

# CATALYST BIOSCIENCES

Corporate Overview  
18 June 2020



# Forward looking statements

This presentation includes forward-looking statements that involve substantial risks and uncertainties. All statements included in this presentation, other than statement of historical facts, are forward-looking statements. Examples of such statements include, but are not limited to, potential markets for MarzAA, DalcA and CB 2782-PEG, potential benefits of subcutaneous dosing, potential use of MarzAA as a subcutaneous therapy for patients with hemophilia A or B with inhibitors, treatment of bleeding, Factor VII deficiency, Glanzmann's Thrombasthenia and other bleeding disorders, potential use of DalcA as a subcutaneous therapy for patients with hemophilia B, potential benefits of CB 2679d-GT as gene therapy, the use of engineered proteases to treat diseases, including dAMD, by mediating the complement cascade, clinical trial results, plans for a registrational trial for MarzAA and a Phase 1/2 trial in Factor VII deficiency, Glanzmann's Thrombasthenia and treatment of bleeding in Hemlibra subjects in Q4 2020, plans to declare development candidates for CB 2679d-GT and in the complement program in Q4 2020, and potential milestone and royalty payments from Biogen. Actual results or events could differ materially from the plans, expectations and projections disclosed in these forward-looking statements.

Various important factors could cause actual results or events to differ materially, including, but not limited to, the risk that the risk that trials and studies may be delayed as a result of the COVID-19 virus and other factors, that trials may not have satisfactory outcomes, that potential adverse effects may arise from the testing or use of MarzAA or DalcA, including the generation of antibodies, which has been observed in patients treated with DalcA, that clinical trials will take longer than anticipated to be completed, that costs required to develop or manufacture the Company's products will be higher than anticipated, that Biogen will discontinue development of CB 2782-PEG, competition and other factors that affect our ability to establish collaborations on commercially reasonable terms and other risks described in the "Risk Factors" section of the Company's annual report on Form 10-K filed with the Securities and Exchange Commission on February 20, 2020, and the Company's quarterly report on Form 10-Q filed on May 11, 2020, and in other filings with the Securities and Exchange Commission. The Company does not assume any obligation to update any forward-looking statements, except as required by law.

## Essential Medicines – Superior Outcomes

### Late-Stage Asset

SQ Marzeptacog alfa  
(activated)  
MarzAA (FVIIa)

**Phase 3 in 2020**

### Hemophilia

SQ MarzAA (FVIIa)

SQ Dalcinonacog  
alfa – DalcA (FIX)

Factor IX Gene Therapy

Factor Xa

### Complement

IVT Anti-C3 Dry AMD  
CB 2782-PEG



SQ Systemic  
Complement  
Inhibitors

Protease Engineering Platform

# Pipeline

## Hemostasis

**SQ Marzeptacog alfa "MarzAA" – (rFVIIa)**

Hemophilia A or B w Inhibitors – ToB

FVIID/Glanzmann/Hemlibra – ToB

**SQ Dalcinonacog alfa "DalcA"**

Hemophilia B (rFIX)

**FIX-Gene Therapy**

Hemophilia B (CB 2679d-GT)

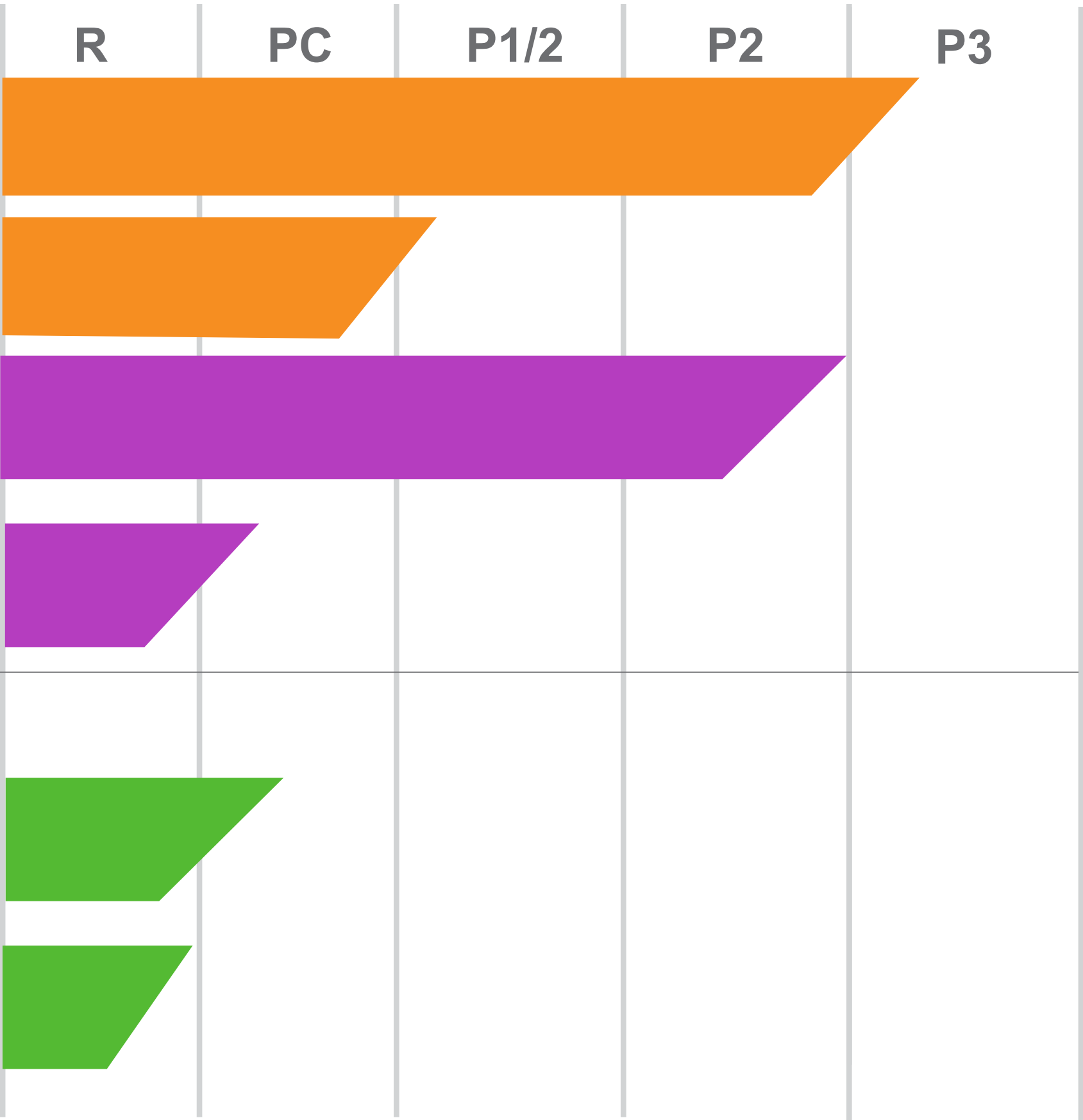
## Complement

**IVT CB 2782-PEG**

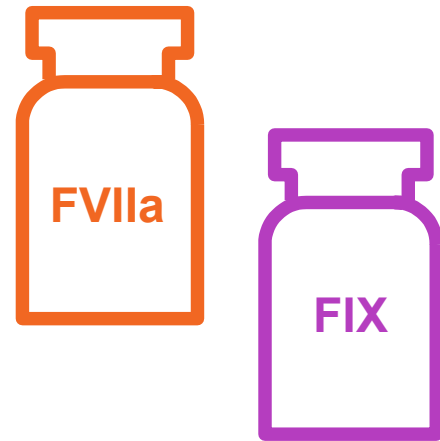
anti-C3 protease for Dry AMD



**SQ Systemic complement inhibitors – CB DC**



# Investment highlights



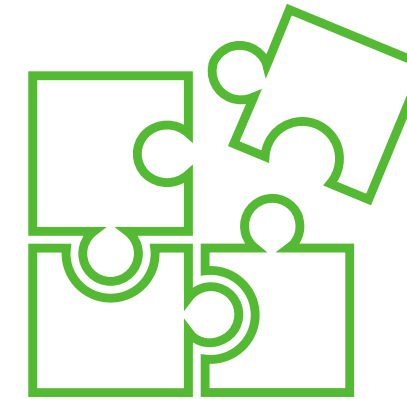
Novel subcutaneous factors with orphan drug designation, **MarzAA** & **DalcA** – P2 efficacy in prophylaxis studies complete



