

Nasdaq: CBIO

# CATALYST BIOSCIENCES

**Corporate Overview**

15 April 2021

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# Forward looking statements



Certain information contained in this presentation and statements made orally during this presentation include forward-looking statements that involve substantial risks and uncertainties. All statements included in this presentation, other than statements of historical facts, are forward-looking statements. Forward-looking statements include, without limitation, statements about the product candidates of Catalyst Biosciences, Inc. (the “Company”) and the benefits of its protease engineering platform, potential markets for and advantages of MarzAA and DalcA; plans to enroll a pivotal Phase 3 registration study of MarzAA; the initiation of a Phase 1/2 trial in patients with FVII Deficiency, Glanzmann Thrombasthenia, and patients treated with Hemlibra; MarzAA as possibly the first prophylactic for FVII Deficiency and Glanzmann Thrombasthenia; the potential for MarzAA and DalcA to effectively and therapeutically treat hemophilia subcutaneously; projected complement market opportunity, solution to fundamental shortcomings in current treatment options, plans to enroll the CB 4332 observational trial in the Company’s complement program in mid-2021, and ongoing updates related to CB 4322 and the C4b degrader.

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 COVID-19 and other factors, that trials may not have satisfactory outcomes, that human trials will not replicate the results from earlier trials, 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 its agreement with the Company, competition 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 (“SEC”) on March 4, 2021, and in other filings with the SEC. The forward-looking statements in this presentation represent the Company’s view as of the date of this presentation and the Company does not assume any obligation to update any forward-looking statements, except as required by law.

## The Protease Medicines Company

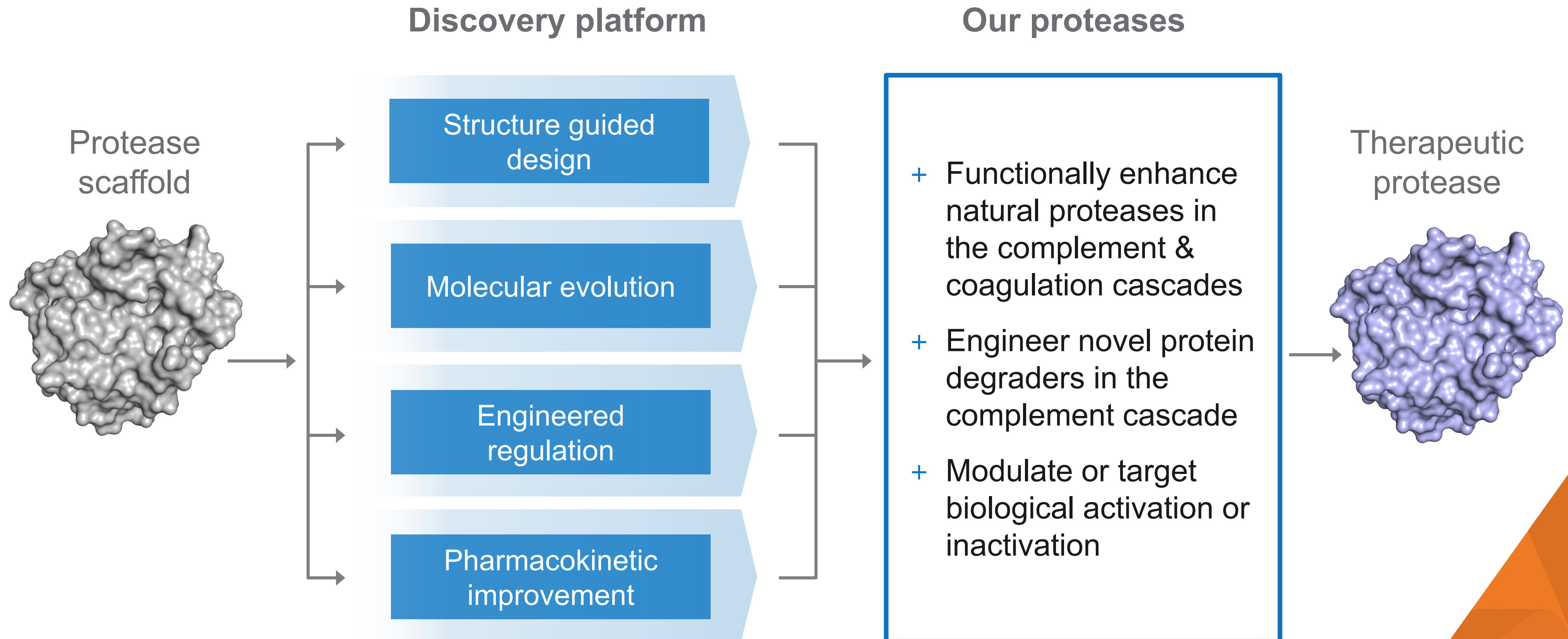
Harnessing the catalytic power of proteases

