Phase 2b Trial to Evaluate the Safety & Factor IX Levels Resulting from a Daily Subcutaneous Prophylaxis Treatment Regimen of Dalcinonacog Alfa in Haemophilia B

Johnny Mahlangu, Howard Levy, Claude Negrier, Mathilde Fretigny, Frank Del Greco, Linda Neuman, Grant E. Blouse

EAHAD 07 February 2020
Session 6: Slam OR07

Haemophilia Comprehensive Care Centre, Johannesburg, South Africa; Catalyst Biosciences, South San Francisco, CA; CHRU Lyon Hopital, France, Secteur Biologie Moléculaire et Diagnostic Prénatal des pathologies de l'Hémostase, Bron, France

EAHAD 2020

13th ANNUAL CONGRESS OF THE EUROPEAN ASSOCIATION FOR HAEMOPHILIA AND ALLIED DISORDERS

THE HAGUE NETHERLANDS 5–7 February 2020

Disclosure for Johnny Mahlangu

In compliance with COI policy, EAHAD requires the following disclosures to the session audience:

Shareholder	**No relevant conflicts of interest to declare**
Grant / Research Support	**BioMarin, CSL, Freeline Therapeutics, Novo Nordisk, Novartis, Pfizer, Sanofi, Roche, uniQure**
Consultant	**CSL Behring, Catalyst Biosciences, Freeline Therapeutics, Novo Nordisk, Roche, Sanofi, Spark and Takeda**
Employee	**No relevant conflicts of interest to declare**
Paid Instructor	**No relevant conflicts of interest to declare**
Speaker bureau	**No relevant conflicts of interest to declare**
Other	**No relevant conflicts of interest to declare**

Presentation includes discussion of the following off-label use of a drug or medical device:

N/A

Unmet needs in Haemophilia B therapy

Continuous convenient protection against bleeding

Current haemophilia B replacement therapy issues:

- Breakthrough bleeds as a result of low extravascular FIX levels
- Require intravenous administration

There is a need for haemophilia therapy with

+ Simple subcutaneous dosing (particularly for children)
+ Continuously protective levels
  - Protection during strenuous activities
  - Prevention of microbleeding
  - Distribution to the extravascular space
+ Low volume injection
+ No need for reconstitution before administration

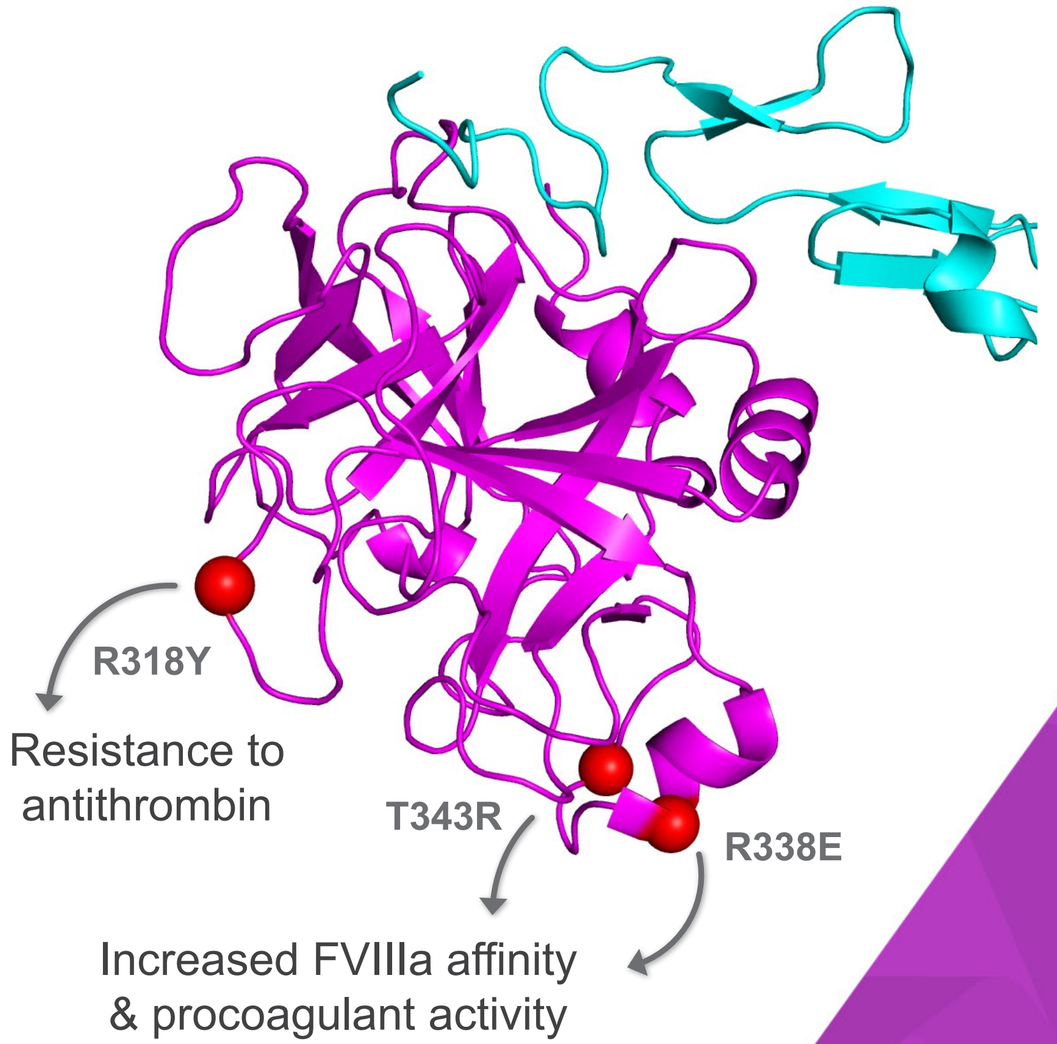
Dalcinonacog alfa: a novel SQ FIX product