Multibillion-dollar market opportunities



Strong balance sheet, \$104.5 M cash – Q1



**Anti-C3 Dry AMD** with Biogen

**SQ systemic complement regulator** research program



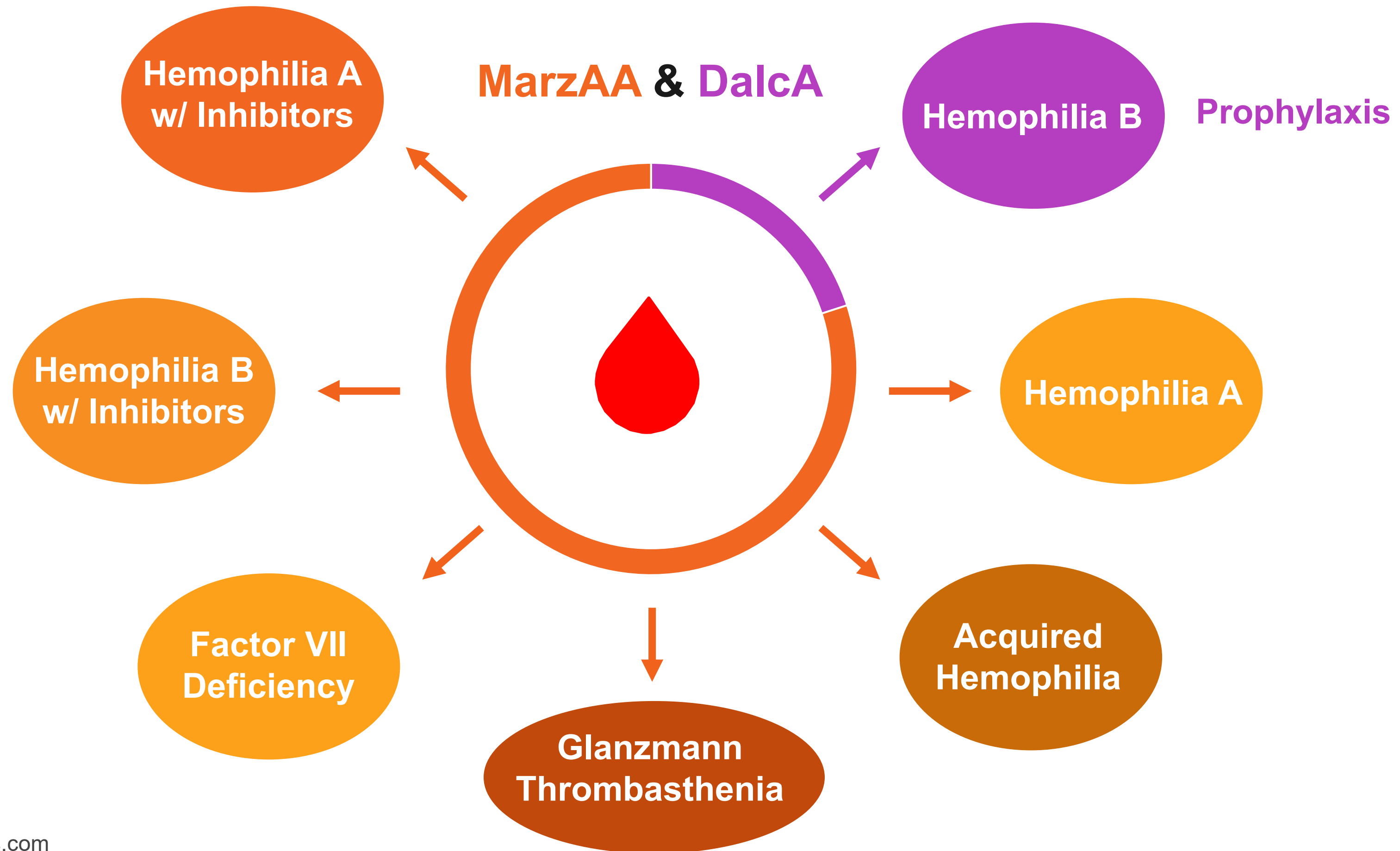
Experienced team



177 worldwide patents  
CBIO retains full ownership of all compounds

# Addressing unmet needs in orphan bleeding disorders

**SQ treatment of episodic bleeding and prophylaxis – \$4B+ market**





# The Catalyst Biosciences subcutaneous solution



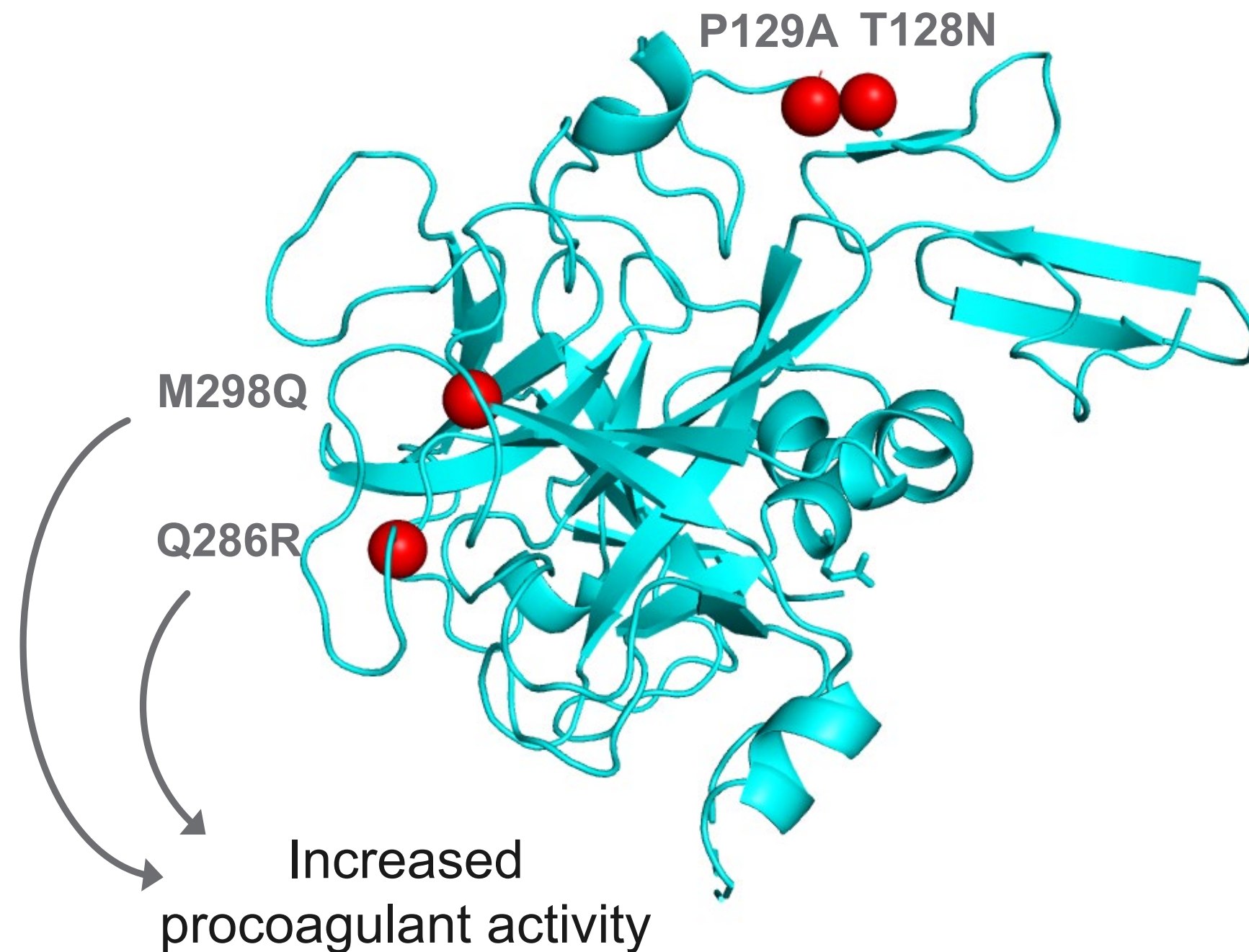
## Our highly potent candidates

- + Quick & simple self-administered SQ injection
- + SQ dosing is the future in hemophilia, other rare hematology indications & complement mediated diseases
- + Significantly increases half-life
- + Much higher & more stable factor levels for prophylaxis
- + Enables SQ treatment of bleeds
- + Ideal for children and adolescents



# Marzeptacog alfa (activated): MarzAA rFVIIa

**Addresses a clear unmet need in hemophilia & other bleeding disorders**



## Four amino acid substitutions

- + Multiple advantages over NovoSeven RT
- + 9-fold higher activity vs NovoSeven RT
- + Potency allows for SQ dosing

## Only SQ bypass agent for on demand treatment

- + Simple, small volume SQ administration
- + Improved bioavailability & prolonged half-life

