

Nasdaq: CBIO

# CATALYST BIOSCIENCES

**Corporate Overview**

17 September 2020

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# 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. Forward-looking statements include statements about the potential benefits of products based on Catalyst's engineered protease platform; potential markets for and advantages of MarzAA and DalcA; plans in Q4 2020 to enroll a pivotal Phase 3 registration study of MarzAA, initiate a Phase 1/2 trial in FVII Deficiency, Glanzmann Thrombasthenia, and patients treated with Hemlibra and initiate a pivotal non-human primate study of CB 2679d-GT; the potential for MarzAA and DalcA to effectively and therapeutically treat hemophilia subcutaneously; potential markets for our anticomplement and gene therapy programs; potential payments from Biogen; plans to declare a development candidate in our systemic complement program in Q4 2020; the superiority of CB 2679d-GT over other gene therapy candidates; and the Company's collaboration with Biogen for the development and commercialization of pegylated CB 2782 for the potential treatment of geographic atrophy-associated dry age-related macular degeneration (AMD). Actual results or events could differ materially from the plans, intentions, expectations and projections disclosed in the forward-looking statements.

Various important factors could cause actual results or events to differ materially, including, but not limited to, the risk that trials and studies may be delayed as a result of the novel coronavirus (COVID-19) outbreak and other factors, that trials may not have satisfactory outcomes, that additional human trials will not replicate the results from earlier trials, that potential adverse effects may arise from the testing or use of DalcA or MarzAA, including the generation of neutralizing antibodies, which has been observed in patients treated with DalcA, the risk that costs required to develop or manufacture the Company's products will be higher than anticipated, including as a result of delays in development and manufacturing resulting from COVID-19 and other factors, the risk that Biogen will terminate Catalyst's agreement, competition and other risks described in the "Risk Factors" section of the Company's quarterly report filed with the Securities and Exchange Commission on August 6, 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.



## Protease engineering platform

### 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



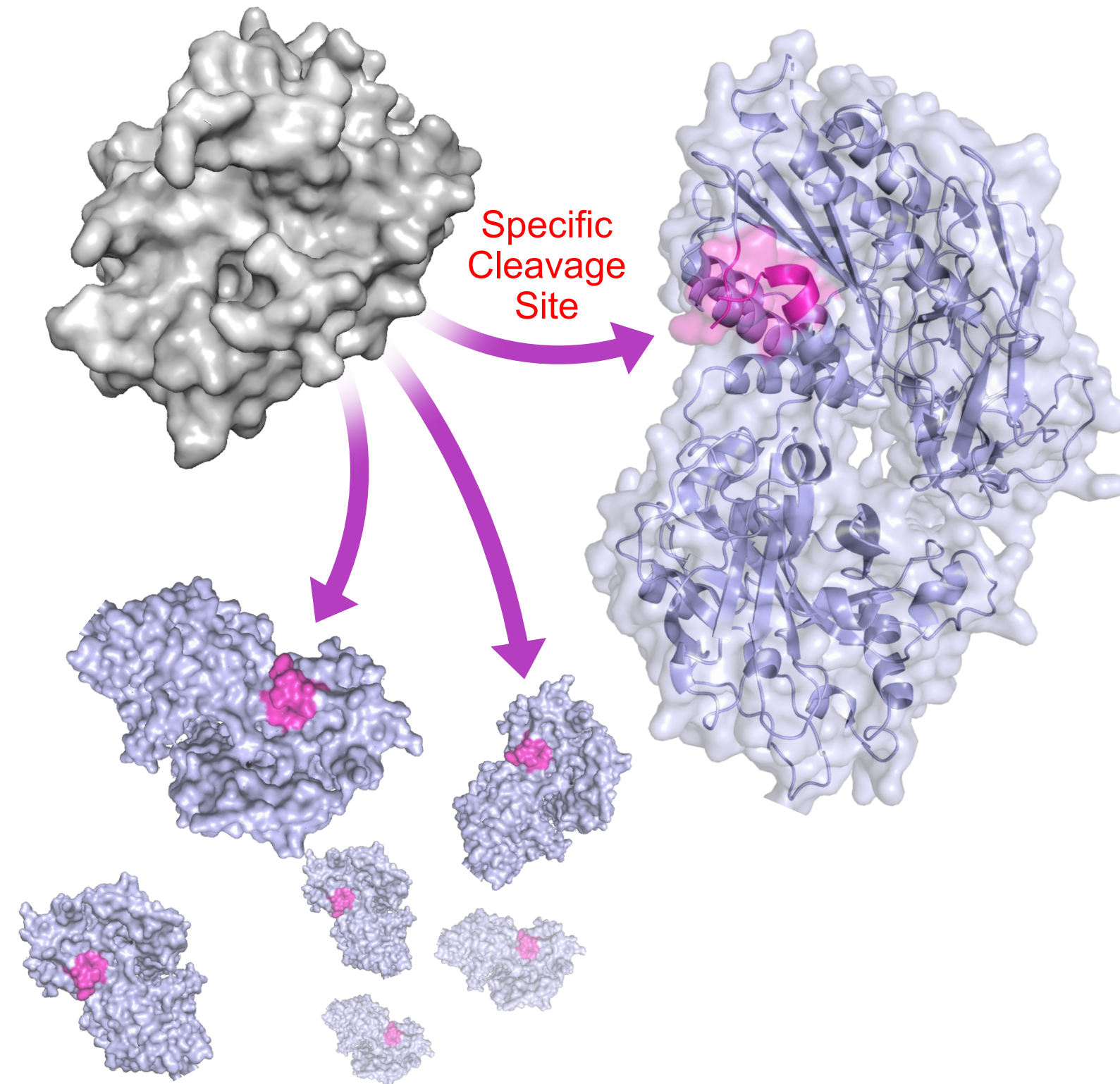
# Harnessing the catalytic power of proteases

One protease molecule activates or inactivates 1000s of target molecules



Therapeutic  
Protease

Target  
Protein



## An adaptable protease platform

- ✓ Functionally enhanced natural proteases (FVIIa, FIX)
- ✓ Engineered novel protein degraders (Anti-C3)
- ✓ Extended half-life variants
- ✓ Increased potency
- ✓ Proven efficacy of clinical stage assets

## Advantages

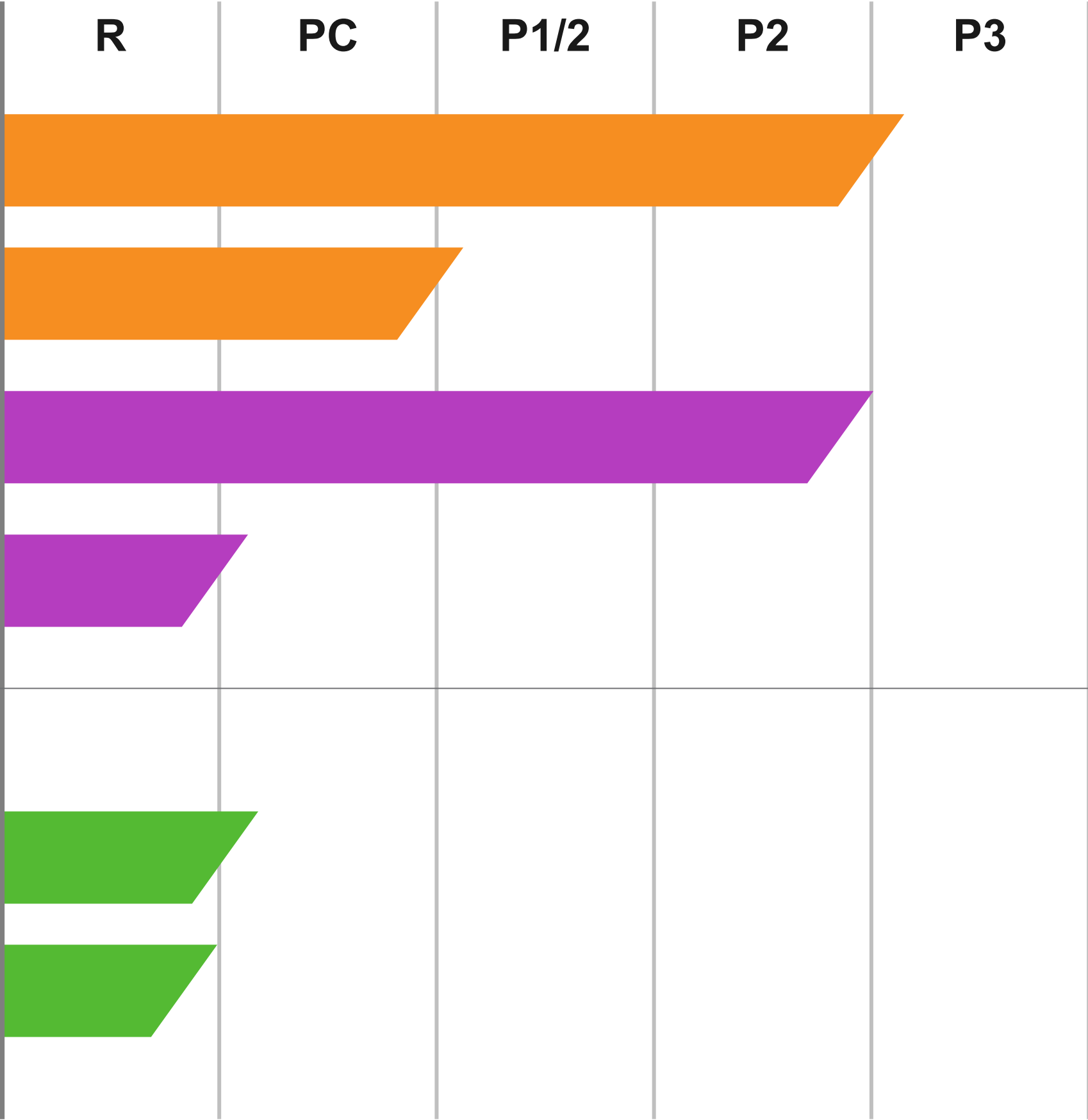
- ✓ Quick & simple SQ dosing for systemic use
- ✓ Less frequent intravitreal dosing in ophthalmology
- ✓ Low vector dose gene therapy constructs
- ✓ Ideal for high concentration drug targets or controlling amplification cascades

