Crimson 1 Study: Phase 3 study to evaluate the efficacy and safety of subcutaneous marzeptacog alfa (activated) for on-demand treatment and control of bleeding episodes in subjects with hemophilia A or hemophilia B, with inhibitors

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Catalyst Biosciences, Inc.

Disclosure for All Authors

Conflict	Disclosure
Current Employee	Catalyst Biosciences
Shareholder/Equity Holder	Catalyst Biosciences

Background

Hemophilia A and Hemophilia B with Inhibitors

+ Hemophilia A and B are X-linked bleeding disorders caused by a deficiency of Factor VIII (HA) or Factor IX (HB)

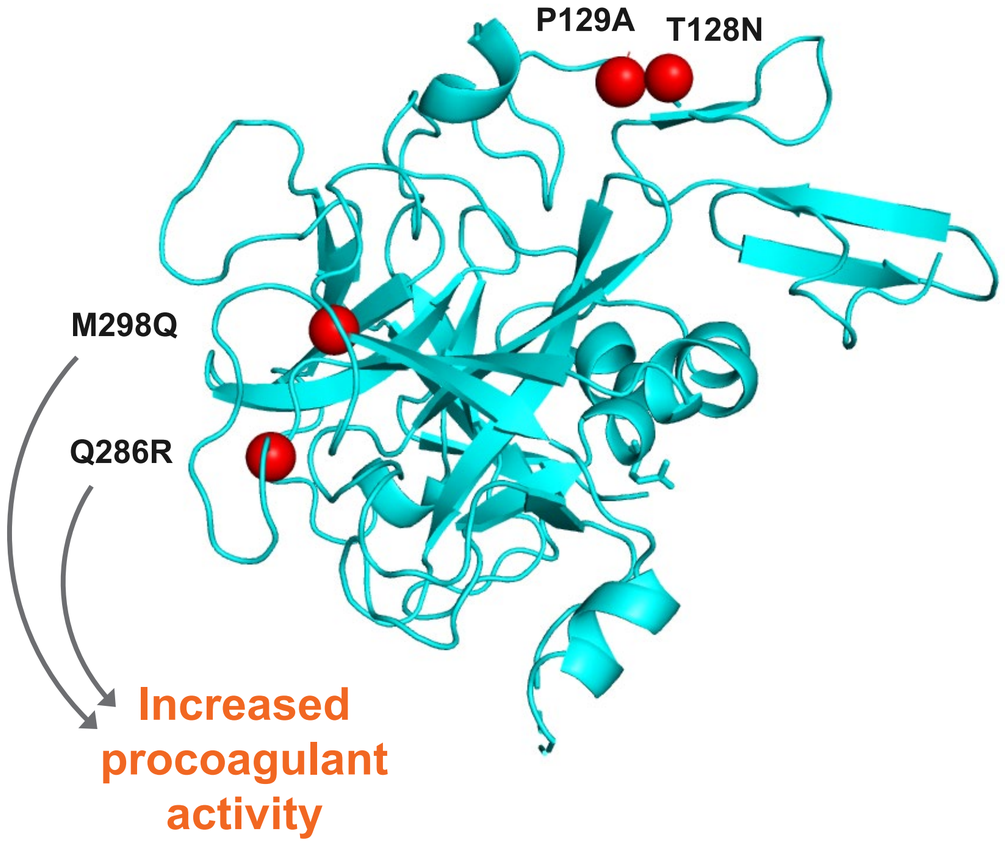
+ A significant number of individuals with HA and HB develop inhibitors against the wild-type FVIII or FIX, respectively, and thereby become refractory to factor treatment

+ Standard of Care (SOC) treatment of episodic bleeding in these individuals requires technical expertise to gain intravenous (IV) access, is often associated with pain and delay in treatment

+ Currently approved bypassing agents require multiple doses and take 6-24 hours to achieve hemostasis and maintain efficacy

Marzeptacog alfa (activated): MarzAA rFVIIa

Addresses a clear unmet need in hemophilia & other bleeding disorders



9-fold higher activity *vs* NovoSeven RT

+ Potency allows for SQ dosing that prolongs half-life
+ Simple, small volume SQ administration