Three substitutions within the FIX protein:

+ Resistance to antithrombin inhibition
+ Higher affinity for FVIIIa
+ Increased catalytic activity
+ 22-fold increased potency over BeneFIX

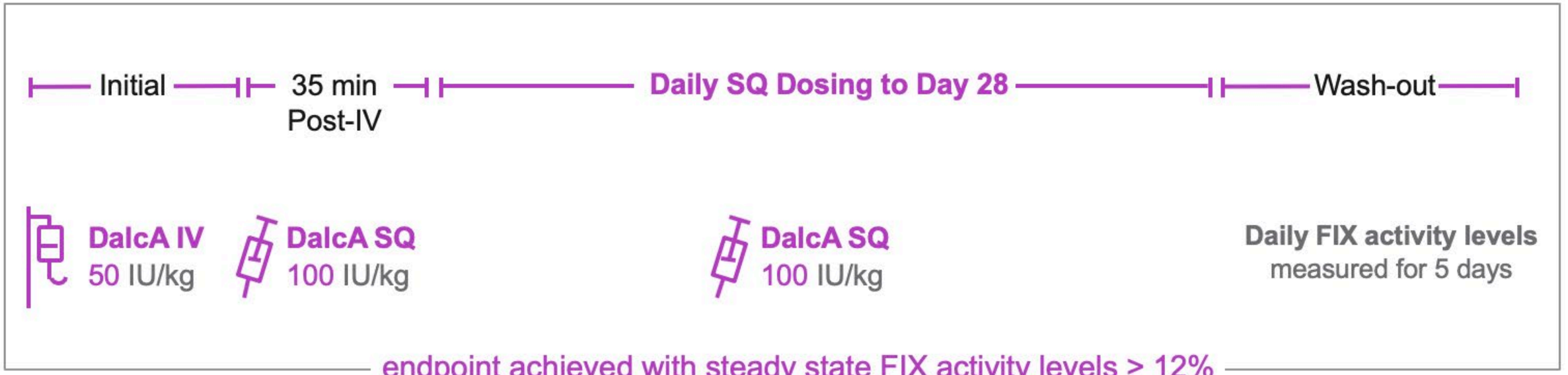
Differentiated from marketed IV FIXs:

+ Simple SQ administration
+ Potential to maintain continuous protective levels
+ Small volume injection
+ Enhanced pharmacokinetics with prolonged half-life



