OR11: Phase 2/3 Trial of Subcutaneous Engineered FVIIa Marzeptacog Alfa (Activated) in Hemophilia A or B with Inhibitors: Pharmacokinetics, Pharmacodynamics, Efficacy and Safety

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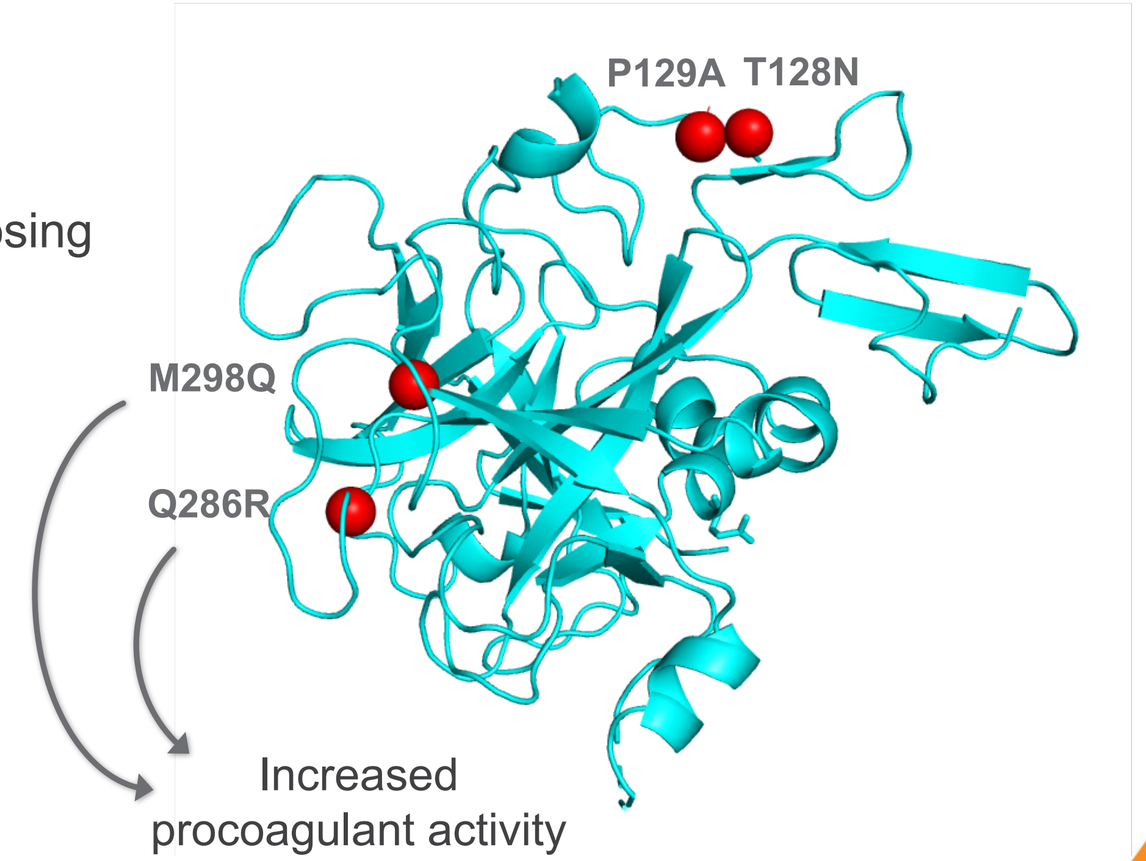
CATALYST BIOSCIENCES

Marzeptacog alfa (activated)