# Pipeline



## Hemostasis

- SQ Marzeptacog alfa "MarzAA" – (rFVIIa)**  
Hem A or B w/ Inh – ToB
- FVIID/Glanzmann/Hemlibra – ToB**
- SQ Dalcinonacog alfa "DalcA"**  
Hem B (rFIX)
- FIX-Gene Therapy**  
Hem B (CB 2679d-GT)

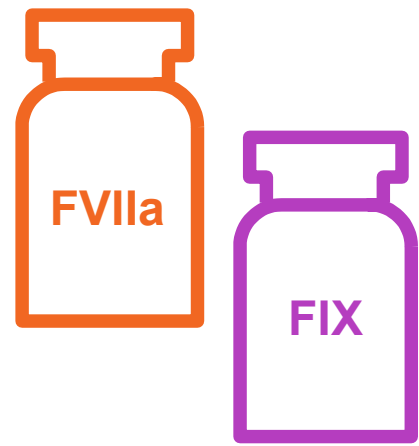


## Complement

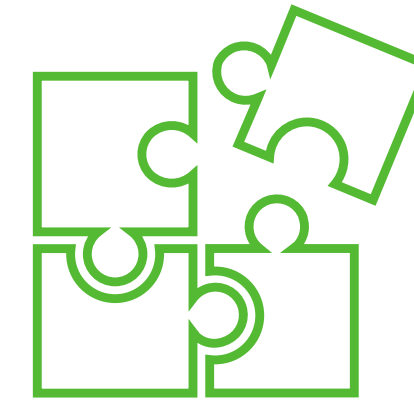
- IVT CB 2782-PEG**  
Anti-C3 protease for Dry AMD
- SQ systemic complement inhibitors – CB DC**



# Investment highlights



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



**Anti-C3 Dry AMD** with Biogen  
**SQ systemic complement regulator** research program



Multibillion-dollar market opportunities



Experienced team



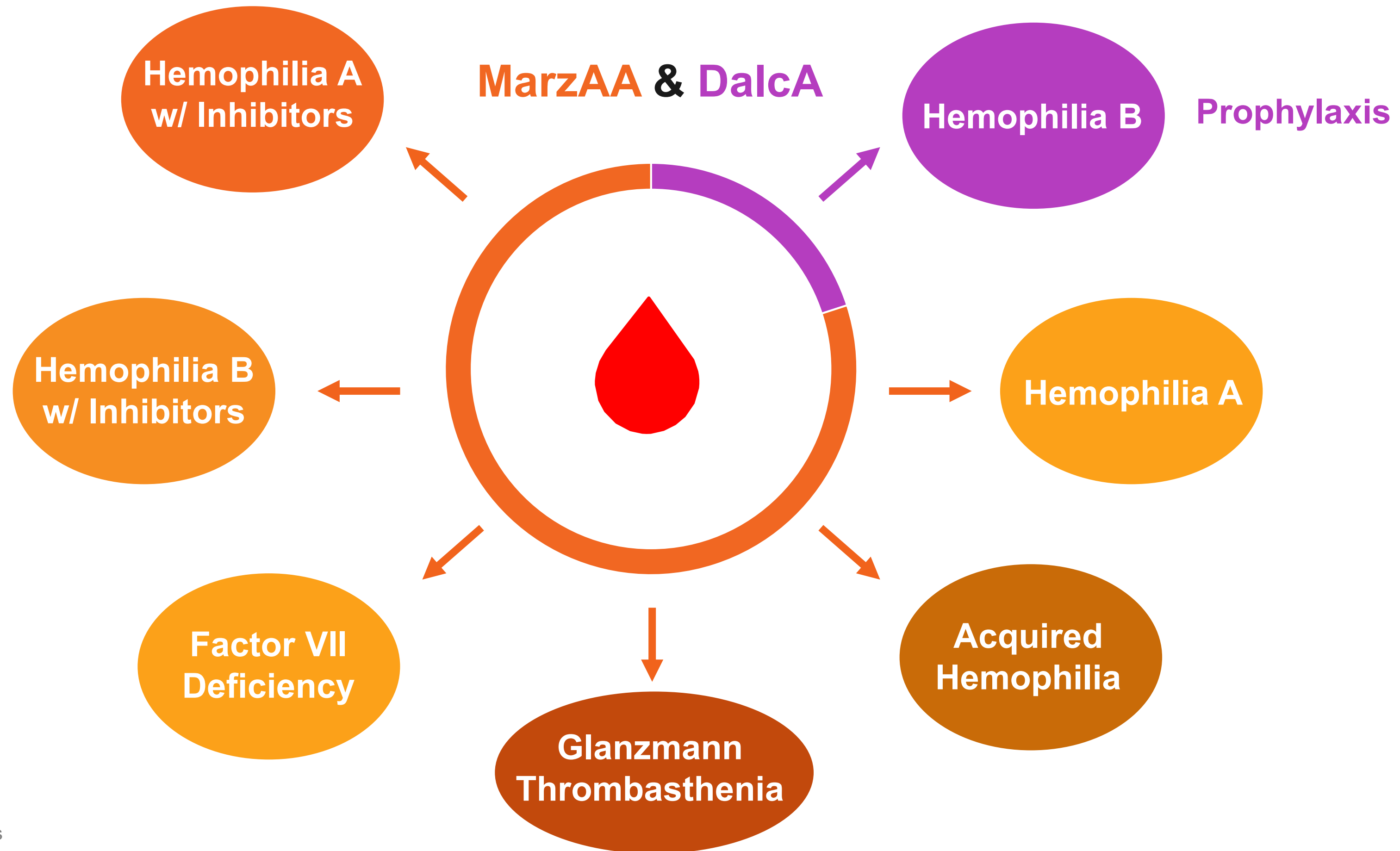
Strong balance sheet,  
\$117.4 M cash – Q2



177 worldwide patents  
CBIO retains full ownership of all compounds

# Addressing unmet needs in rare bleeding disorders

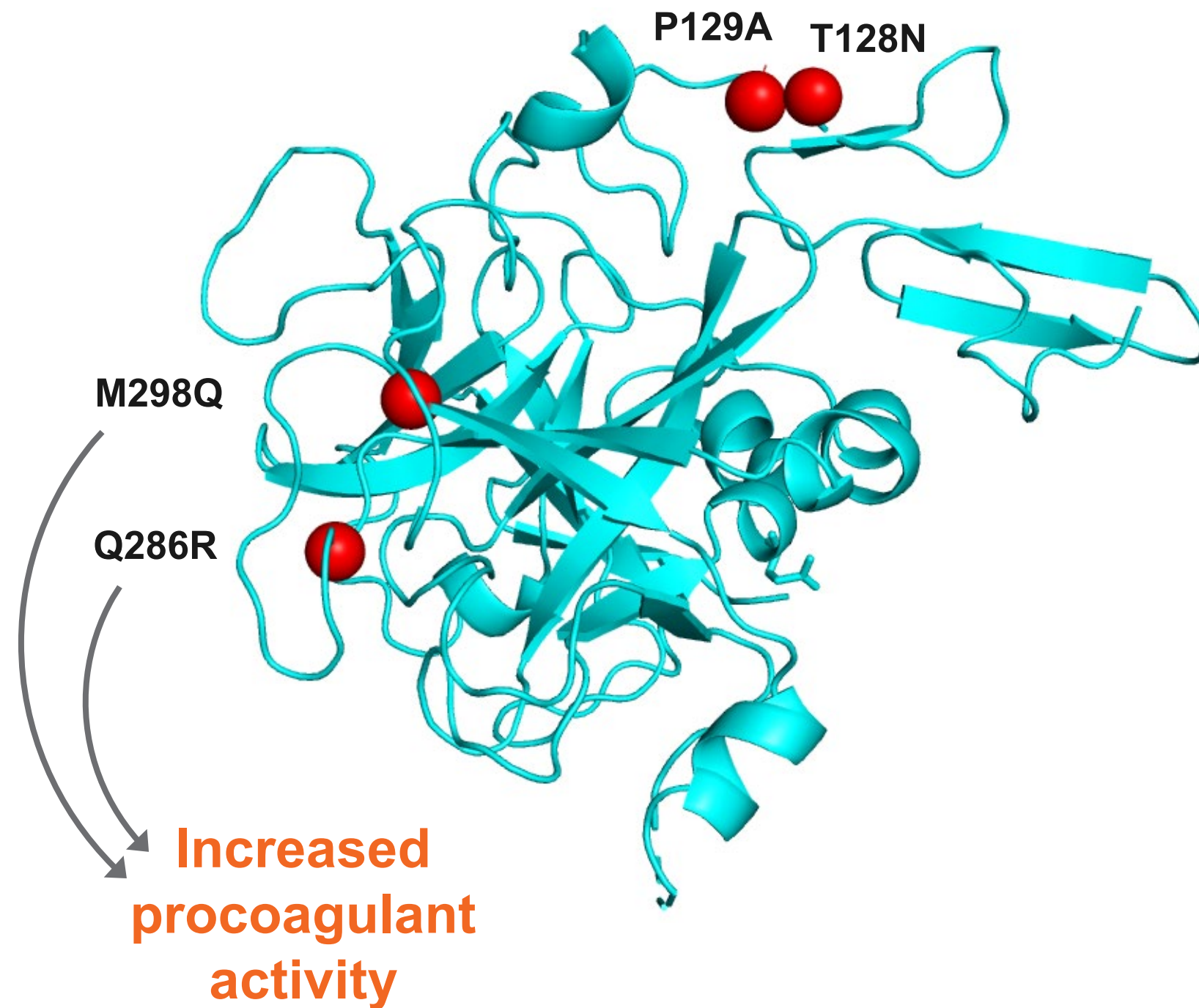
SQ treatment of episodic bleeding and prophylaxis – \$4B+ market





# 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

- + Small volume SQ administration
- + Improved bioavailability
- + Prolonged half-life