- ✓ Novel differentiated protease medicines
- ✓ Robust complement portfolio
- ✓ Clinical-stage hemophilia assets
- ✓ Late-stage asset in Phase 3

# Catalyst's protease platform generates differentiated therapeutics



Unique expertise in protease biology enables design of optimized protease therapeutics



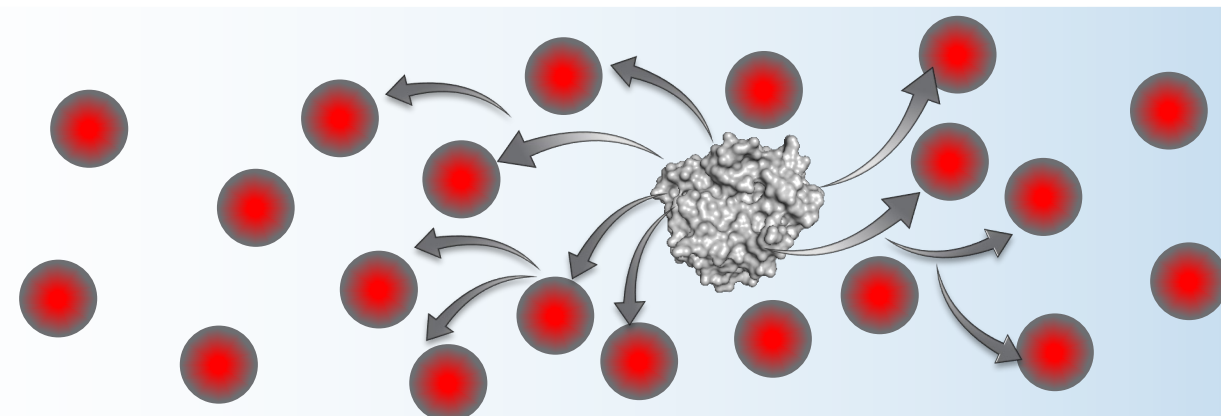
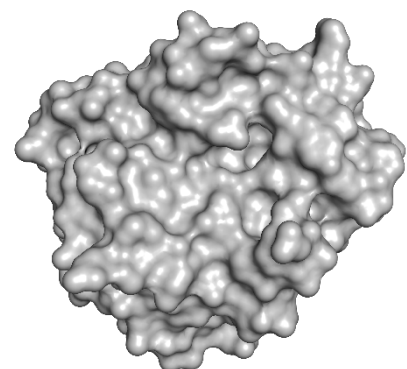