## Orphan Drug Designation in US and EU

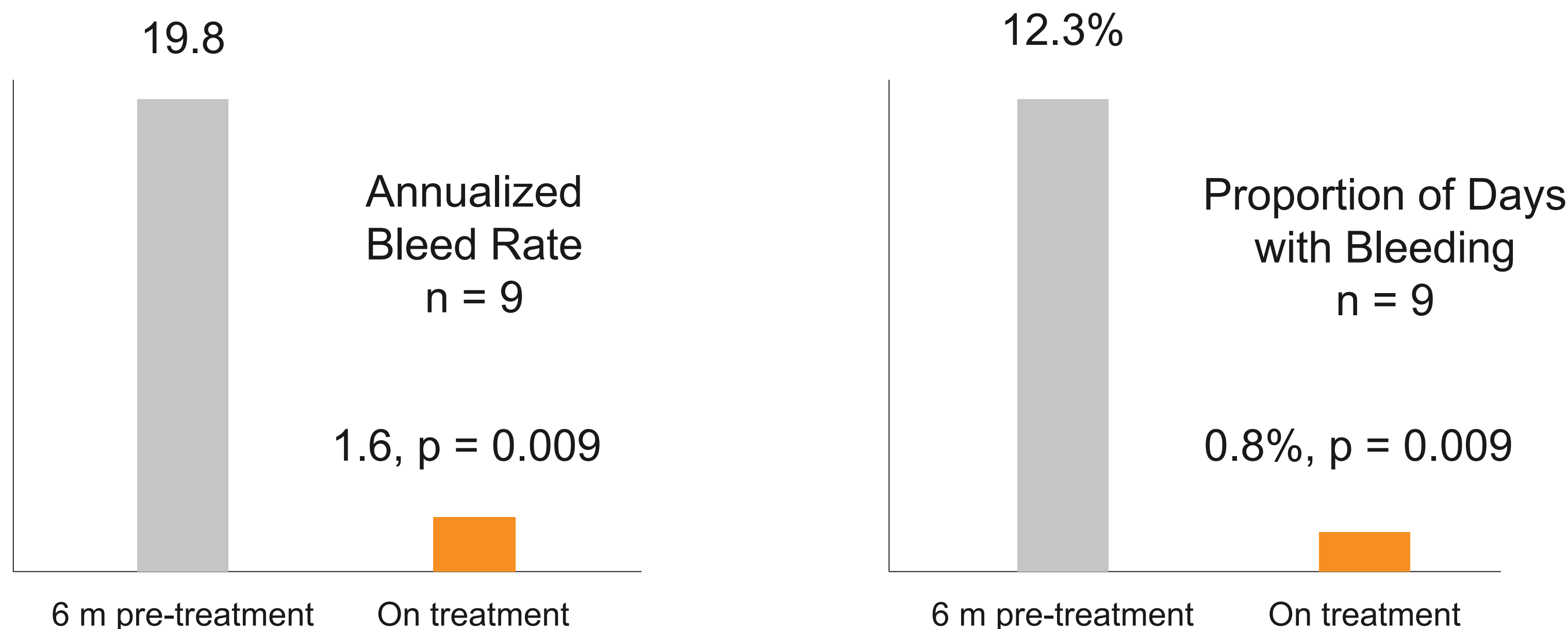


# MarzAA Phase 2 demonstrates efficacy in prophylaxis

Greater than 90% reduction in all bleeding – Median ABR = 0

7 of 9 subjects had no bleeding at final dose level

Safe & well tolerated, ~1% ISR (6/517 doses) & no ADA



# In a world of SQ prophylaxis

## Patients & KOLs want SQ treatment of a bleed

Individuals on Hemlibra® have breakthrough bleeds

NovoSeven® is safe but is administered IV

FEIBA should not be used with Hemlibra and is given IV

## MarzAA has optimal properties

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- ✓ Fast & easy to administer
- ✓ Achieves therapeutic levels rapidly
- ✓ Stops bleeding in multiple preclinical models
- ✓ Can be combined with Hemlibra *in vitro* without increased thrombogenicity

# MarzAA P3: On demand treatment of episodic bleeding

## CRIMSON-1 Registration Study – A Global Clinical Trial

### Phase 1 & 2 trials demonstrated the clinical impact of SQ MarzAA

- MAA-102 rapidly achieved target activity levels
- MAA-201 demonstrated efficacy in prophylaxis, safe & well tolerated with no ADA
- Clinically support P3 SQ MarzAA treatment of episodic bleeding

### Open label trial evaluating the safety & efficacy of SQ MarzAA in episodic bleeding

- Primary endpoint: Hemostatic efficacy using a standard 4-point assessment scale
- ~230 bleeding episodes to be treated in ~75 HA/HB individuals with inhibitors
- Anticipate first patient enrolled by end of 2020

### Opportunity in multiple bleeding disorders

- ✓ Hemophilia A or B with inhibitors
- ✓ Hemlibra breakthrough bleeds
- ✓ Factor VII deficiency
- ✓ Glanzmann thrombasthenia
- Acquired hemophilia



# MarzAA development plan in 2020

**Phase 3 HA/HB w Inhibitors – ToB**

**Phase 1/2 study in FVIID, Glanzmann & Hemlibra ToB**

Large commercial opportunity across multiple rare bleeding disorders

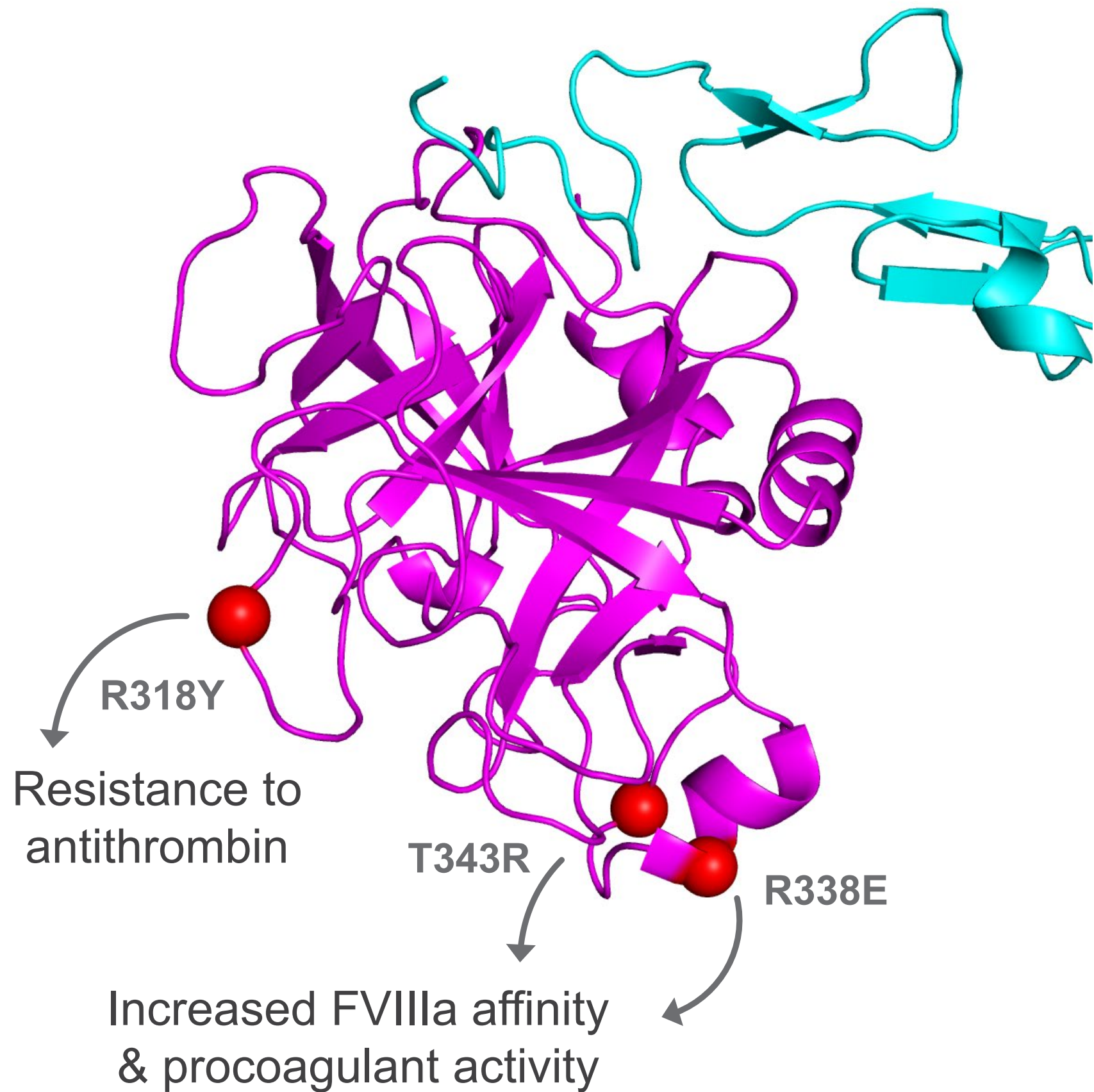
Phase 1 PK/PD data support on demand as well as prophylactic treatment of bleeding

Phase 2 demonstrated clinical efficacy & tolerability for prophylaxis indications

Efficacy demonstrated for SQ on-demand treatment of bleeding in pre-clinical models