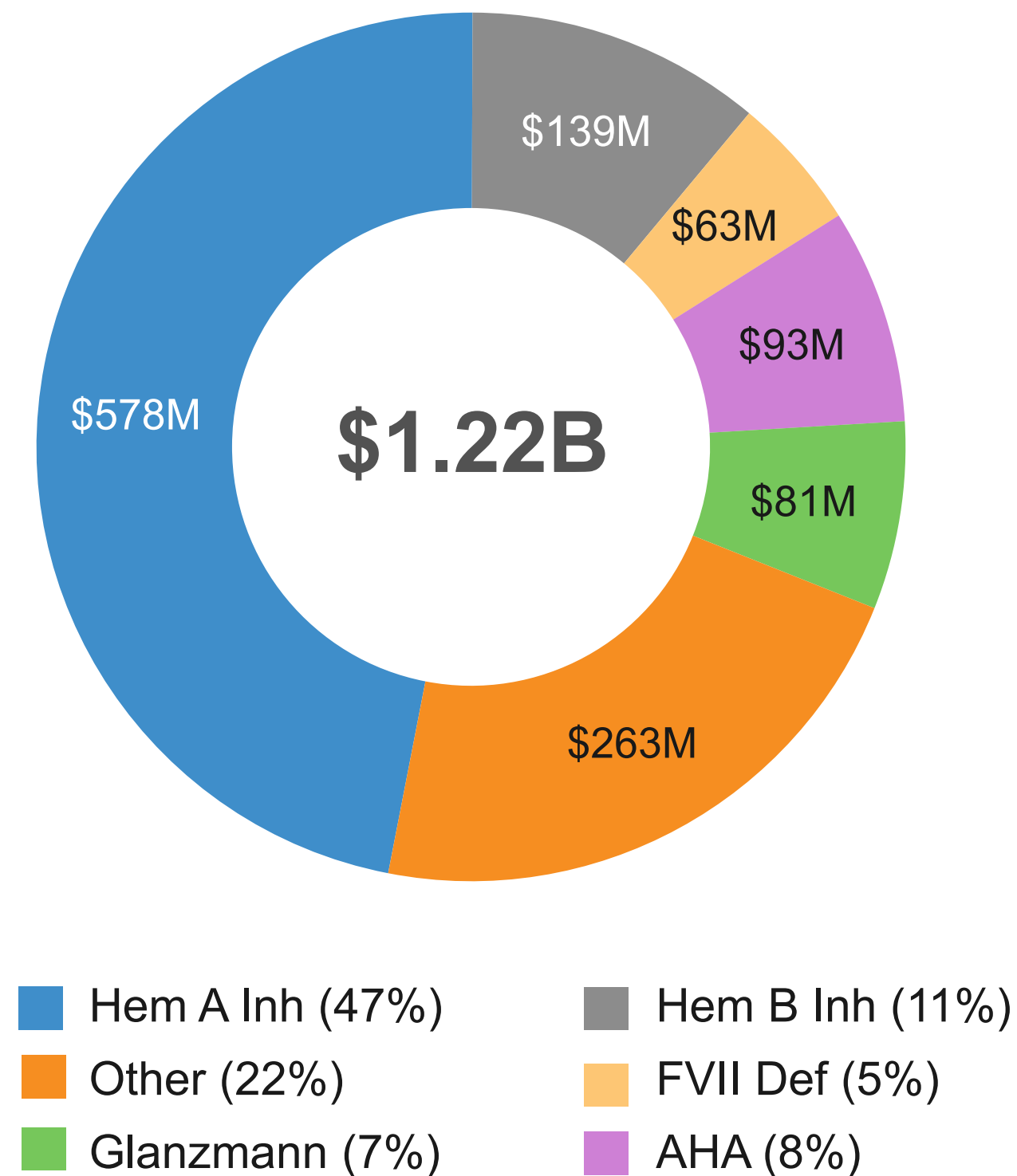
Orphan Drug Designation in US and EU



# SQ treatment of a bleed is a large commercial opportunity



## Global NovoSeven sales breakdown by indication (2019)



## SQ MarzAA has a superior profile

- ✓ Faster & easier to administer vs N7 dosed every 2 hours IV
- ✓ MarzAA half-life ~8x longer than N7
- ✓ 9-fold higher activity vs N7
- ✓ Potential to reduce rebleeding
- ✓ Stops bleeding in multiple preclinical models
- ✓ Can be combined with Hemlibra *in vitro* without increased thrombogenicity
- ✓ Potential for prophylaxis
- ✓ Ideal for pediatrics and patients with venous access issues

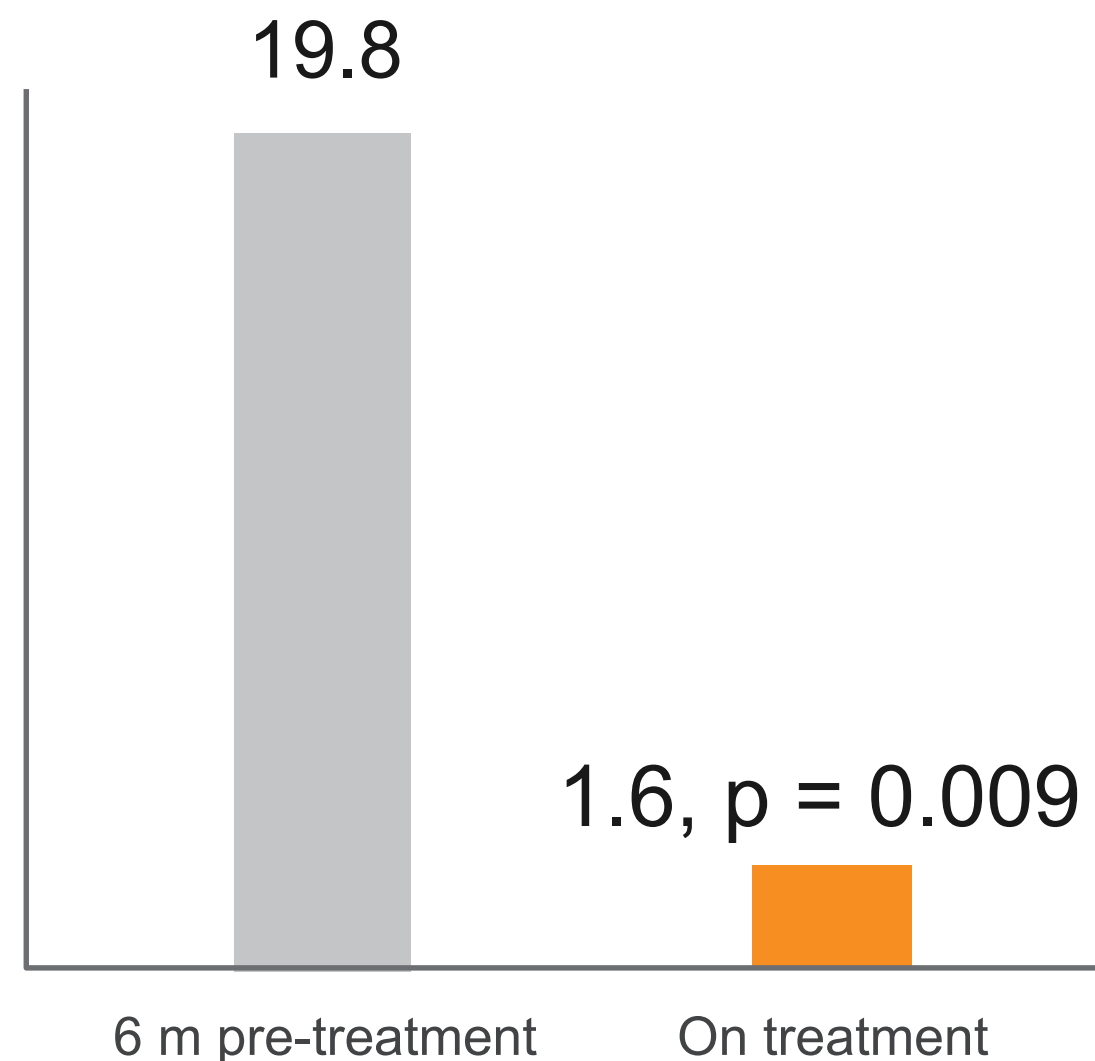
Source: Adivo Associates market research; Catalyst Biosciences market research. Data on file