Four engineered amino acid substitutions within the FVIIa protein

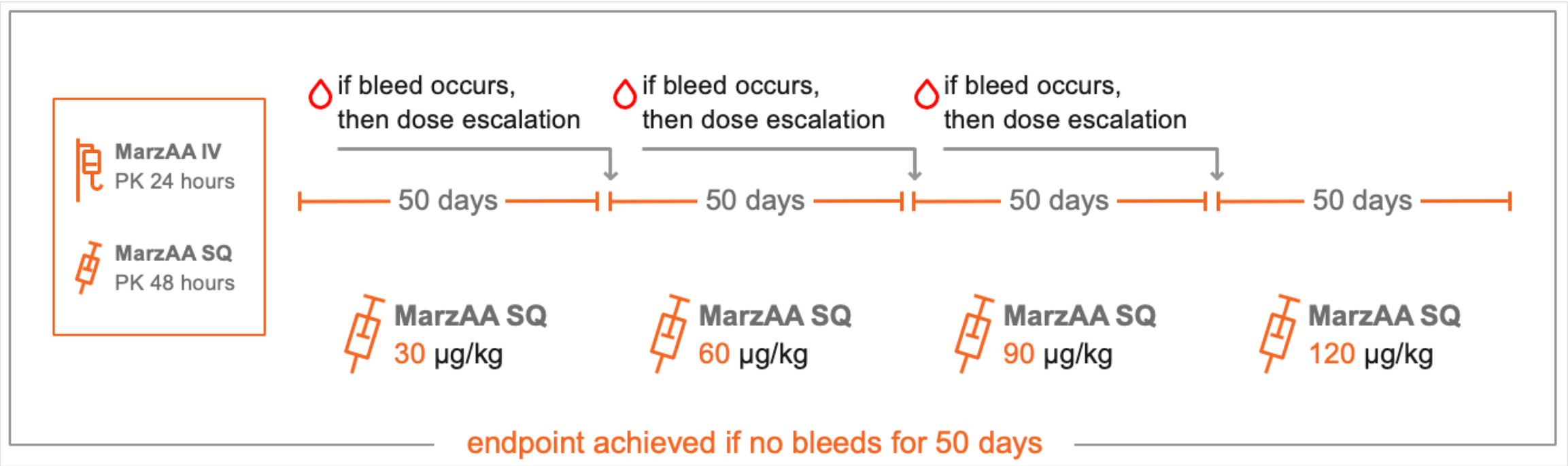
+ Catalytic activity increased
+ 9-fold more potent than NovoSeven RT
+ Allows subcutaneous dosing
+ Half-life prolonged when using subcutaneous dosing

Orphan Drug Designation in US



MarzAA phase 2/3 SQ clinical trial design

+ Individualized dose escalation if needed **+ Enrollment completed**



- Open label SQ study with individual dose escalation if needed
- Hemophilia A or B with inhibitors
- Adult patients with documented annual bleeding rate (ABR) >12
- Primary endpoint: reduction in annualized bleed rate **at final dose level**
- Secondary endpoints: safety and tolerability, no inhibitor formation

Subject demographics & disposition

Nasdaq: CBIO

Subject ID	Age	Highest Inhibitor level BU	Age when inhibitor diagnosed	Hem A or B	Subject Status	ABR	ABR on treatment	Proportion of days with bleeding	Proportion of days with bleeding on treatment
2680101	36	16	15	A	Revoked consent	12.2	n/a	6%	n/a
2680301	18	5	14	A	Complete	26.7	Zero at 60 µg/kg 3.8 overall	18%	Zero at 60 µg/kg 1% overall
2680302	30	2.7	26	A	Fatal unrelated SAE	18.3	n/a	11%	n/a
6430201	29	4.2	27	A	Complete	15.9	Zero	12%	Zero
6430202	35	4.7	35	A	Complete	16.6	Zero	11%	Zero
0510101	43	5.5	39	A	Complete	22.2	Untreated traumatic hematoma Day 4. ABR 7.3	22%	2%
6430203	23	4.5	21	A	Complete	15.2	Zero	4%	Zero
0510104	31	1.7	31	B	Complete	21.2	Zero at 60 µg/kg 3.8 overall	18%	Zero at 60 µg/kg 1.8% overall
6430204	18	56	6	A	Complete	15.9	Treated traumatic hematoma Day 36. ABR 7.3	9%	2%
0510106	47	1.07	40	A	Dosing	20.5	n/a	8%	n/a
6160101	31	27.5	10	A	Dosing	24.3	n/a	9%	n/a

+ Patients can have a very different proportion of days with bleeding despite similar ABR

Subject status to date

Clinical efficacy demonstrated

+ 17 subjects have been consented and 12 enrolled; 3 active subjects; is no longer recruiting
+ ABR: Mean 19.0; Range 12.2-26.7
+ Proportion of days with bleeding: Mean 12.2%; Range 4-22%
+ 7 subjects have completed dosing
  - Clinically significant reduction in ABR
  - 2 subjects had dose escalation to 60 µg/kg
  - 5 subjects had no bleeds (traumatic or spontaneous) at their final dose level
  - Statistically significant reduction in proportion of days with bleeding