MarzAA can be safely combined with Hemlibra in human plasma *in vitro*

# Dalcinonacog alfa: novel FIX replacement for SQ delivery



## Three amino acid substitutions

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

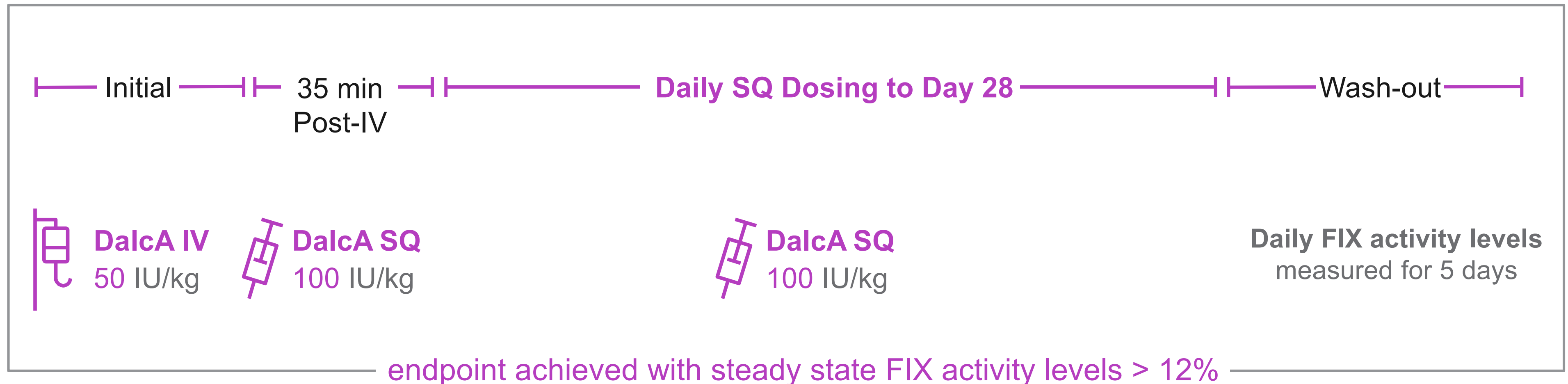
## Differentiated from marketed IV FIXs

- + Simple, small volume SQ administration
- + Enhanced pharmacokinetics with prolonged half-life
- + Excellent extravascular distribution
- + Potential to maintain continuous protective levels

## Orphan Drug Designation in US & EU

# Dalcinonacog alfa phase 2b SQ clinical trial

## Trial completed

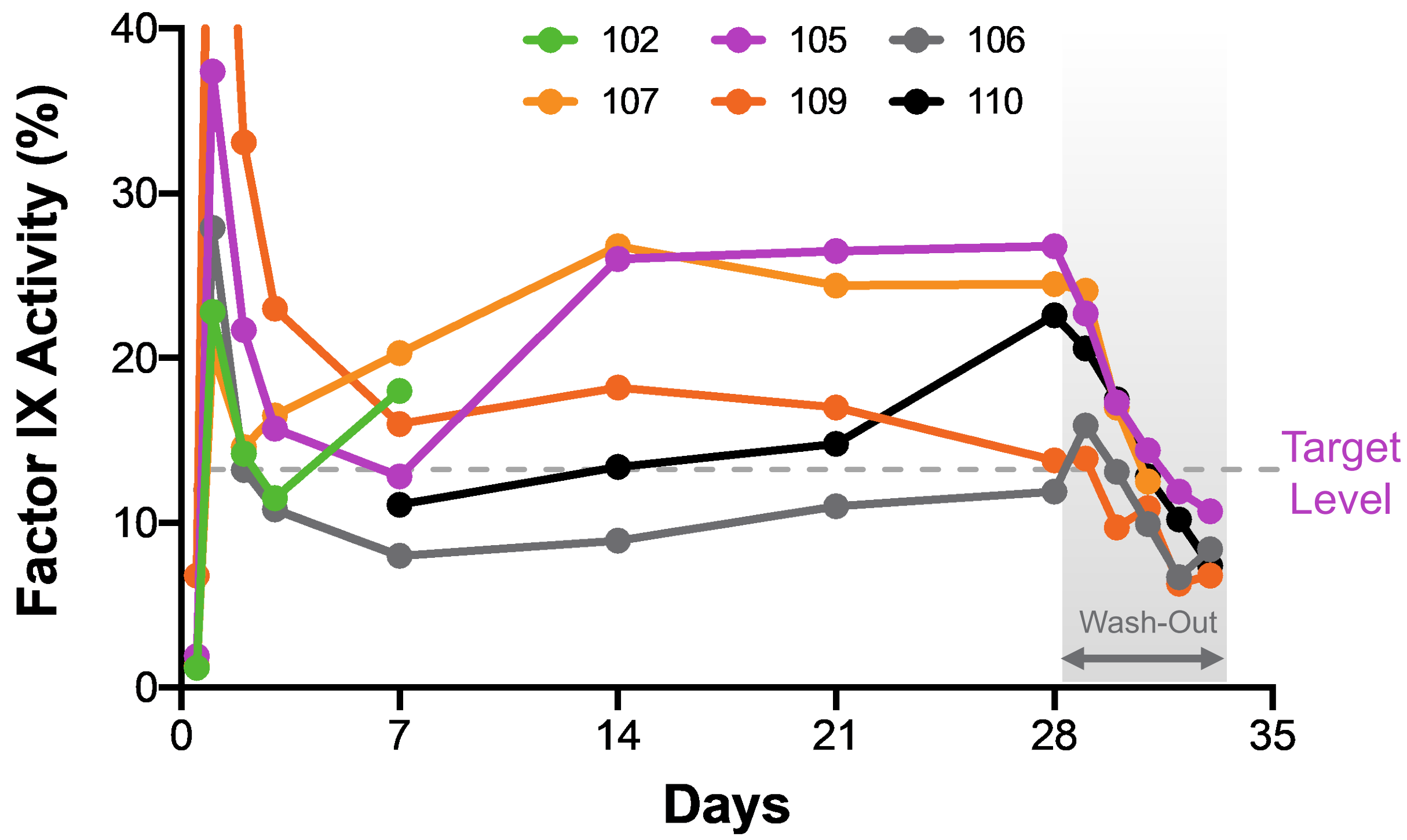


- + Primary endpoint: **Steady state FIX activity** level above 12% with daily dosing
- + Secondary endpoints: **safety including weekly ADA testing**, pharmacokinetics, pharmacodynamics, bleeding events
- + 6 severe Hemophilia B subjects dosed
- + Rare propeptide mutation excluded
- + HLA profile associated with nAb risk was excluded



# DalcA P2b efficacy & safety demonstrated

Target levels >12% achieved with 100 IU/kg dosing for 28 Days



- + Dosed 6 severe HB subjects
  - 102 withdrew on Day 7
- + **Steady state FIX levels up to 27%** achieved after 14 days
- + **No breakthrough bleeds**
- + **No neutralizing ADAs**
- + Consistent PK profiles
- + Terminal half-life is 2.5 - 5.1 days

## Potential to provide effective SQ prophylaxis for individuals with Hemophilia B

Phase 2b trial complete

Excellent protective therapeutic FIX activity levels achieved

No bleeding events during treatment demonstrates effective prophylaxis

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

Mild to moderate ISR primarily with initial injections – transient & self-limiting

Long half-life – demonstrates potential to lower dose / reduce dosing frequency

# FIX gene therapy: CB 2679d-GT for hemophilia B

## CB 2679d-GT in combination with a novel chimeric AAV capsid provides significant improvements

- + Stable **high activity levels** in a mouse hemophilia B model – **no nAb**
- + Vector dose **reduced 10-fold** compared to current constructs
- + Potential for an improved efficacy & safety profile
- + AAV license and sponsored research agreement with Stanford University School of Medicine



## Superior preclinical efficacy of CB 2679d-GT vs Padua

- + 4 to 5-fold reduction in bleeding time
- + Activity levels elevated throughout the study - **no nAb**