# MarzAA Phase 2 demonstrates efficacy with daily prophylaxis



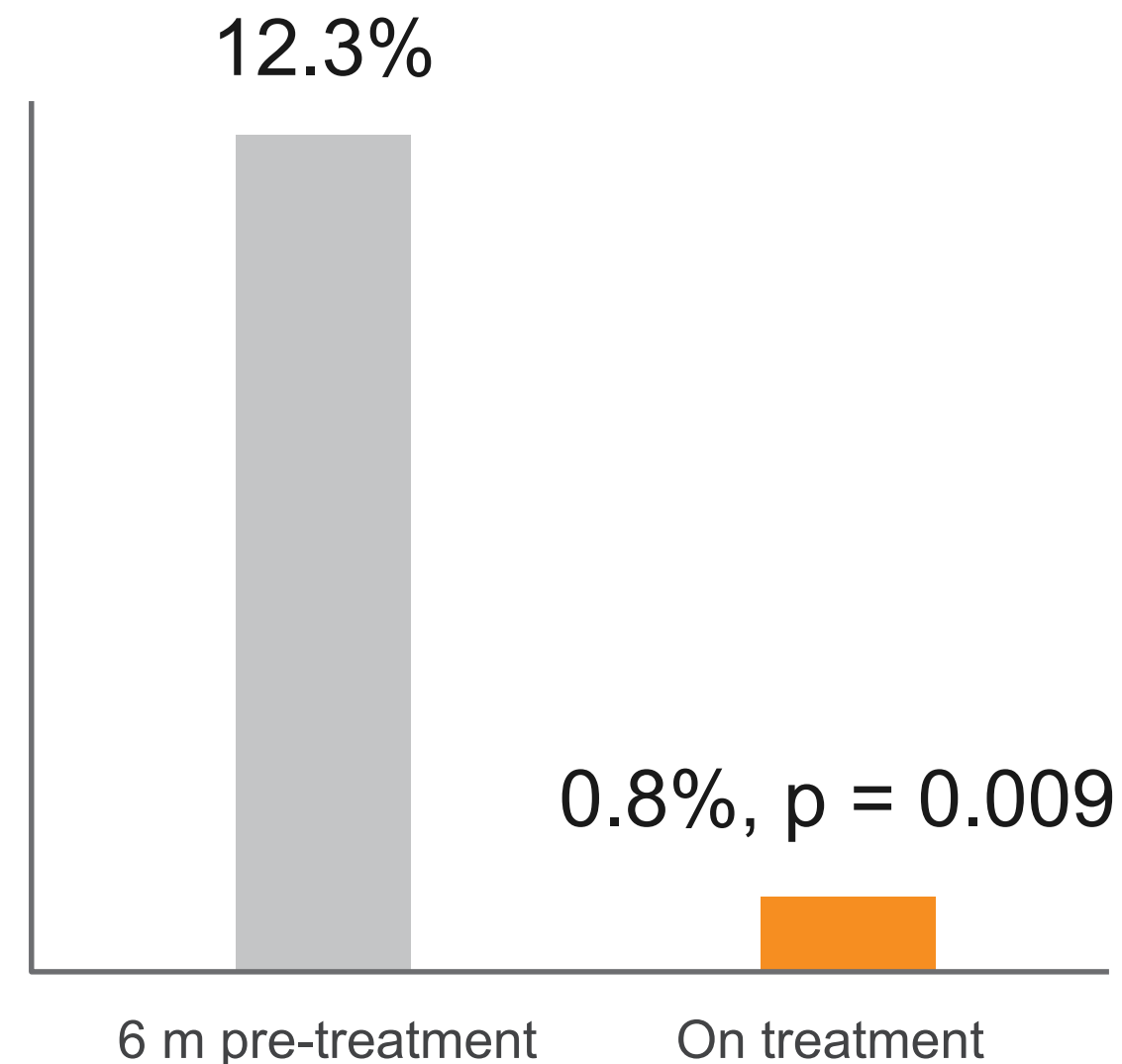
## Annualized bleed rate

n = 9



## Proportion of days with bleeding

n = 9



- + 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

# Current bypass agents require multiple IVs over the course of hours



Patients identify a need for an easy to administer treatment to stop bleeds quickly

## NovoSeven

### 6 Hours

- + Patients reported needing an average of **6 hours and 3 injections** of NovoSeven to resolve bleeds, with certain bleeds requiring up to or longer than 72 hours to resolve bleeding episodes<sup>1,2,3</sup>

72

Hours



*"I have trouble securing a vein for IV administration due to the fact that my veins are very scarred from years of IV injections. My veins are prone to collapse."*

- Hemophilia Patient

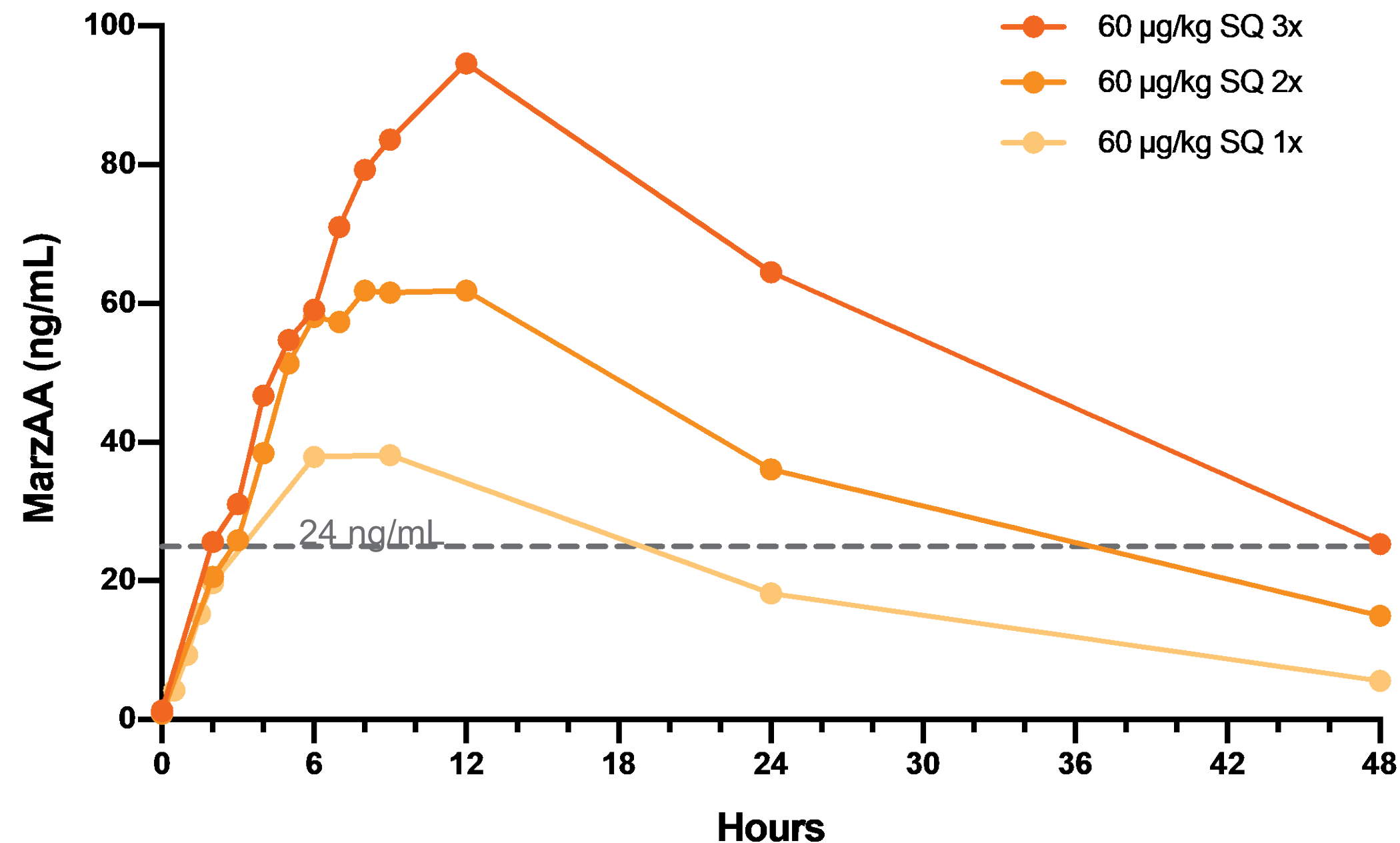
*"Wish we could do [treatment of a bleed] via something outside of IV, we would love the convenience of a subcutaneous administration."*

- Hemophilia Patient



Source: <sup>1</sup>NovoSeven PI Rev 7/2020; <sup>2</sup>Adivo Associates market research; <sup>3</sup>Catalyst Biosciences market research. Data on file

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

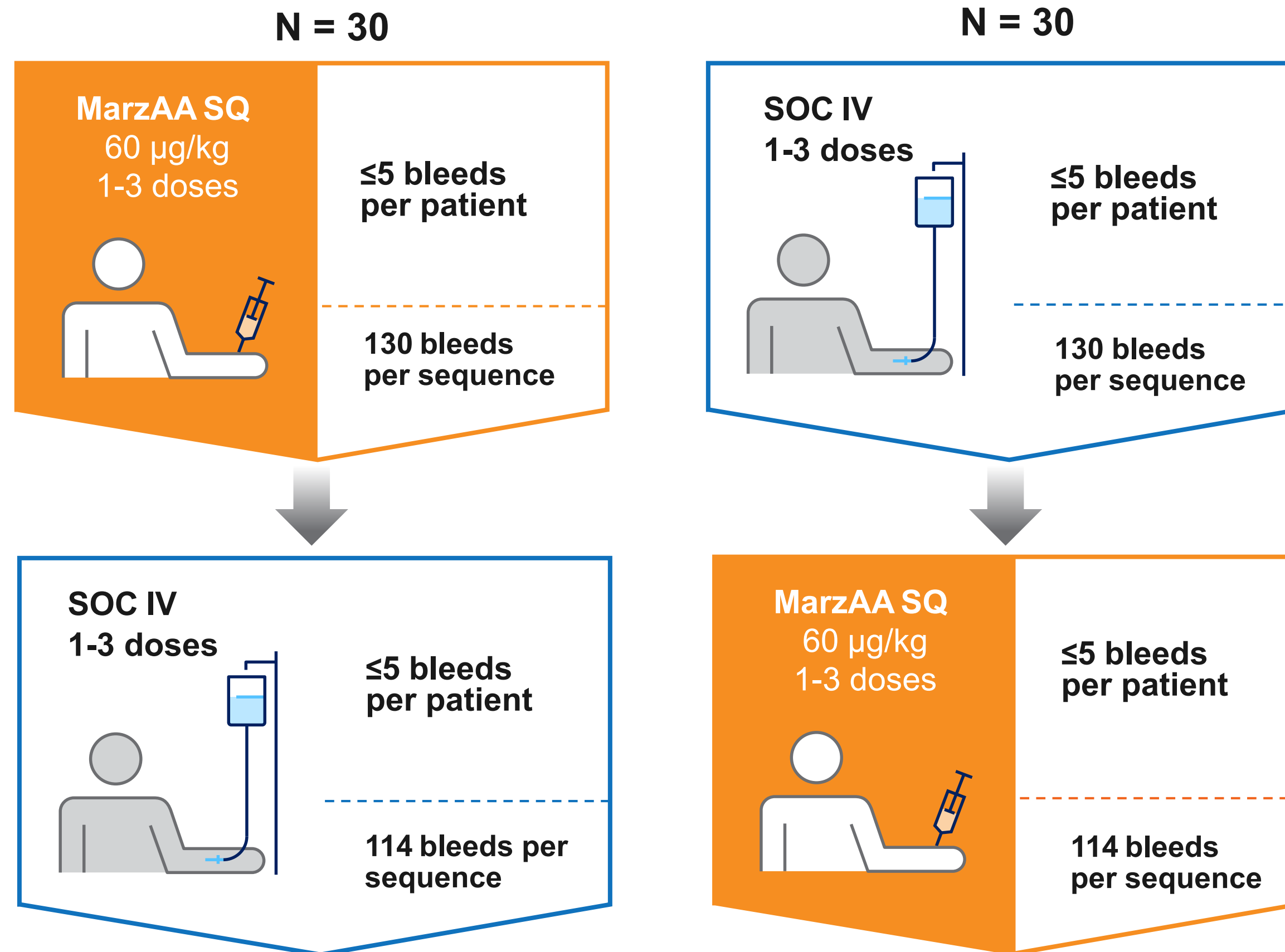


- + Target of 24-120 ng/mL to treat a bleed is based on continuous infusion levels of NovoSeven for surgery
- + Target levels are rapidly achieved
- + 25% and 50% of  $C_{max}$  at 1 and 2 hours, respectively
- + Dose-proportional increases in  $C_{max}$  and AUC
- + Target levels can be maintained for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