Preclinical efficacy of SQ on-demand treatment

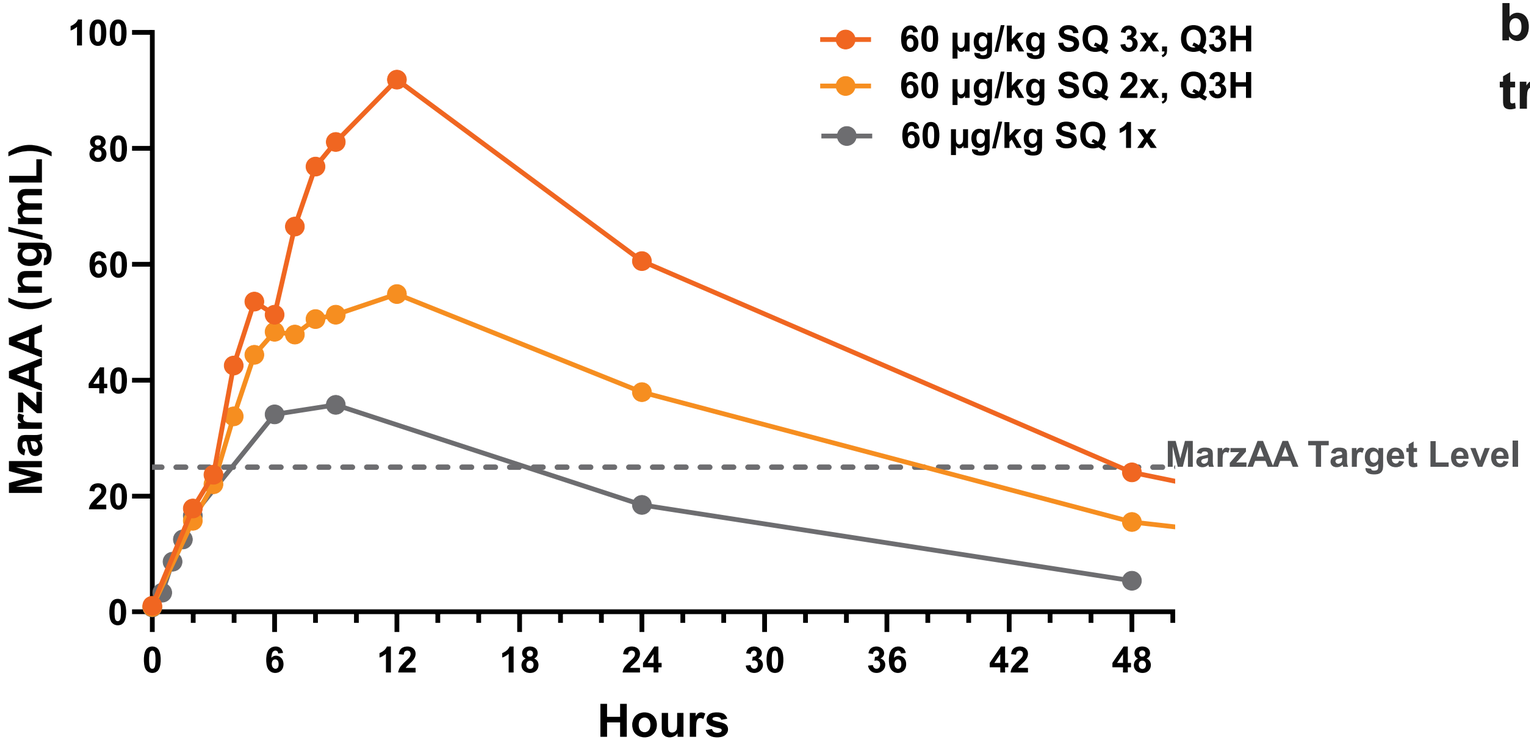
+ HA mouse after tail cut; HA dog; HA rat

P2/3 prophylaxis efficacy & safety in HA or HB with inhibitors

+ 47 patients treated to date including: single dose IV, up to 3 SQ doses/day, & daily SQ up to 97 days

Marzeptacog Alfa (activated)