# Proteases are ideal for high abundance targets & cascades



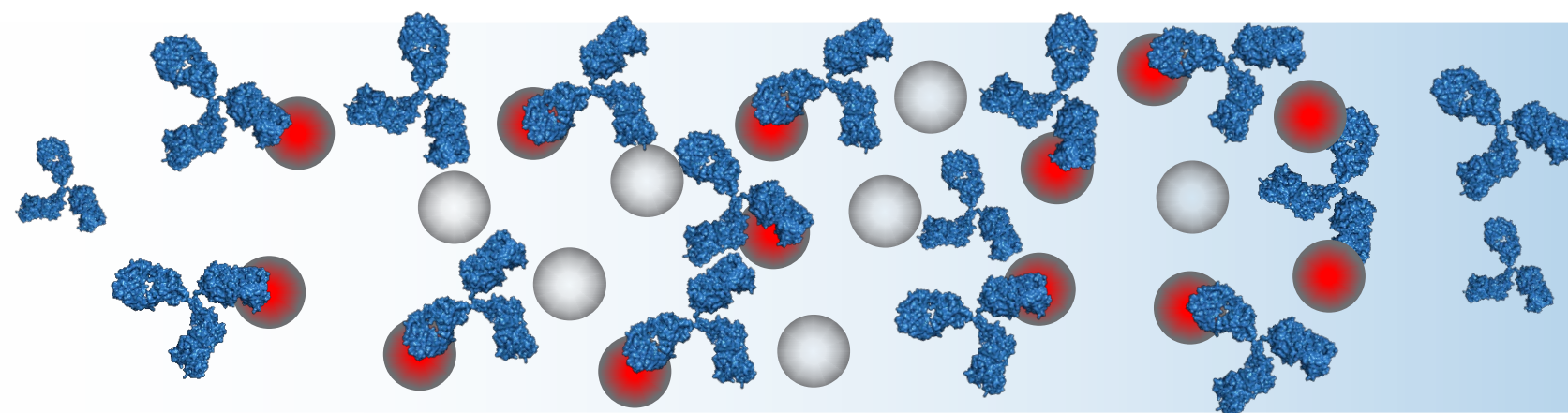
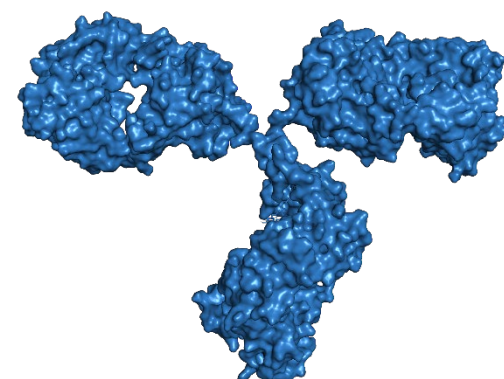
**A better way to regulate biological processes compared with antibodies & small molecules**

Proteases



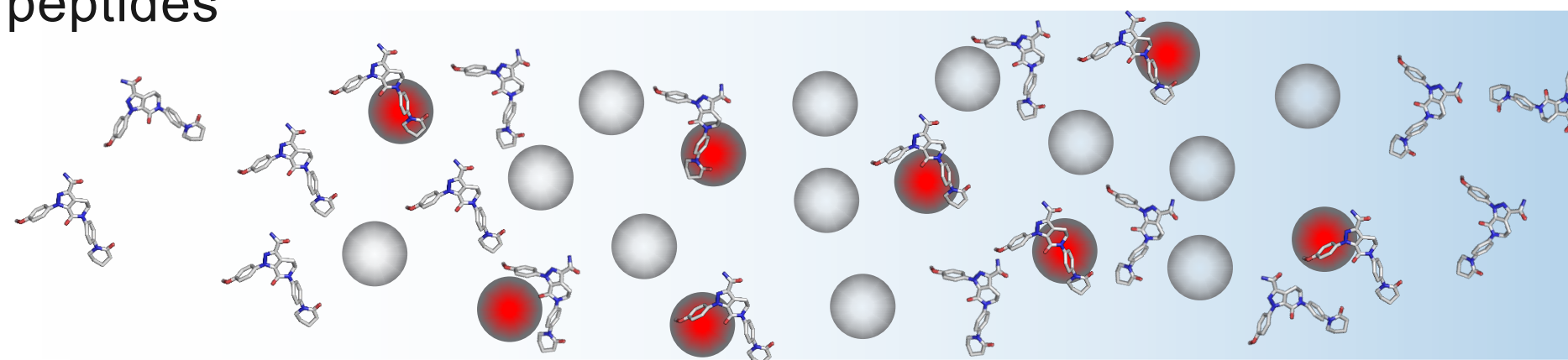
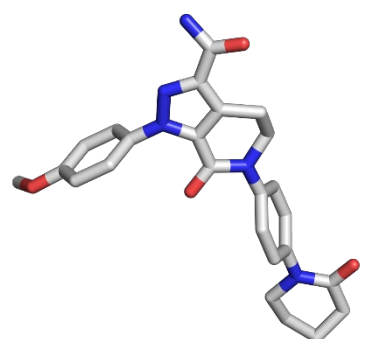
Efficient regulation at low concentrations of therapeutic protease