# Crimson 1 Phase 3 study: Treatment of episodic bleeding

Hemophilia A or B with inhibitors, ABR  $\geq 8$



- **Primary endpoint**

Non-inferior hemostatic efficacy:  
standard 4-point scale

- **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%**

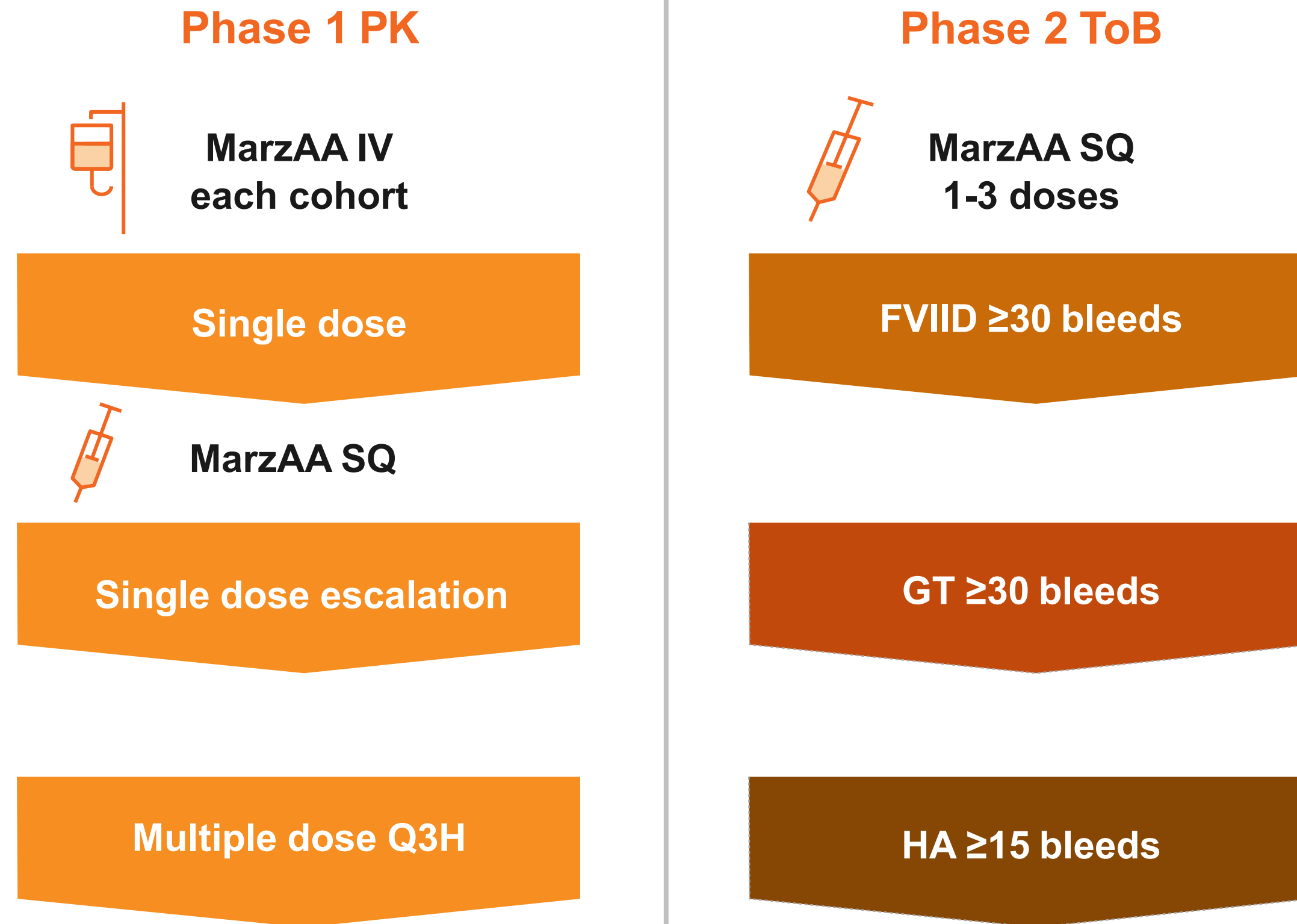
+ **2.5%** significance, one-sided

+ **90%** power

# MAA-202 Phase 1/2 study design



**FVII deficiency, Glanzmann thrombasthenia and HA on Hemlibra: N = 8 each**



- **Phase 1**

**Primary endpoints:**

Pharmacokinetics

**Secondary endpoints:**

Pharmacodynamics

- **Phase 2 ToB**

**Primary endpoints:**

Hemostatic efficacy at 24 hours

**Secondary endpoints:**

Effective hemostasis at successive timepoints; doses needed; rescue meds

**Safety:**

Adverse events and ADA

# MarzAA clinical development plan for treatment of bleeds

**Large commercial opportunity across multiple rare bleeding disorders**

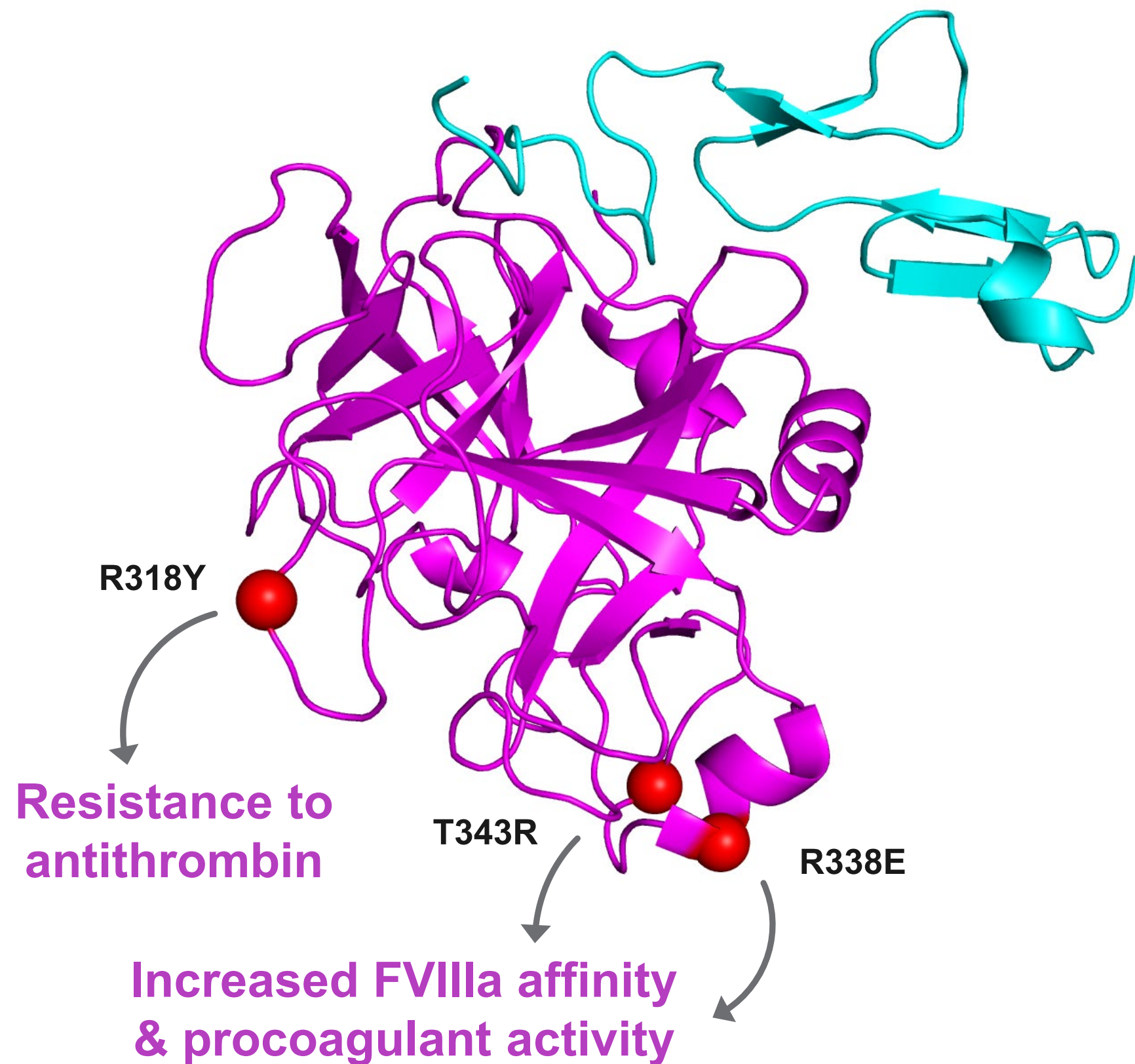


- **Initiate P3 Crimson 1 study in Q4 2020**
- **HA/HB with inhibitors**

- **Initiate P1/2 study MAA 202 in Q4 2020**
- **FVII deficiency, Glanzmann thrombasthenia, Hemlibra breakthrough bleeds**