Recombinant Factor VIIa variant

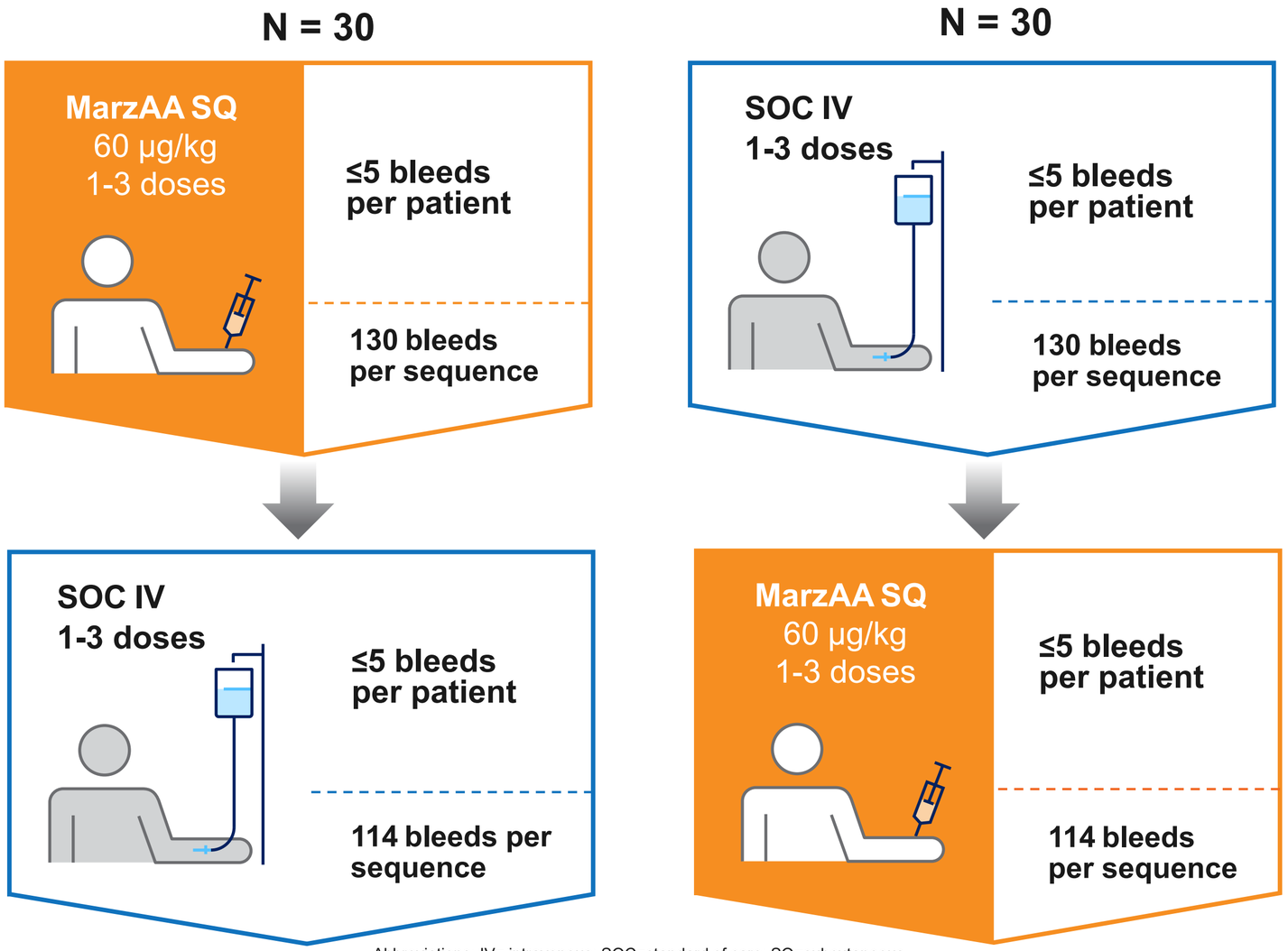


Characteristics of MarzAA as SQ bypassing agent for on-demand treatment

- Simple, small volume SQ administration
- Rapidly achieves target blood levels
- Prolonged half-life with the potential to prevent rebleeds
- Target levels can be maintained for 18 hours with a single SQ dose

Treatment of Episodic Bleeding

Study Design



Abbreviations: IV= intravenous; SOC=standard of care; SQ=subcutaneous

Open-label, global, multi-center, randomized, cross-over trial

- **Primary endpoint**
  Non-inferior hemostatic efficacy: standard 4-point scale at 24-hours
- **Secondary endpoints**
  Time to bleed resolution; number of doses; rescue meds
- **Safety**
  Adverse events, anti-drug antibodies (ADA); thrombosis

Statistics

+ **SOC estimate 85%**
  Excellent/good treatment of bleeds
+ Non-inferiority margin of **12%**
+ **2.5%** significance, one-sided
+ **90%** power

Inclusion and Exclusion Criteria

Key Inclusion Criteria

- Confirmed diagnosis of HA and HB with inhibitors requiring bypassing agents to treat episodic bleeding
- Historic ABR of ≥8
- Age ≥12 years (male or female)
- Investigator-confirmed subject's ability to identify and treat bleeding episodes
- Investigator-confirmed subject's ability to administer SQ MarzAA and infuse SOC IV

Key Exclusion Criteria

- Previous exposure to SQ administration of rFVIIa or exposure to any other variant rFVIIa
- Known positive antibody to MarzAA, FVIIa, or FVIIa variants
- History of other coagulation disorder(s)
- History of atherosclerotic disease or venous thromboembolism within 24 months or at high risk for thromboembolic events
- Platelet count <50,000/μL

Study Objectives

Primary

+ Percentage of treated bleeds resulting in effective hemostasis (excellent or good) at 24 hours after the initial dose

Secondary

+ Time to cessation of bleeding
+ Percentage of treated bleeds resulting in effective hemostasis at 1, 3, 6, 9, 12, 24 and 48-hour timepoints
+ Percentage of successfully treated bleeding events at 24 hours that maintain hemostasis through 48 hours after the initial dose
+ The use and amount of rescue therapy needed in treatment failures

Safety

+ Adverse events
+ Thrombotic events
+ Binding and/or neutralizing anti-drug antibodies

Exploratory

+ Patient satisfaction with the Treatment Satisfaction Questionnaire for Medicine-9
+ Pain assessment using the Wong Baker Faces Pain Scale
+ Time required to administer treatment

Current Trial Status

Actively enrolling subjects

+ Number of sites: ~50 global sites

+ Number of countries: ~19 countries

+ Current enrollment status:
  - Sites are open for enrollment
  - Patient Recruitment has begun

THANK YOU