Antibodies



Requires high concentrations in excess of the target

Small molecules / peptides



Requires high concentrations & frequent dosing

# Pipeline



## Hemostasis

- SQ Marzeptacog alfa (FVIIa) "MarzAA"**  
Hemophilia A or B with inhibitors – ToB
- FVIID/Glanzmann/Hemlibra – ToB**

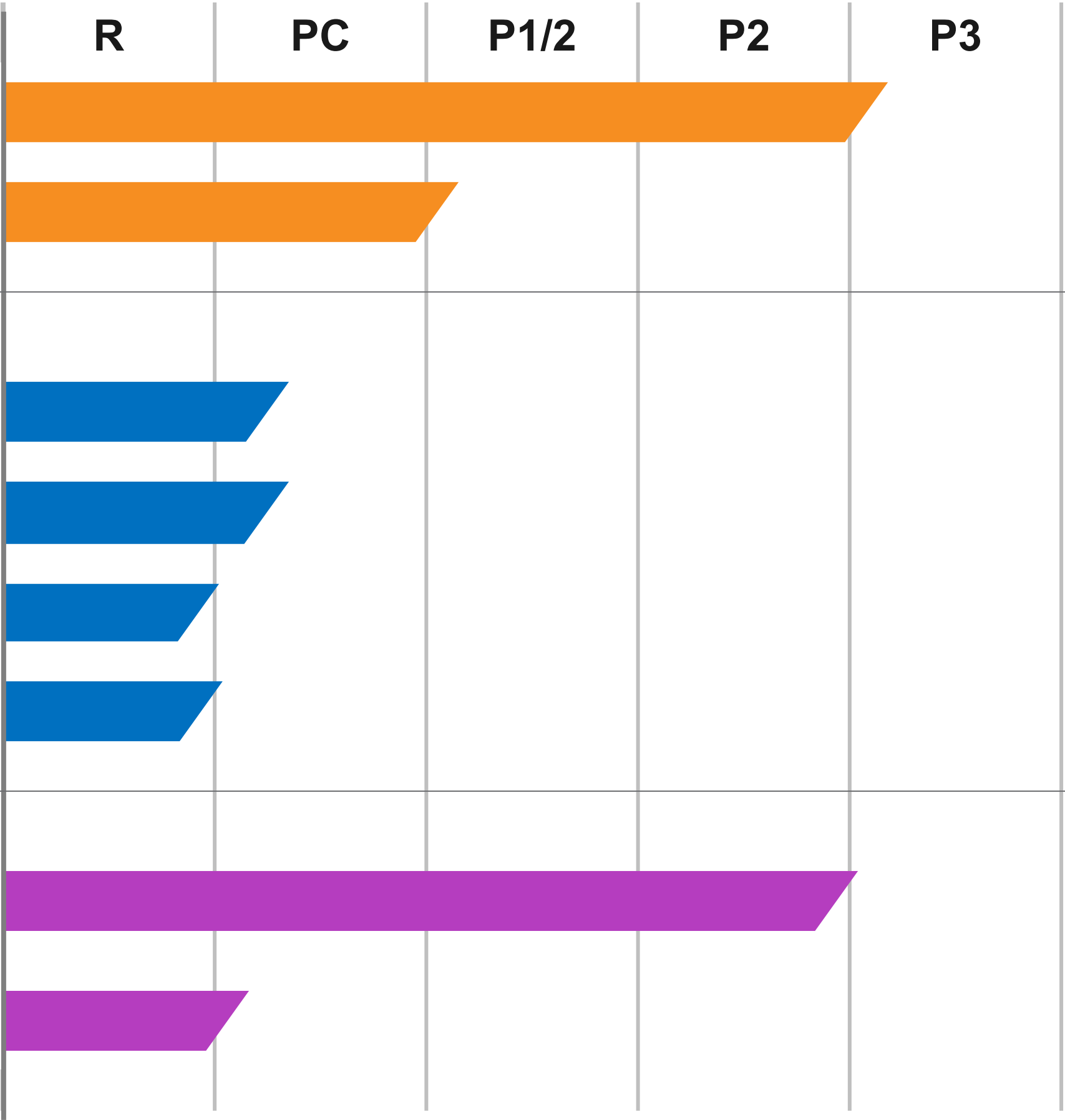
## Complement

- IVT CB 2782-PEG**  
C3 degrader for Dry AMD
- SQ CB 4332** Enhanced CFI
- C4b Degradar**
- Additional programs**



## Hemostasis

- SQ Dalcinonacog alfa (FIX) "DalcA"**  
Hemophilia B
- CB 2679d-GT**  
Hemophilia B FIX Gene Therapy