- **Data expected in 2021 & 2022**

# 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

- + 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

Endpoint achieved with steady state FIX activity levels >12%

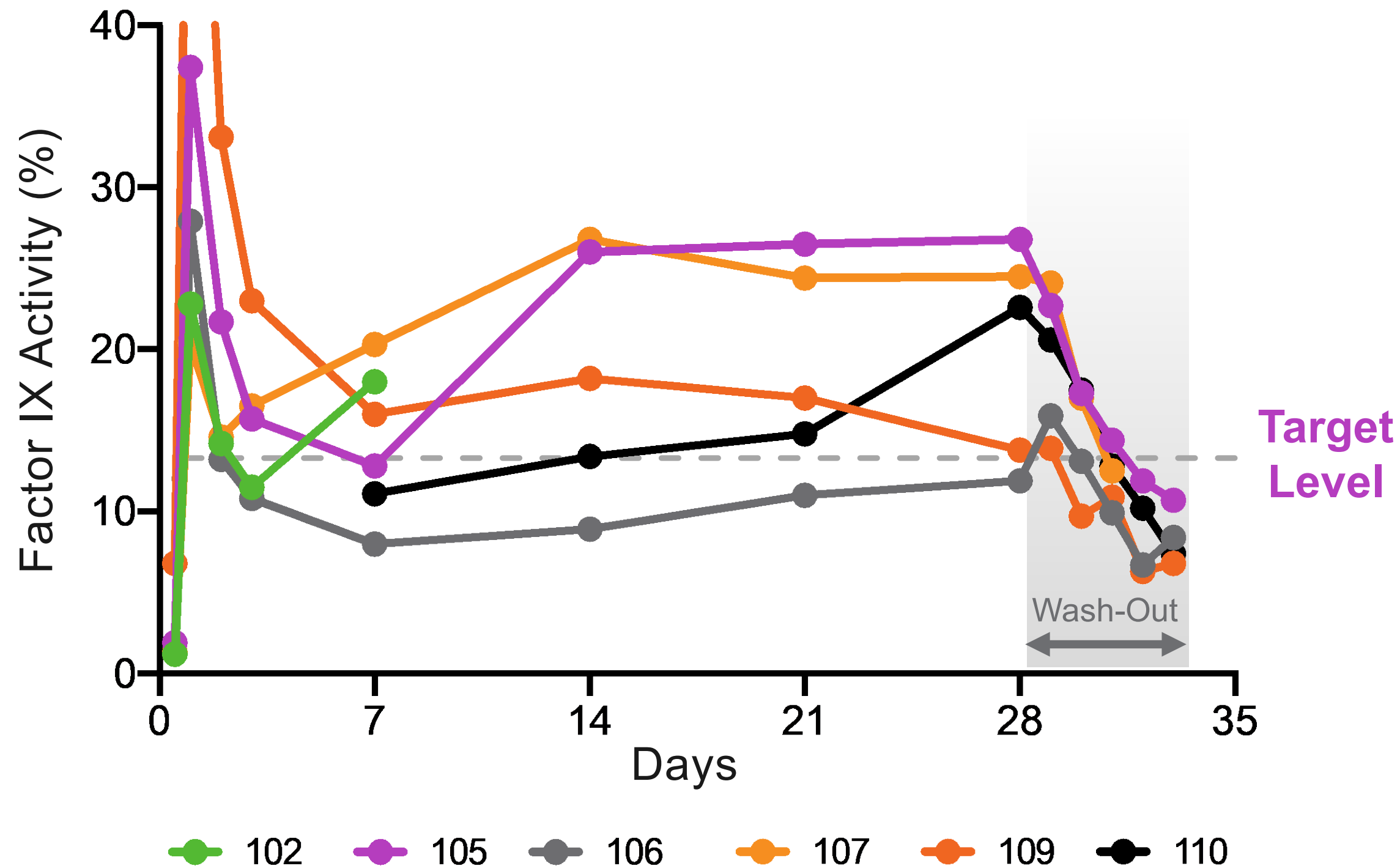


- + Primary endpoint: **Steady state FIX activity** level above 12% with daily dosing
- + Secondary endpoints: **safety including weekly ADA testing**, pharmacokinetics, pharmacodynamics, bleeding events
- + 6 severe Hemophilia B subjects dosed
- + Rare propeptide mutation excluded
- + HLA profile associated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

# DalcA P2b demonstrated proof of safety and efficacy



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



- + Dosed 6 severe HB subjects
  - Subject 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

# Dalcinonacog alfa



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

- ✓ Phase 2b trial complete
- ✓ Protective therapeutic FIX activity levels achieved
- ✓ No bleeding events during treatment indicates effective prophylaxis
- ✓ No SAEs, systemic hypersensitivity, nAb
- ✓ Mild to moderate ISR primarily with initial injections – transient & self-limiting
- ✓ Long half-life – potential for lower dose/reduced dosing frequency

# Catalyst's CB 2679d - gene therapy



## Limitations of 1st generation GTs create an opportunity



### AAV serotype

- High vector doses needed to achieve stable expression
- Preexisting neutralizing antibodies to the capsids limit efficacy & eligible patients
- Variable tissue tropism can limit effectiveness

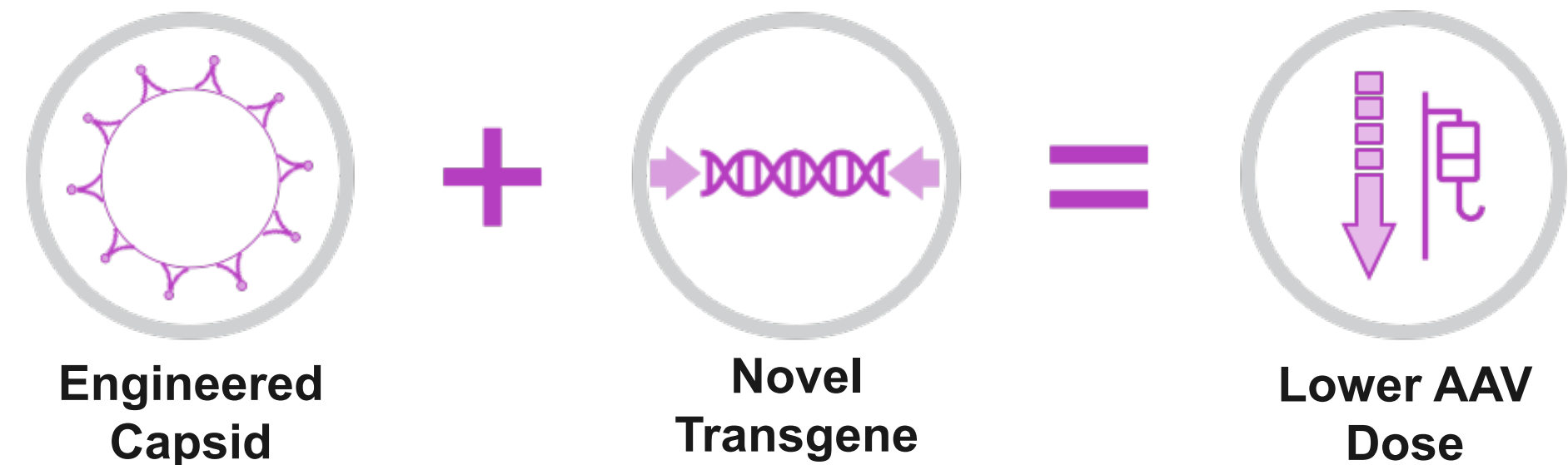


### Durability

- + FIX transgenes encode the Padua high-activity FIX variant
- Gene therapies have yet to demonstrate durable and clinically meaningful FIX expression 5 years post-infusion
- FIX activity has decreased over time



# CB 2679d-GT for hemophilia B



FIX Transgene	AAV Capsid	Study Dose (vg/kg)	FIX Activity (U/mL)
CB 2679d-GT	Novel Chimeric	$8.0 \times 10^{10}$	20
Padua	TAK-748*	$7.4 \times 10^{11}$	20
Padua	TAK-748*	$7.4 \times 10^{10}$	1

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



**Stanford**  
University

License & sponsored research agreement

## ✓ CB 2679d-GT has a superior profile vs Padua in preclinical studies

- + Stable high activity levels with a vector dose reduced 10-fold in a mouse hemophilia B mode
- + 4 to 5-fold reduction in bleeding time when compared to the Padua transgene in mice
- + Potential for an improved efficacy & safety

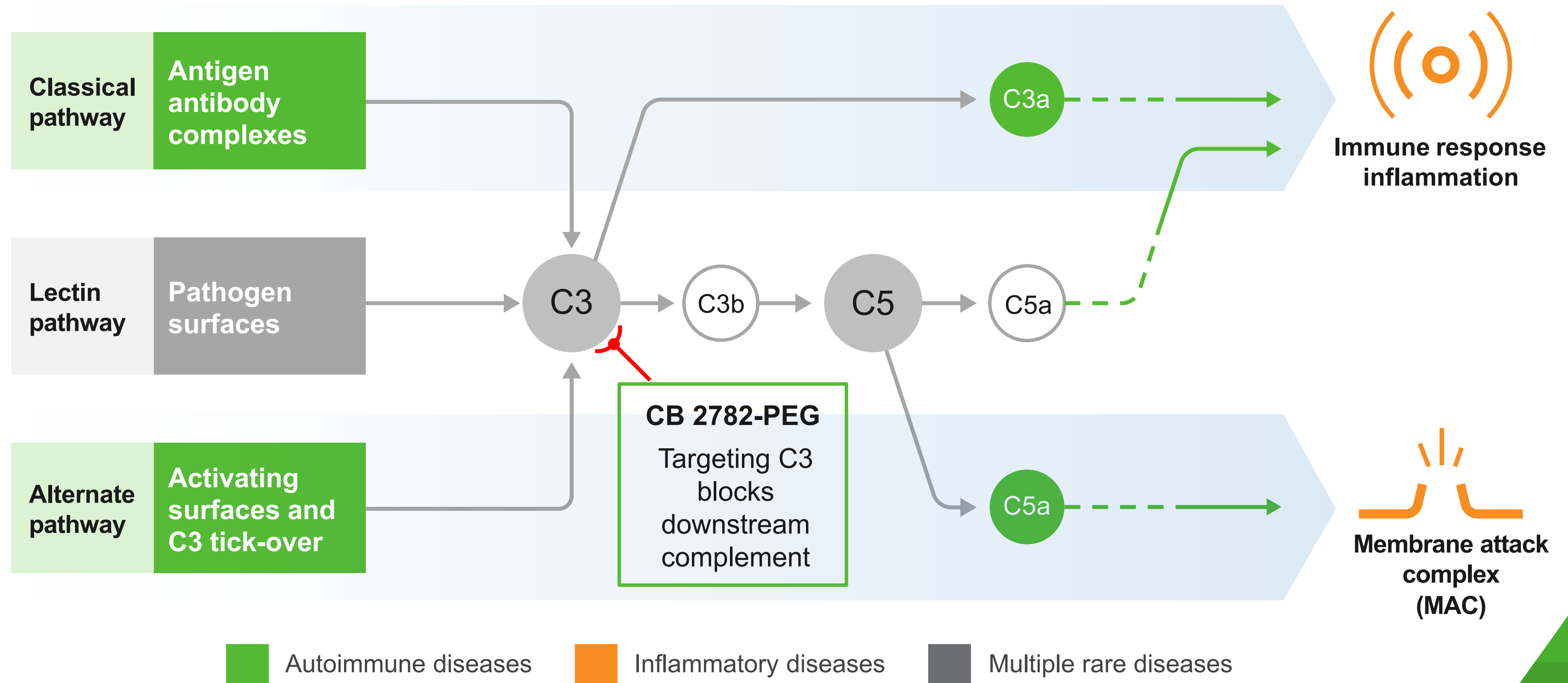
## ✓ Achieved high initial FIX levels in NHPs