MarzAA reduces annualized bleed rate (ABR)

Nasdaq: CBIO

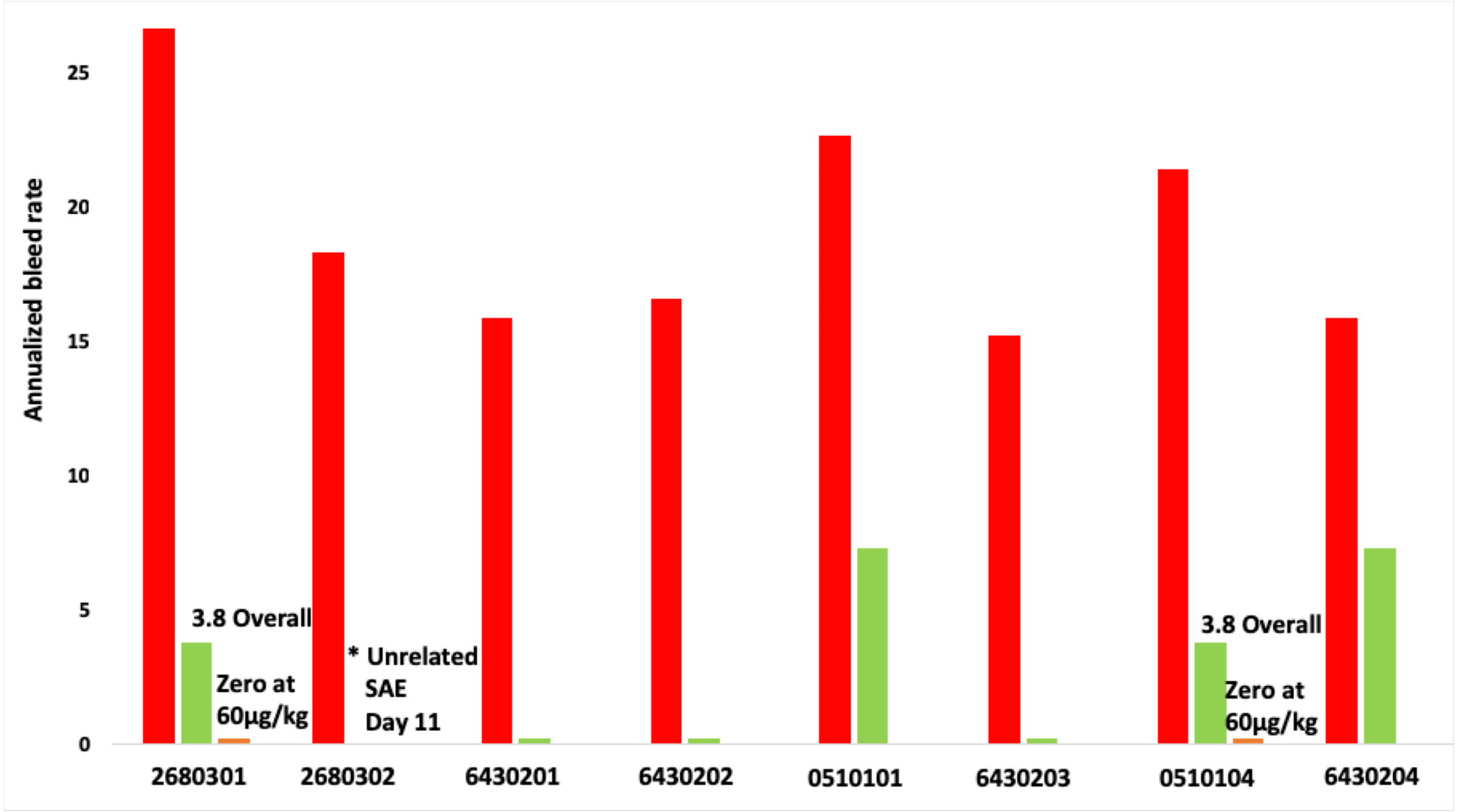
The width of each red bar represents bleed duration: 1 to 9 days