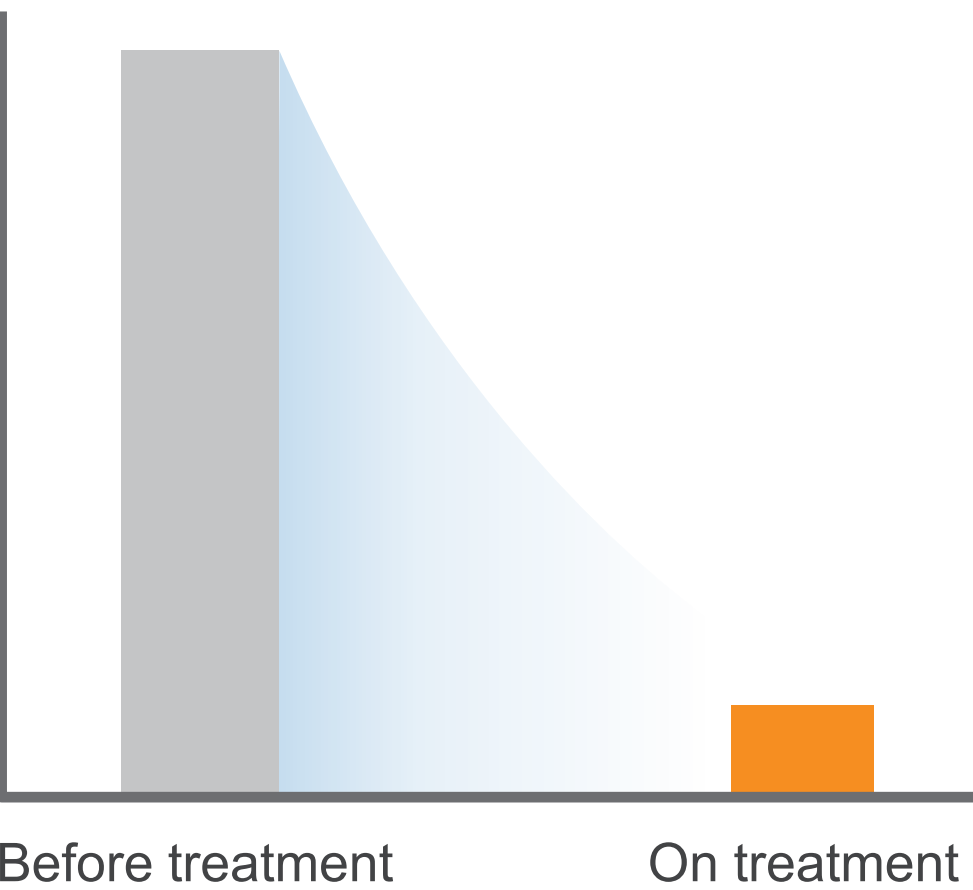


# Clinical & partnering success of the CBIO protease platform