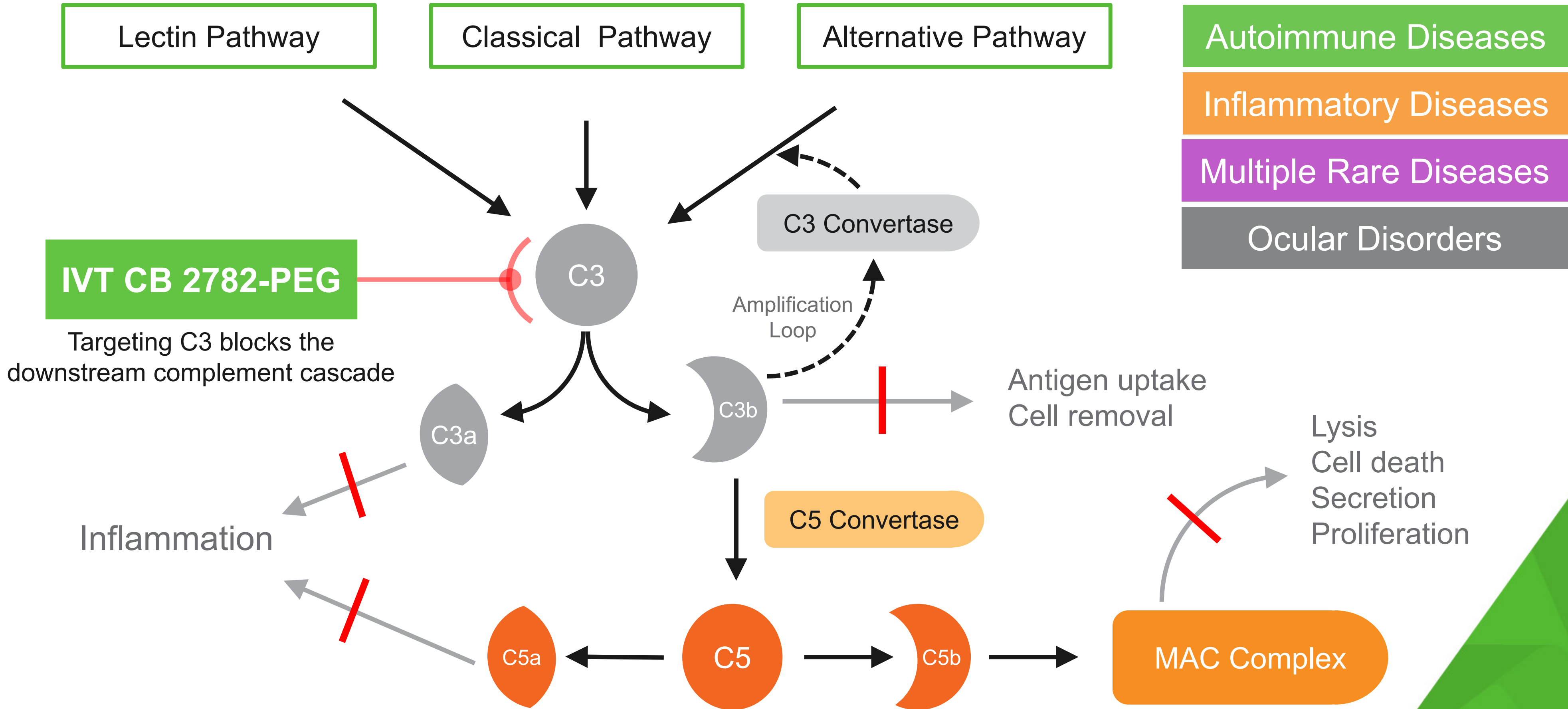
## Wholly-owned & issued patents covering gene therapy

| FIX Transgene | AAV Capsid     | Study Dose (vg/kg)   | FIX Activity (U/mL) |
|---------------|----------------|----------------------|---------------------|
| CB 2679d-GT   | Novel Chimeric | 8.0x10 <sup>10</sup> | 20                  |
| Padua         | TAK-748*       | 7.4x10 <sup>11</sup> | 20                  |
| Padua         | TAK-748*       | 7.4x10 <sup>10</sup> | 1                   |

\*Weiller *et al.* (2019) *Blood* Vol. 134, Supplement S1 P4633

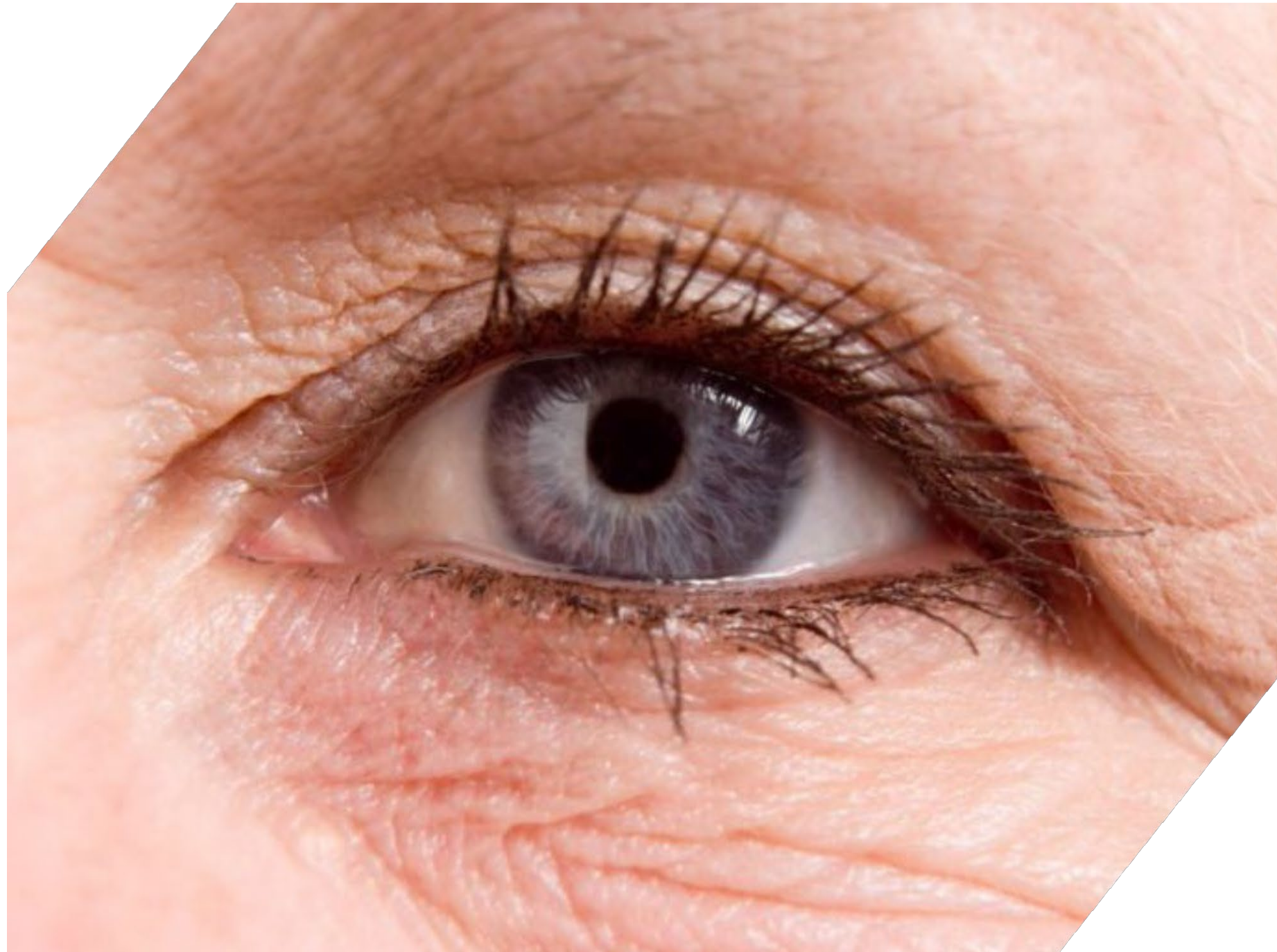


# Complement cascade is regulated by proteases



# CB 2782-PEG: Complement factor 3 (C3) cleaving protease

## Geographic Atrophy in Dry AMD can result in blindness



- + Geographic atrophy is an advanced stage of dry age-related macular degeneration (dAMD)
- + Dry AMD affects ~1M people in the US and over 5M worldwide
- + Global market estimated at >\$5B
- + C3 is the only clinically (randomized P2) validated target for the treatment of dAMD
- + No currently approved drugs

Sources: National Eye Institute. Facts About Age-Related Macular Degeneration, Tufail 2015, The Eye Diseases Prevalence Research Group 2004, GlobalData

# CB 2782-PEG long acting anti-C3 protease

## Best-in-class anti-C3 profile for dry AMD

- + Generated from Catalyst's proprietary **protease engineering platform**
- + Potent, selective and long acting anti-C3 protease that degrades C3 into inactive fragments
- + Preclinical NHP PK & PD data\* predict **best-in-class** human intravitreal dosing three or four times a year

## Biogen Collaboration

- + Announced December 19, 2019
- + \$15M upfront, up to \$340M in milestones and tiered royalties up to low double digits
- + Catalyst to perform fully funded pre-clinical and manufacturing activities
- + Biogen responsible for IND-enabling activities, worldwide clinical development & commercialization