6-month recorded bleeds | **Treatment Period** | **Follow-up Period**

MarzAA 30 µg/kg & 60 µg/kg

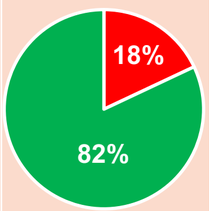
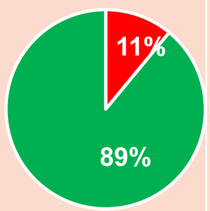
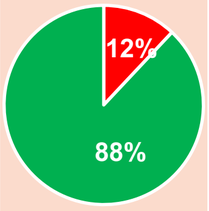
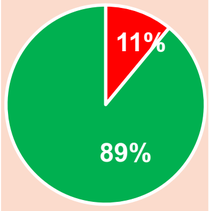
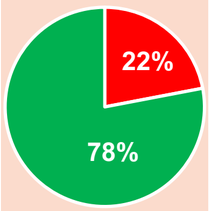
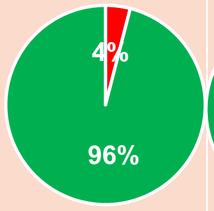
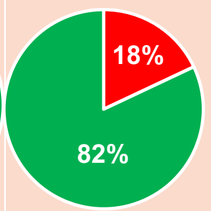
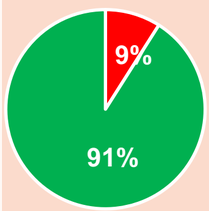
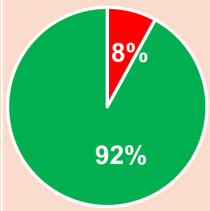
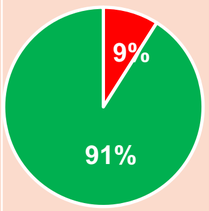
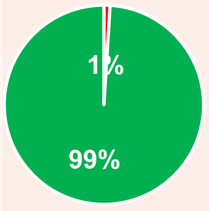
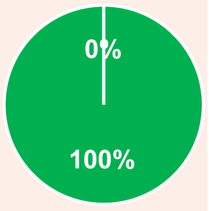
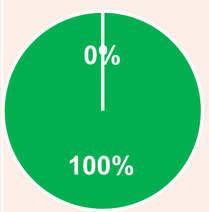
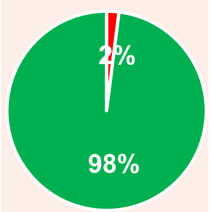
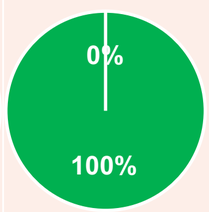
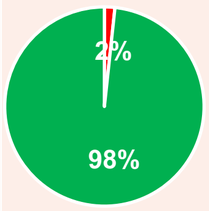
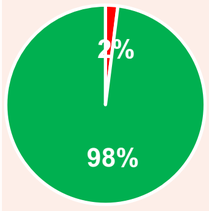
Significant reduction in ABR on-treatment

Nasdaq: CBIO



Pre- and on-treatment proportion of bleeding days efficacy

Nasdaq: CBIO

Subject	2680301	2680302	6430201	6430202	0510101	6430203	0510104	6430204	0510106	6160101	Subject
Pre-treatment											Pre-treatment
On-treatment		Unrelated SAE									On-treatment

Red denotes the proportion of days with bleeding during period of observation

- The average percentage of days of bleeding in the pre-treatment period was 12.2% (SD 5.2%) [median = 11.0%]
- In the treatment period, these percentages were reduced to 1.0% (SD 5.2%) [median 1.0%]
- The analysis of these pairwise differences by a randomization paired t-test yields p=0.016 (and p=0.0001 by Wilcoxon signed-rank test)

Current MAA-201 trial status

High pre-treatment ABRs reduced to a median of zero on treatment

+ 7 subjects have completed dosing with clinically significant reduction in ABR
+ 5 subjects had no bleeds at their final dose level
+ SQ half-life increases to 13.1 hours from an IV half-life 3.9 hours in Part 1
+ No anti-drug antibodies have been detected to date
+ More than 450 SQ injections have been administered
  - 6 injection site reactions in 2 subjects
    - Moderate swelling that resolved without sequelae
    - Mild or moderate redness that resolved without sequelae

Conclusions on the marzeptacog alfa (activated) program

Nasdaq: CBIO

Moving forward in clinical development after clinical proof of concept

Clinical efficacy and tolerability demonstrated

Additional clinical data at ISTH 2019

Pivotal trial guidance obtained from EMA & MHRA and we will confirm with FDA at end-of-phase 2 meeting in late 2019