## Marzeptacog alfa (activated)

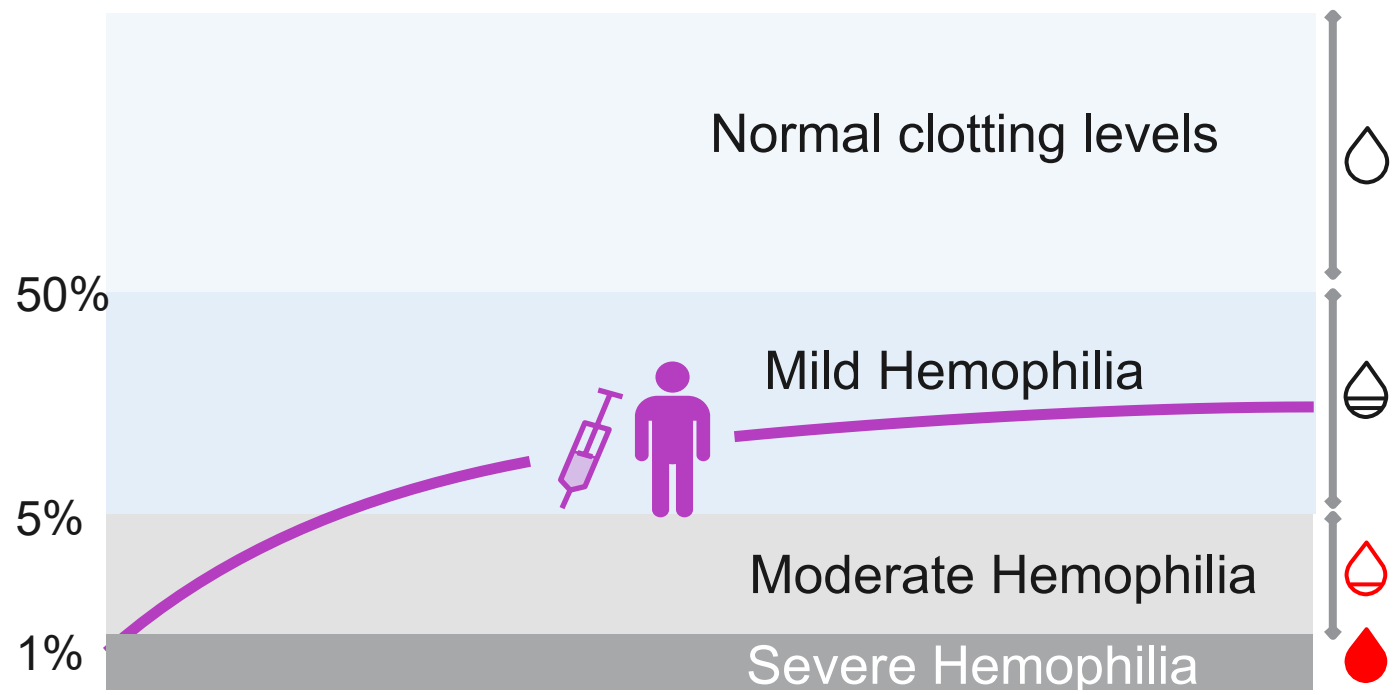
90% reduction  
in annualized bleed rate