- + Presented at World Federation of Hemophilia Virtual Summit 2020 (June 19, 2020)
- + Additional vector optimization & dose ranging studies ongoing

## ✓ Wholly-owned & issued patents covering gene therapy

# Targeting complement – a pathway regulated by proteases

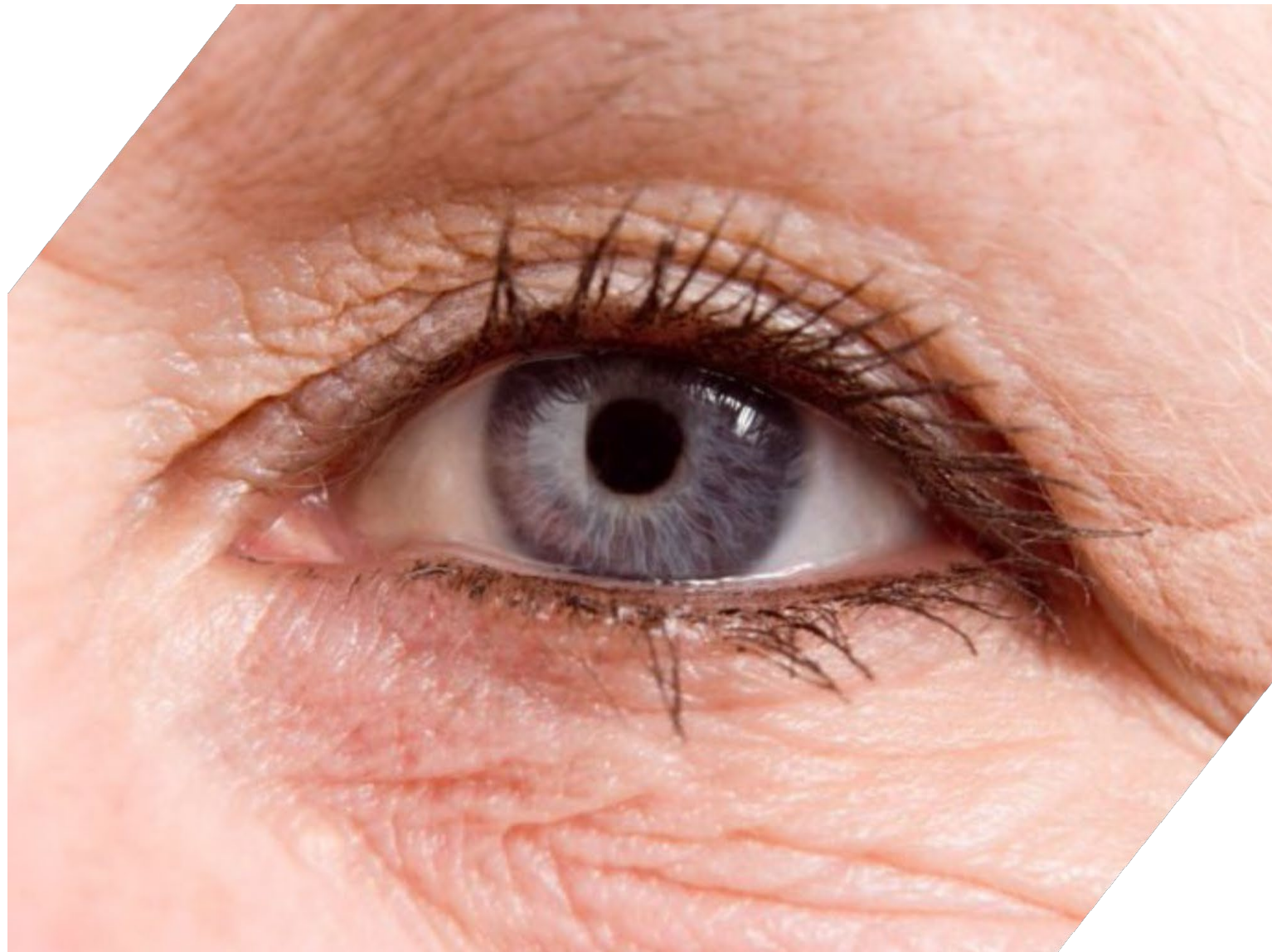
Dysregulated complement activity is associated with a broad range of disorders and a logical fit for our protease platform



# 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 therapy

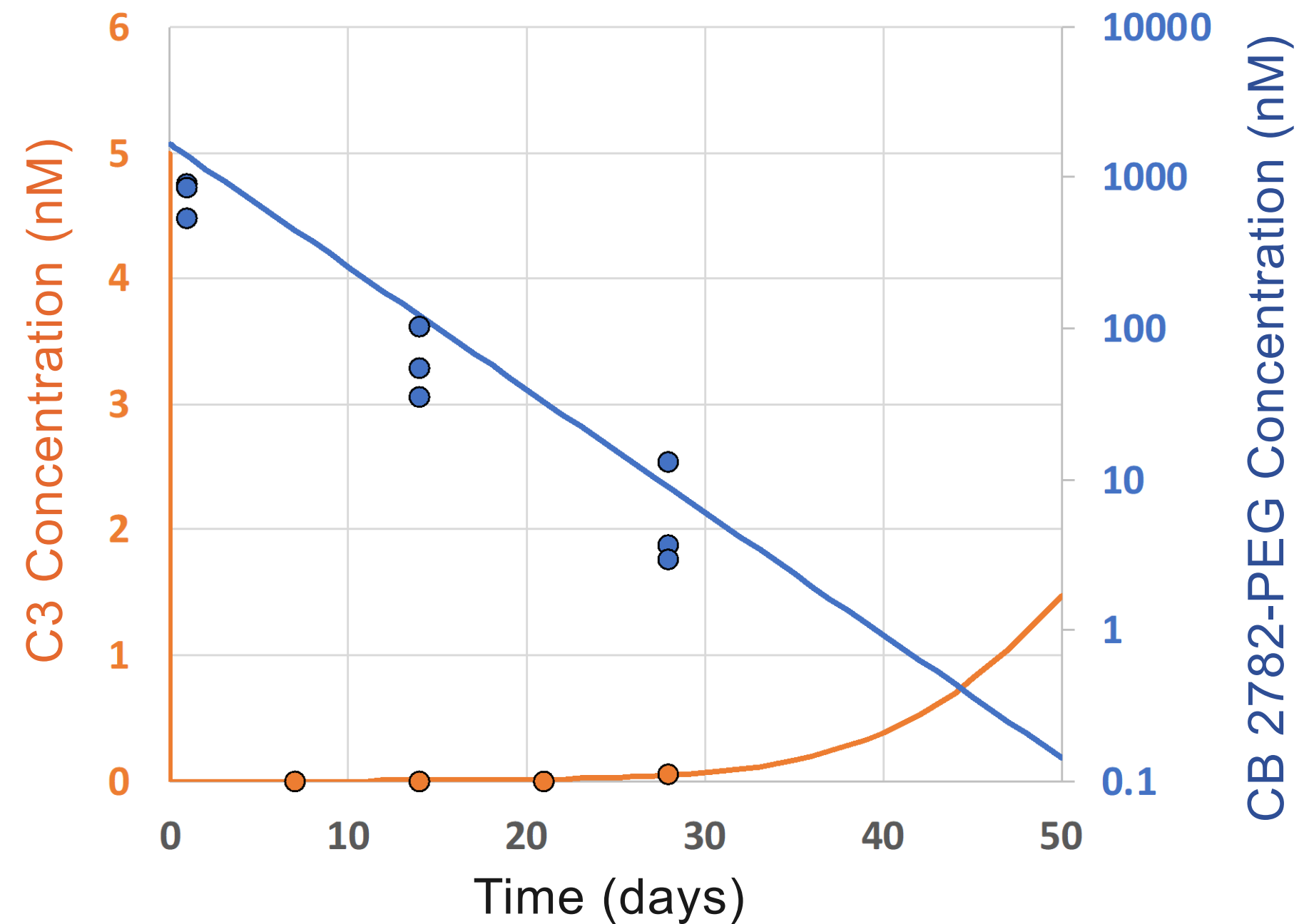
Sources: National Eye Institute. Facts About Age-Related Macular Degeneration, Tufail 2015, The Eye Diseases Prevalence Research Group 2004, GlobalData