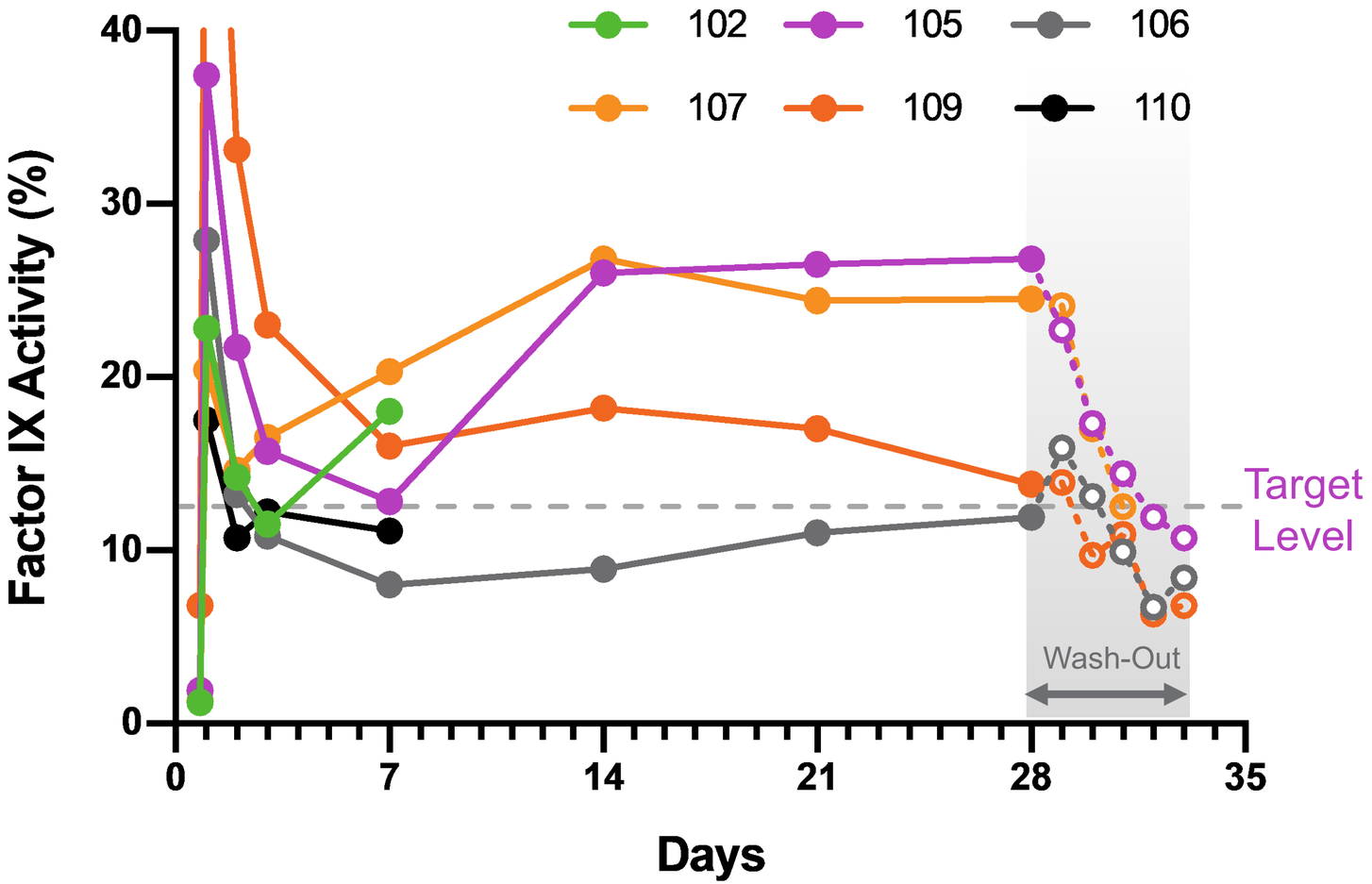
Dalcinonacog alfa phase 2b SQ clinical trial design

Enrollment complete



+ Primary endpoint: **Steady state FIX activity** level above 12% with daily dosing
+ Secondary endpoints: **safety including weekly ADA testing**, pharmacokinetics, pharmacodynamics, bleeding events
+ 10 severe HB patients screened; 6 dosed
+ Rare propeptide mutation excluded

Target levels achieved with 100 IU/kg dosing for 28 Days



Target FIX >12% Achieved

- Dosed 6 severe HB subjects
  - 110 continues dosing*
  - 102 withdrew on Day 7
- **Steady state FIX levels up to 27%** achieved after 14 days
- Consistent PK profiles
- Terminal half-life is 70-112 hrs
- **No breakthrough bleeds through washout**

*Data cutoff 05 Feb 2020

Safety

No anti-drug antibodies detected

+ No ADA or nAb against DalcA, and no de novo inhibitor to FIX*
+ There were no serious adverse events (SAEs) reported, no systemic hypersensitivity
- Patients reported injection site reactions (ISRs)
  - The majority of were mild in severity and abated with continued dosing
    - Pain; redness; swelling
- Adverse events in 2 subjects
  - Subject 102 had moderate ISRs Days 1-3 that resolved without sequelae
  - Subject 105 had moderate haematomas that resolved without sequelae

*Data cutoff 05 Feb 2020

Conclusions

+ **SQ dalcinonacog alfa provides stable therapeutic levels of Factor IX**
+ **Demonstrates the potential to be an effective prophylaxis treatment for individuals with Haemophilia B**

Trial enrollment complete

Excellent & consistent therapeutic FIX activity levels attained

Prolonged half-life with SQ administration

No SAEs, systemic hypersensitivity, ADAs or nAb to DalcA or wild-type FIX

Mild to moderate ISR’s primarily with initial injections

No bleeding events through washout demonstrates effective prophylaxis