✓ Engineered  
rFVIIa protease

## Dalcinonacog alfa

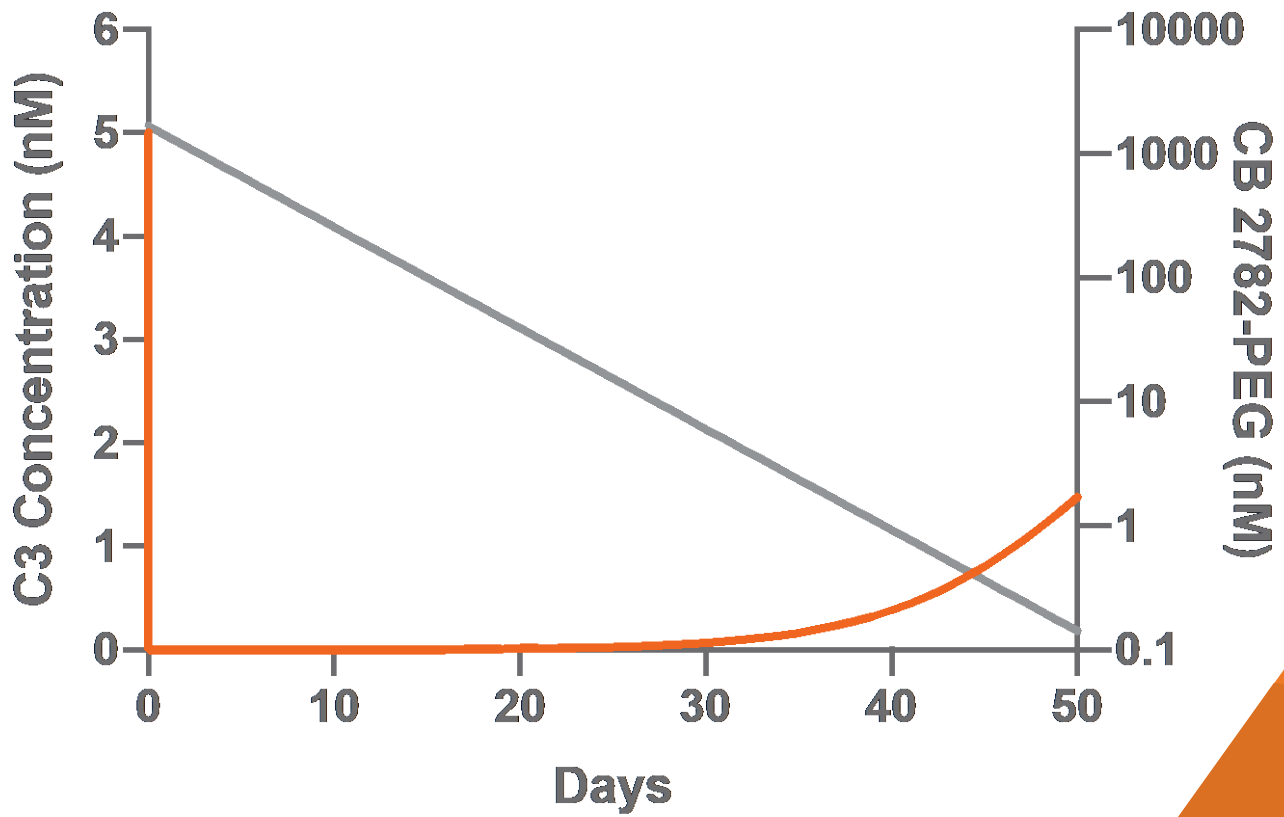
Achieved sustained  
& high target levels of FIX