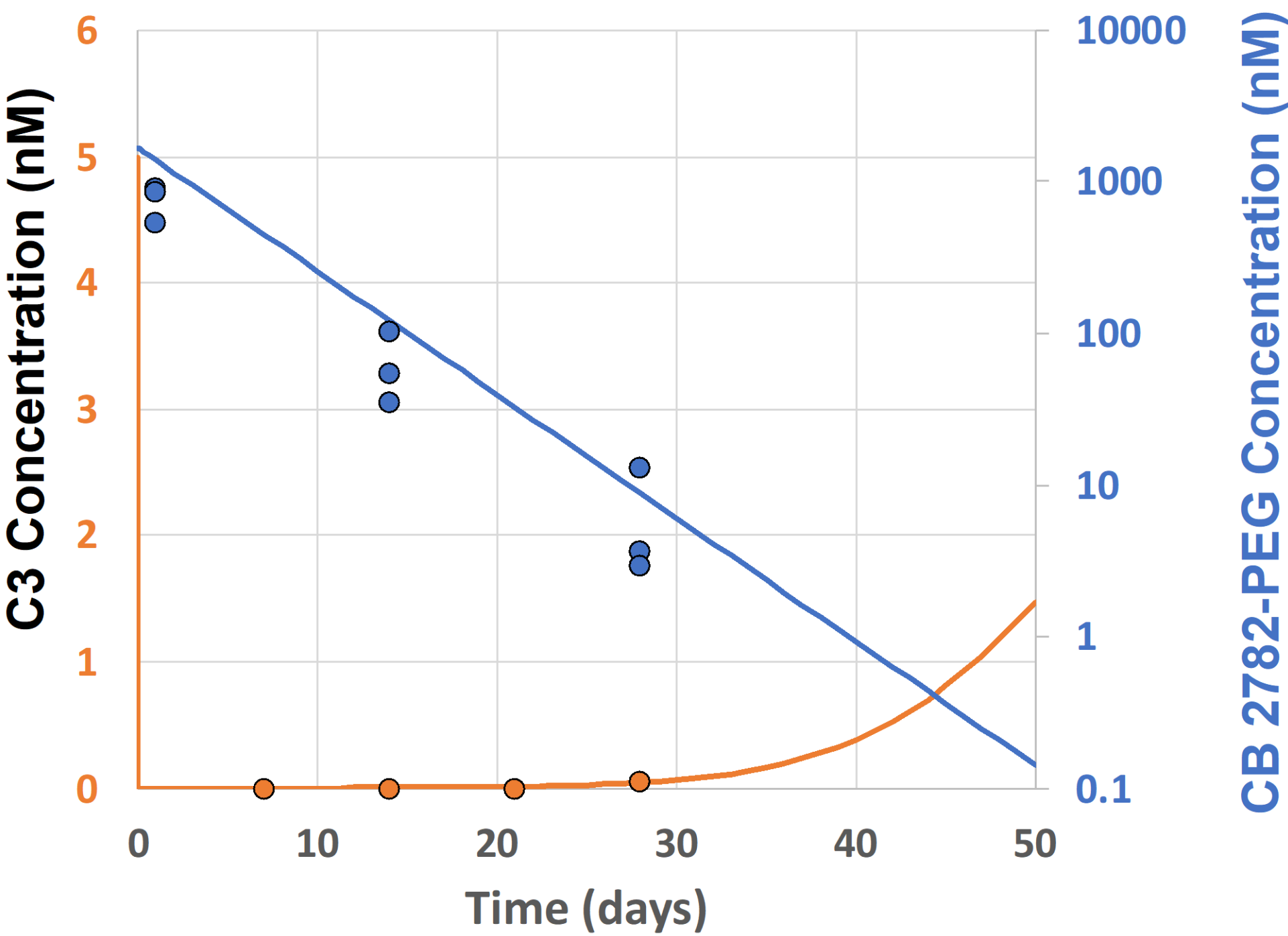




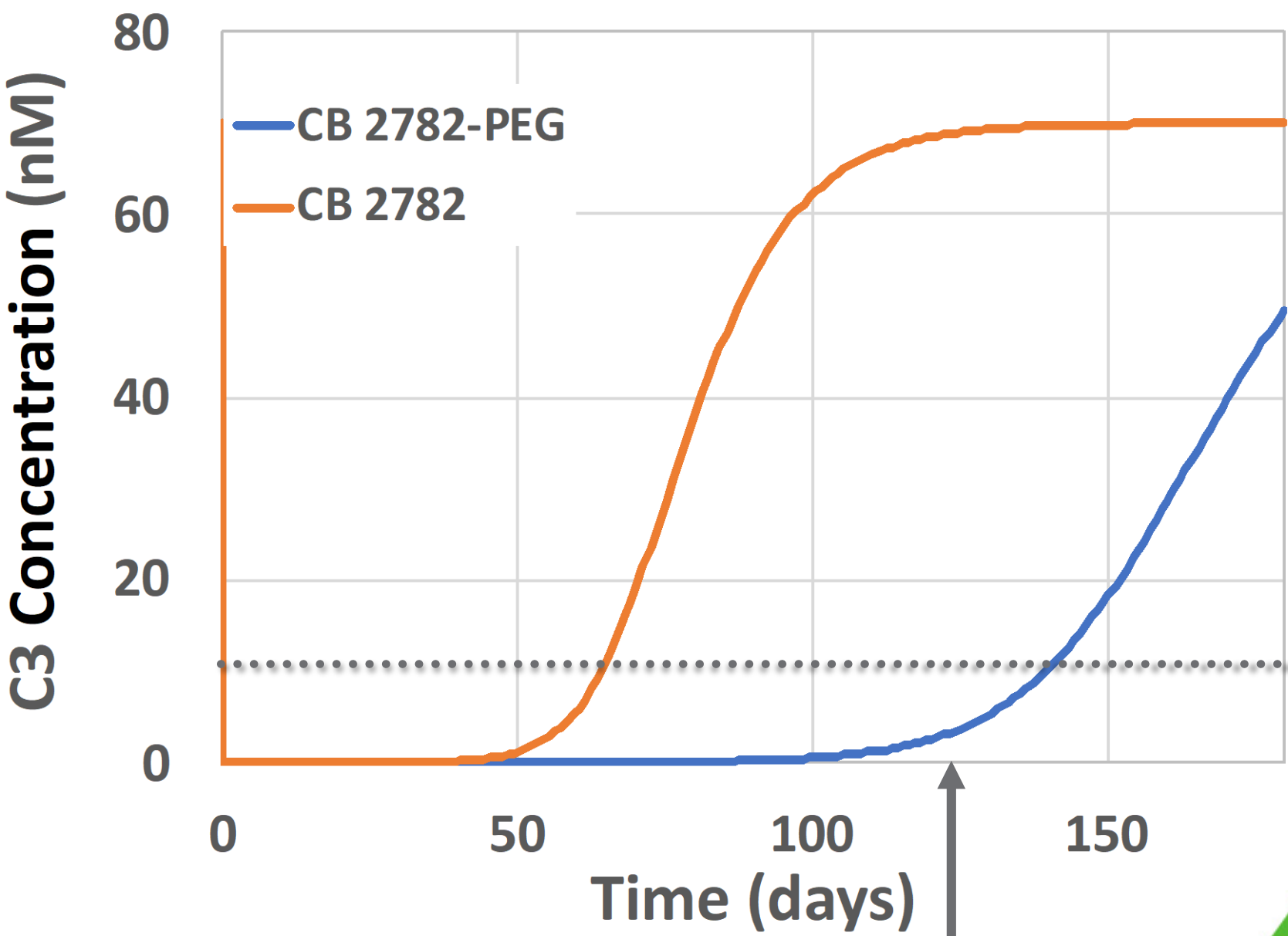
# CB 2782-PEG long acting anti-C3 protease