# CB 2782-PEG long acting anti-C3 protease

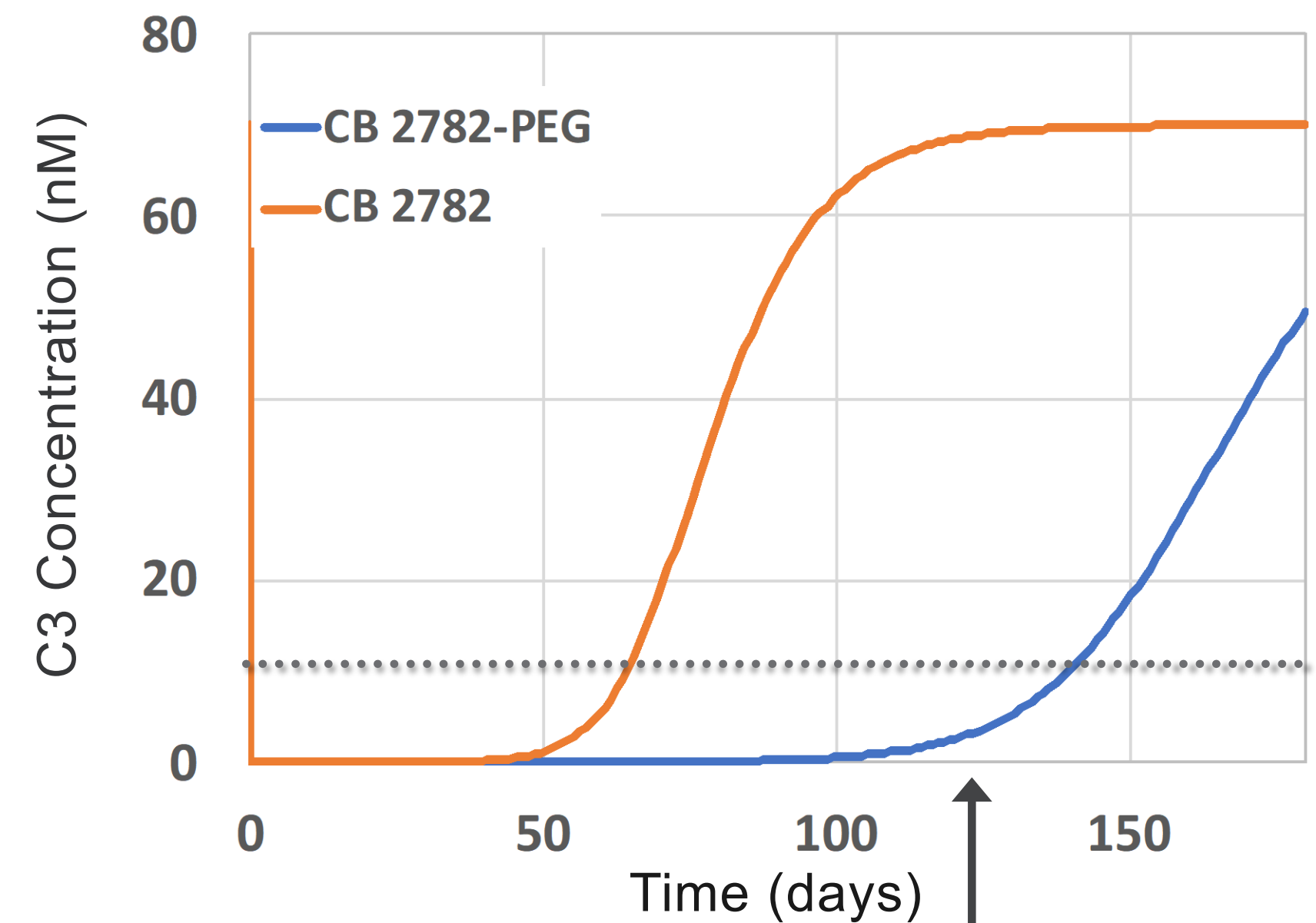
Best-in-class anti-C3 profile for dry AMD with dosing every 3 to 4 months



## Non-Human Primates



## Human Modeling



Predicted >90% elimination  
of C3 at 4 months



# CB 2782-PEG long acting anti-C3 protease



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

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- + 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

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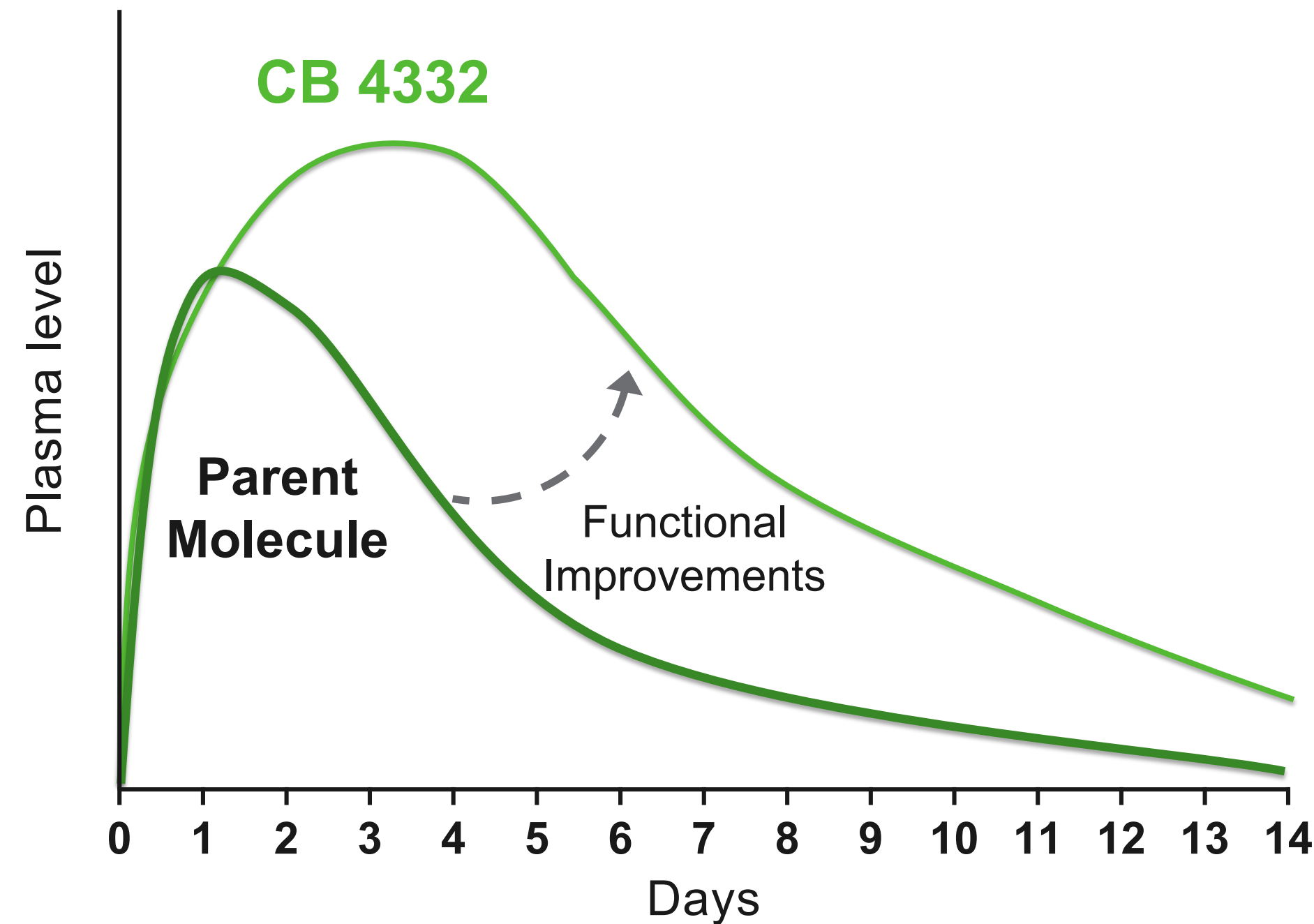
- + Announced December 19, 2019
- + \$15M upfront, up to \$340M in milestones and **tiered royalties up to low double digits**
- + Catalyst to perform fully funded pre-clinical and manufacturing activities
- + Biogen responsible for IND-enabling activities, worldwide clinical development & commercialization

\*Furfine *et al.* ARVO 2019

# CB 4332 SQ long-acting systemic complement regulator



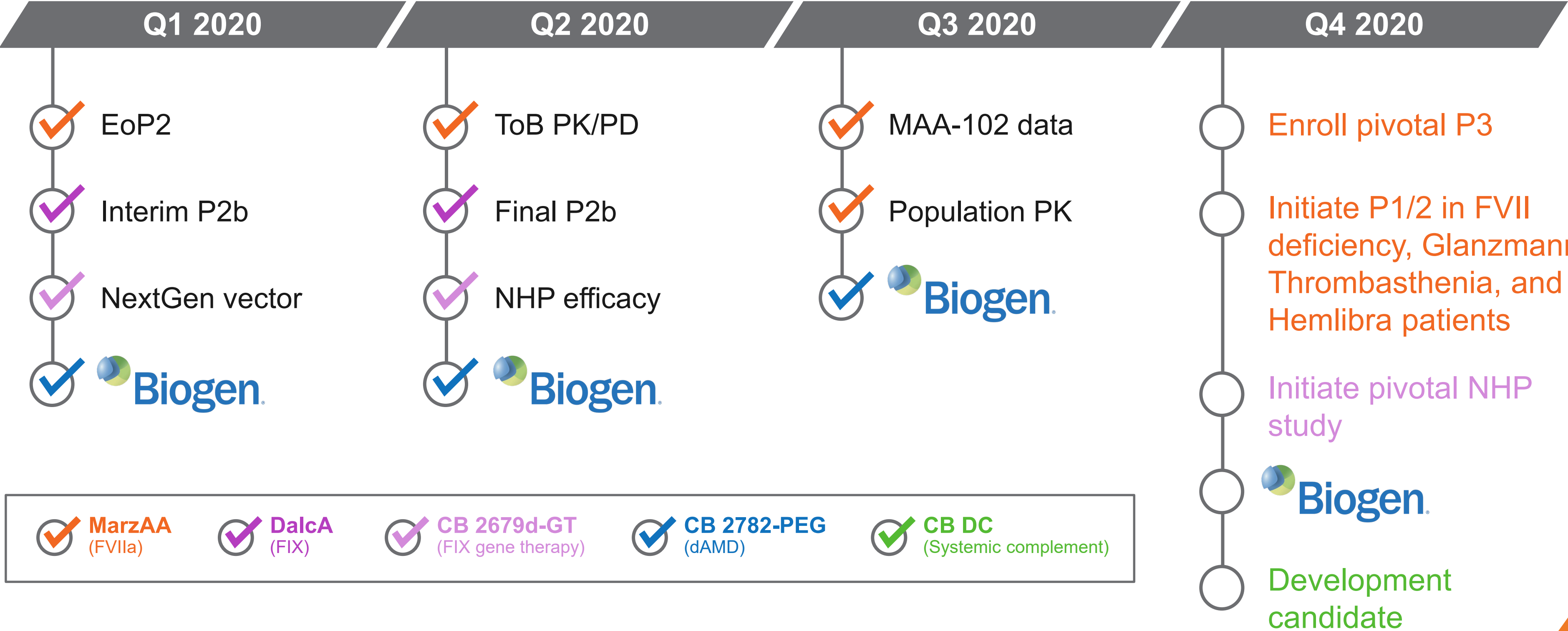
Non-human primate PK supports weekly SQ dosing in humans



## Expanding the complement portfolio

- + Leverages Catalyst's proprietary **protease engineering platform**
- + Designed for **SQ administration & improved bioavailability**
- + **Simple & efficient** production process
- + Program update in Q4

# Milestones – 2020



# Team



**Nassim Usman, Ph.D.**

President & CEO



28 years in biotech

**Grant Blouse, Ph.D.**

SVP Translational Research



13 years in biotech

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

Chief Financial Officer



16 years in biotech & investing/banking

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

SVP Business Development



18 years in biotech

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

Chief Medical Officer



20 years in hematology

**Anju Chatterji, Ph.D.**

SVP Biologics Development & Manufacturing



19 years in biotech

# Summary



## 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 with lower doses

### ✓ 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

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