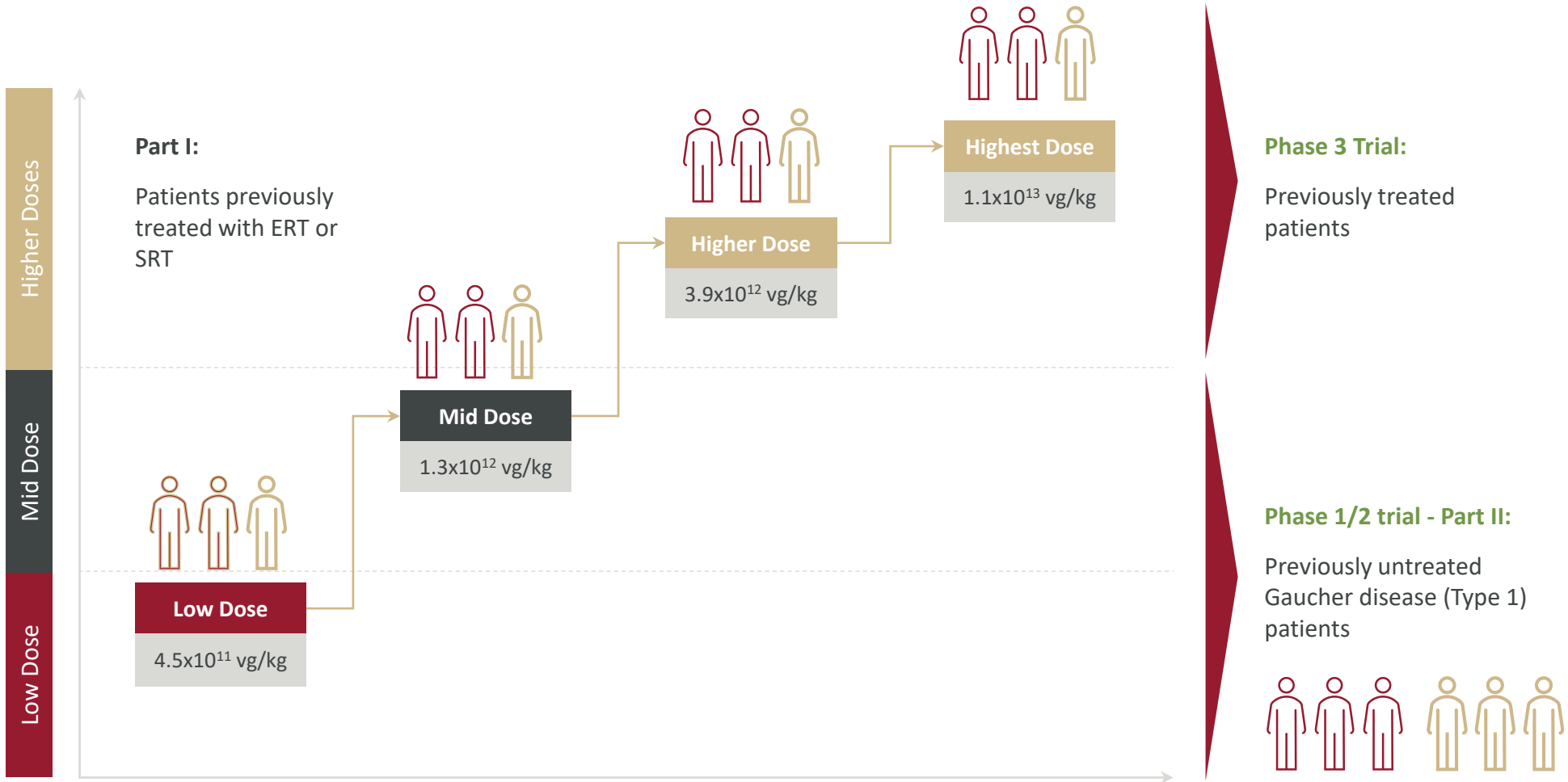
Primary and secondary endpoints

- Primary: Safety as assessed by treatment-emergent adverse events
- Secondary: change from baseline in
  - Plasma and leukocyte GCase activity
  - Glucosylsphingosine in plasma
  - Spleen volume
  - Liver volume
  - Haemoglobin
  - Platelet count

GCase = β-Glucocerebrosidase; ERT = enzyme replacement therapy, LTFU = long-term follow-up; SRT = substrate reduction therapy.

The adaptive dose-escalation design of GALILEO-1 will identify a dose of FLT201 for further development in Phase 3 clinical trial

Study to evaluate the safety and tolerability of FLT201 and establish a dose that delivers sustained increases in GCase to levels that reduce substrate accumulation and improve clinical parameters



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