Best-in-class anti-C3 profile for dry AMD with dosing every 3 to 4 months

Non-Human Primates



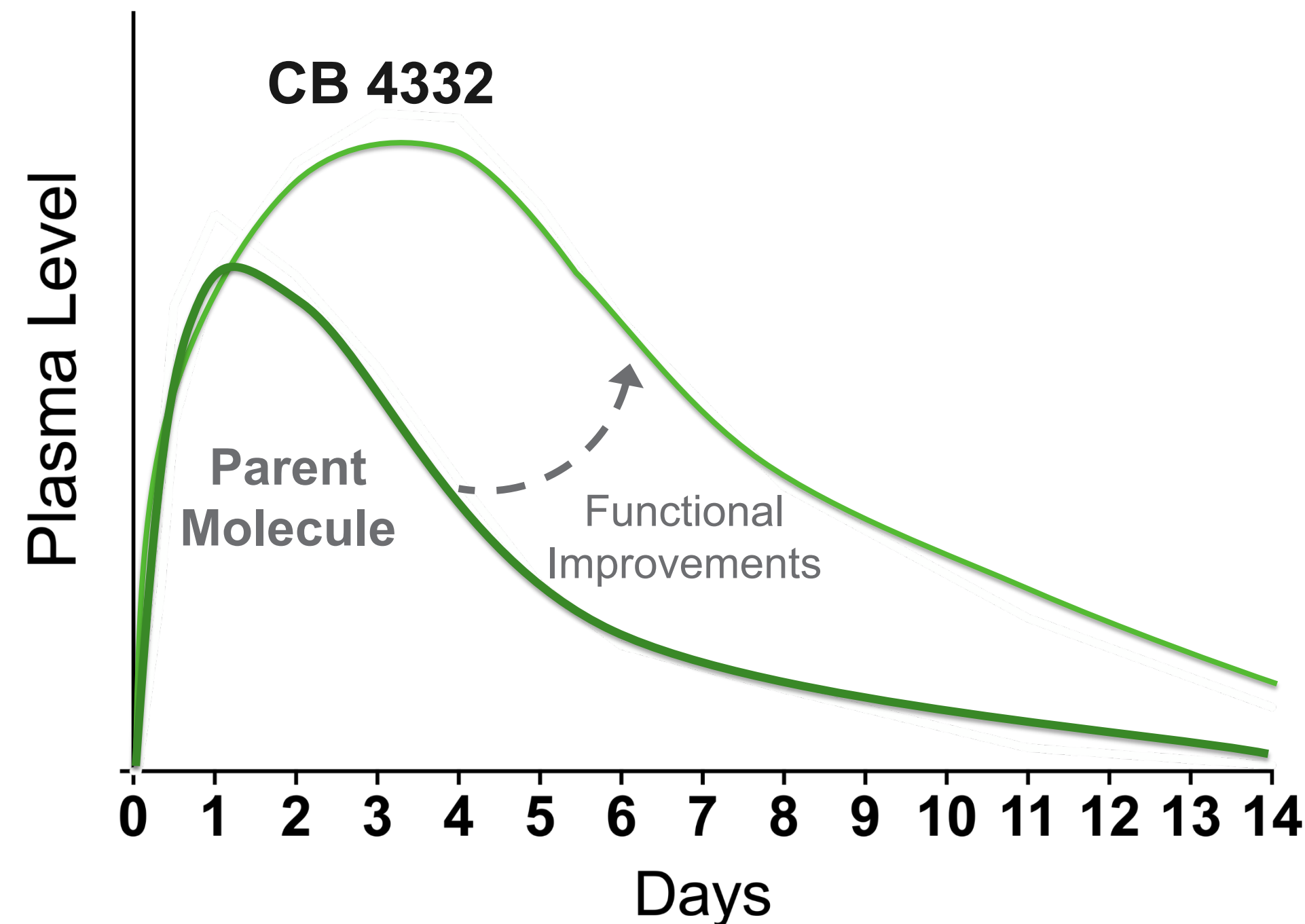
Human Modeling



Predicted >90% elimination of C3 at 4 months

# CB 4332 SQ long-acting systemic complement regulator







Non-human primate PK supports weekly SQ dosing in humans



## Expanding the complement portfolio

- + Leverages Catalyst's proprietary **protease engineering platform**
- + Designed for **SQ administration & improved bioavailability**
- + **Simple & efficient** production process

# Milestones – 2020

|  | Q1   | Q2  | Q3  | Q4   |
|--|--|---|---|--|
| <b>MarzAA</b><br>(FVIIa)                 | <b>EoP2</b><br>             | <b>ToB PK/PD</b><br> | <ul style="list-style-type: none"> <li>• MAA-102 data</li> <li>• Population PK</li> </ul> | <ul style="list-style-type: none"> <li>• Initiate pivotal P3</li> <li>• Initiate P1/2 in FVII Deficiency, Glanzmann Thrombasthenia, and Hemlibra patients</li> </ul> |
| <b>DalcA</b><br>(FIX)                    | <b>Interim P2b</b><br>      | <b>Final P2b</b><br> |   |  |
| <b>CB 2679d-GT</b><br>(FIX Gene Therapy) | <b>NextGen Vector</b><br> | <ul style="list-style-type: none"> <li>• NHP Efficacy</li> </ul>  |   | <ul style="list-style-type: none"> <li>• Development Candidate</li> </ul>  |
| <b>CB 2782-PEG</b><br>(dAMD)             |  |                    |   |  |
| <b>CB DC</b><br>(Systemic complement)    |  |   |   | <ul style="list-style-type: none"> <li>• Development Candidate</li> </ul>  |

# Team

## President & CEO

**Nassim Usman, Ph.D.**



26 years  
in biotech

## Chief Medical Officer

**Howard Levy, M.B.B.Ch., Ph.D., M.M.M.**



18 years  
in hematology

## Chief Financial Officer

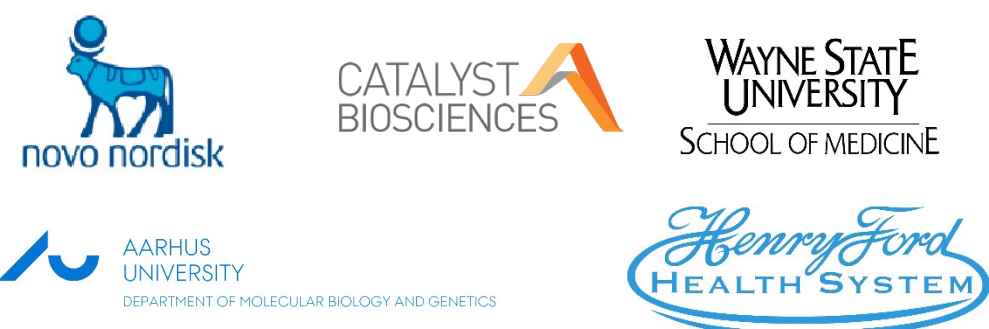
**Clinton Musil, M.B.A**



16 years  
in biotech &  
i-banking

## SVP, Translational Research

**Grant Blouse, Ph.D.**



13 years  
in biotech

## SVP, Business Development

**Jeffrey Landau, M.B.A.**



18 years  
in biotech

## SVP, Technical Operations

**Andrew Hetherington, M.B.A.**



20 years  
in biotech



## Disruptive approach to billion-dollar markets – protease engineering platform

- ✓ **FVIIa: SQ MarzAA ~\$2.2B market**
  - + P1 PK/PD & preclinical data supports ToB
  - + P2 efficacy & safety demonstrated
  - + P3 patient enrollment in Q4 2020
- ✓ **FIX: SQ DalcA >\$1.8B market**
  - + Phase 2b efficacy & safety demonstrated
  - + Potential for less frequent dosing
- ✓ **FIX Gene Therapy: CB 2679d-GT**
  - + Proprietary preclinical gene therapy asset with superior activity vs current clinical constructs
- ✓ **Anti-C3 dAMD: IVT CB 2782-PEG >\$5B market**
  - + Biogen collaboration
  - + \$15M upfront, up to \$340M in milestones, up to low double digits tiered royalties
- ✓ **SQ systemic complement inhibitor program**
  - + Large \$B+ rare-disease opportunity
  - + Multiple indications & applications
  - + 1<sup>st</sup> Development Candidate in Q4 2020
- ✓ **Well capitalized**
  - + Cash runway into 2022

# THANK YOU

Nasdaq: CBIO

[catalystbiosciences.com](http://catalystbiosciences.com)



# MarzAA is only bypass agent for **both** SQ prophylaxis and SQ treatment of bleeds

**Attractive commercial profile targeting an existing \$2.2B bypass agent market**

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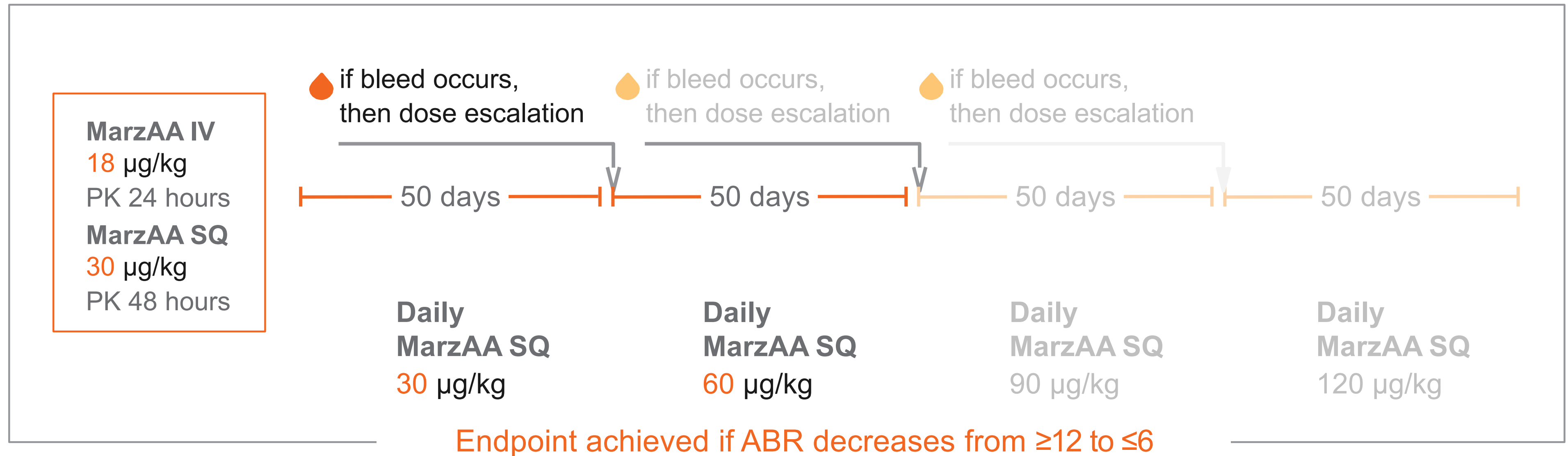
IV NovoSeven (\$1.2B 2019 sales) validates rFVIIa in multiple rare bleeding disorders

- + Hemophilia A or B with inhibitors
- + Severe Factor VII Deficiency
- + Glanzmann Thrombasthenia
- + Acquired Hemophilia A

**SQ MarzAA has a superior profile to IV NovoSeven – over 100 clinicians & 175 patients surveyed**

- + Physicians & patients overwhelmingly prefer SQ MarzAA over IV NovoSeven
- + **SQ MarzAA** can create & expand multiple episodic bleed & prophylaxis markets

# MarzAA phase 2/3 SQ clinical trial MAA-201

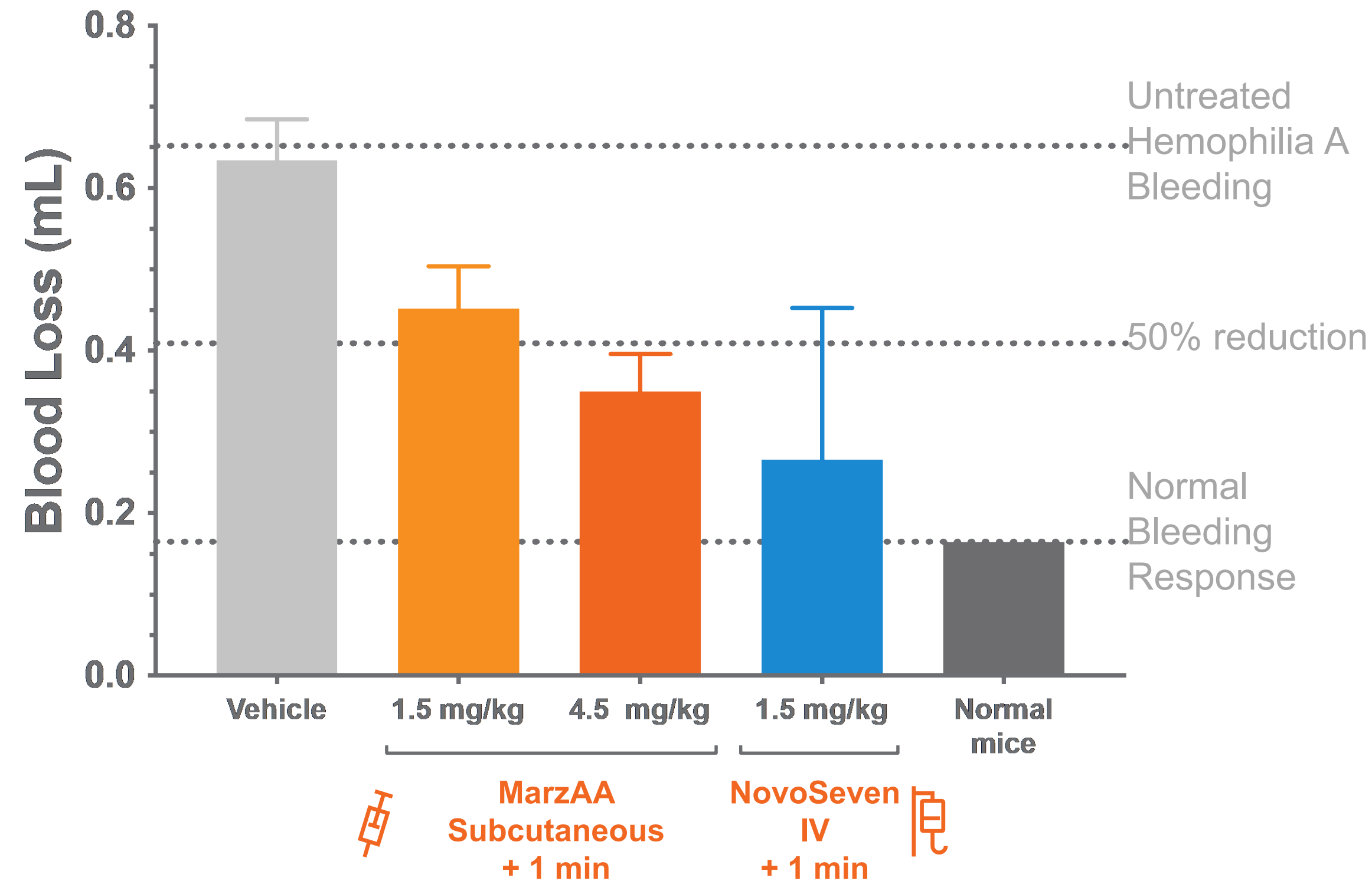


- + Patients with documented annual bleeding rate (ABR)  $> 12$
- + Open label SQ study with individual dose escalation if needed in Hemophilia A or B with inhibitors
- + Primary endpoint: reduction in annualized bleed rate **at final dose level**
- + Secondary endpoints: safety and tolerability, inhibitor formation



# SQ MarzAA reduces bleeding when dosed *After* the Injury

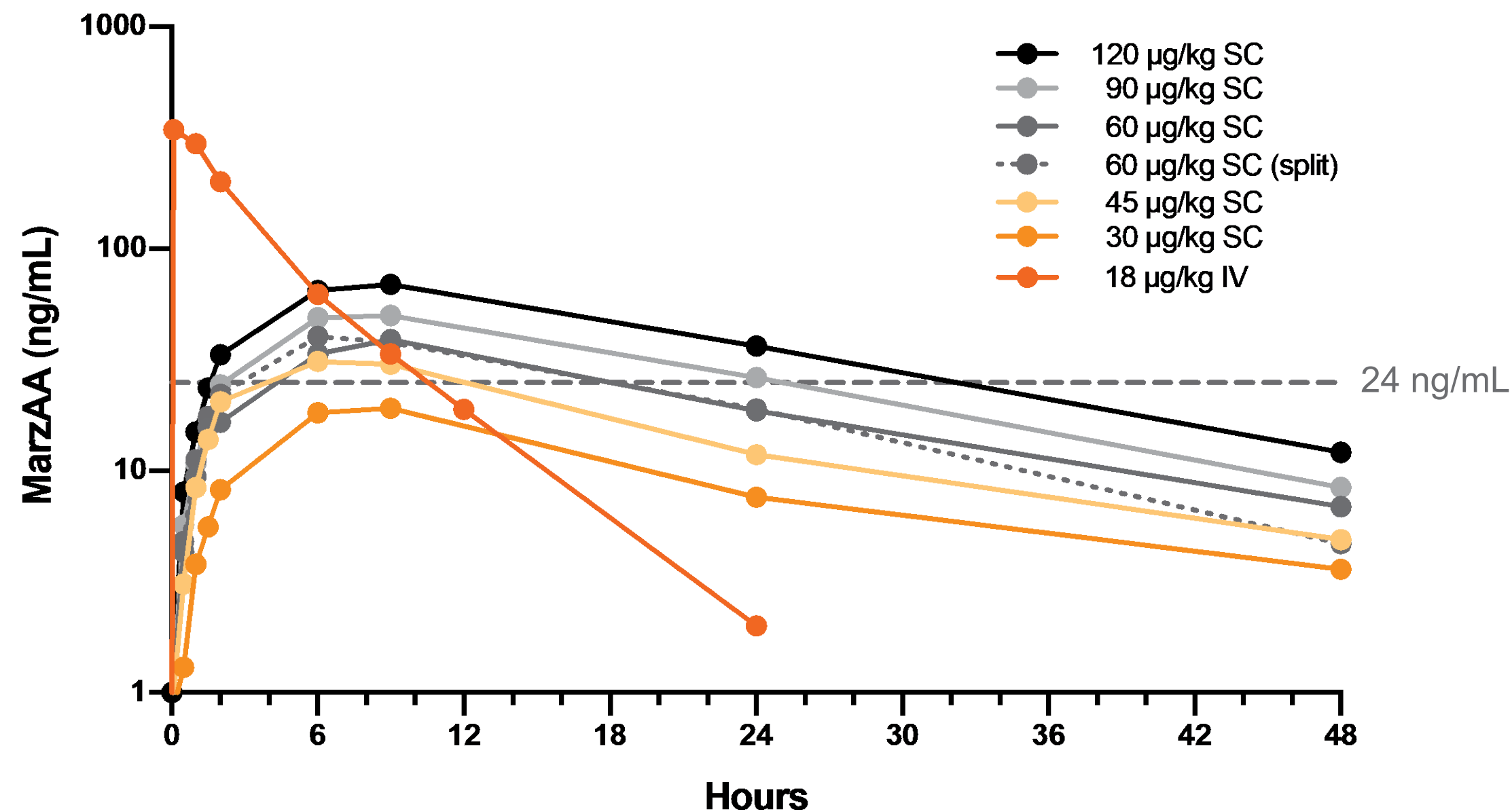
## Acute mouse injury model with dosing *after* the injury



## Reduced bleeding *After* Injury

- + Hemophilic mice bleed **considerably more** than normal mice
- + **SQ treatment** of MarzAA one min after traumatic bleeding has started significantly **reduces blood loss** and **stops the bleed**
- + The effect is **dose dependent**
- + Reduction in blood loss **is comparable with IV NovoSeven**

# MAA-102: PK MarzAA levels support SQ treatment of a bleed Nasdaq: CBIO



- + Target of 24-120 ng/mL to treat a bleed is based on continuous infusion levels of NovoSeven for surgery
- + Target levels are rapidly achieved
- + 25% and 50% of  $C_{max}$  at 1 and 2 hours, respectively
- + Dose-proportional increases in  $C_{max}$  and AUC
- + Target levels can be maintained for 18 hours with a single SQ dose of 60 µg/kg
- + No ADA
- + Multiple dosing cohorts completed
  - 60 µg/kg 3-hourly; twice and thrice