✓ Engineered  
rFIX protease

## CB 2782-PEG Biogen

Best-in-class profile for dry AMD  
Extended pharmacodynamics



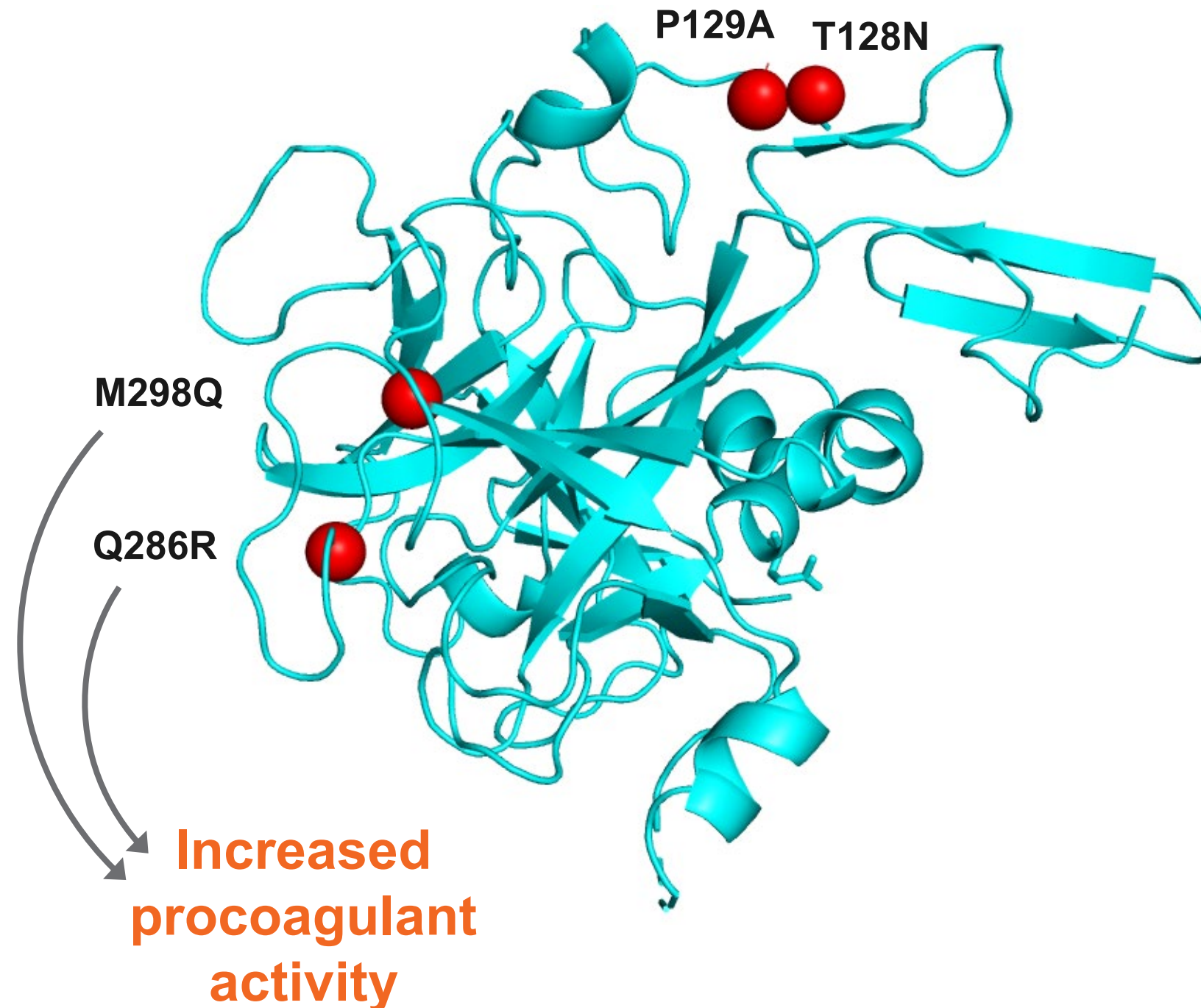
✓ Novel  
C3 degrader





# Marzeptacog alfa (activated) – MarzAA: SQ 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**

- + 46 patients treated including: single dose IV, up to 3 SQ doses/day, & daily SQ up to 97 days – no ADA

## **FDA Fast Track designation for treatment of episodic bleeding in Hem A or B with inhibitors**

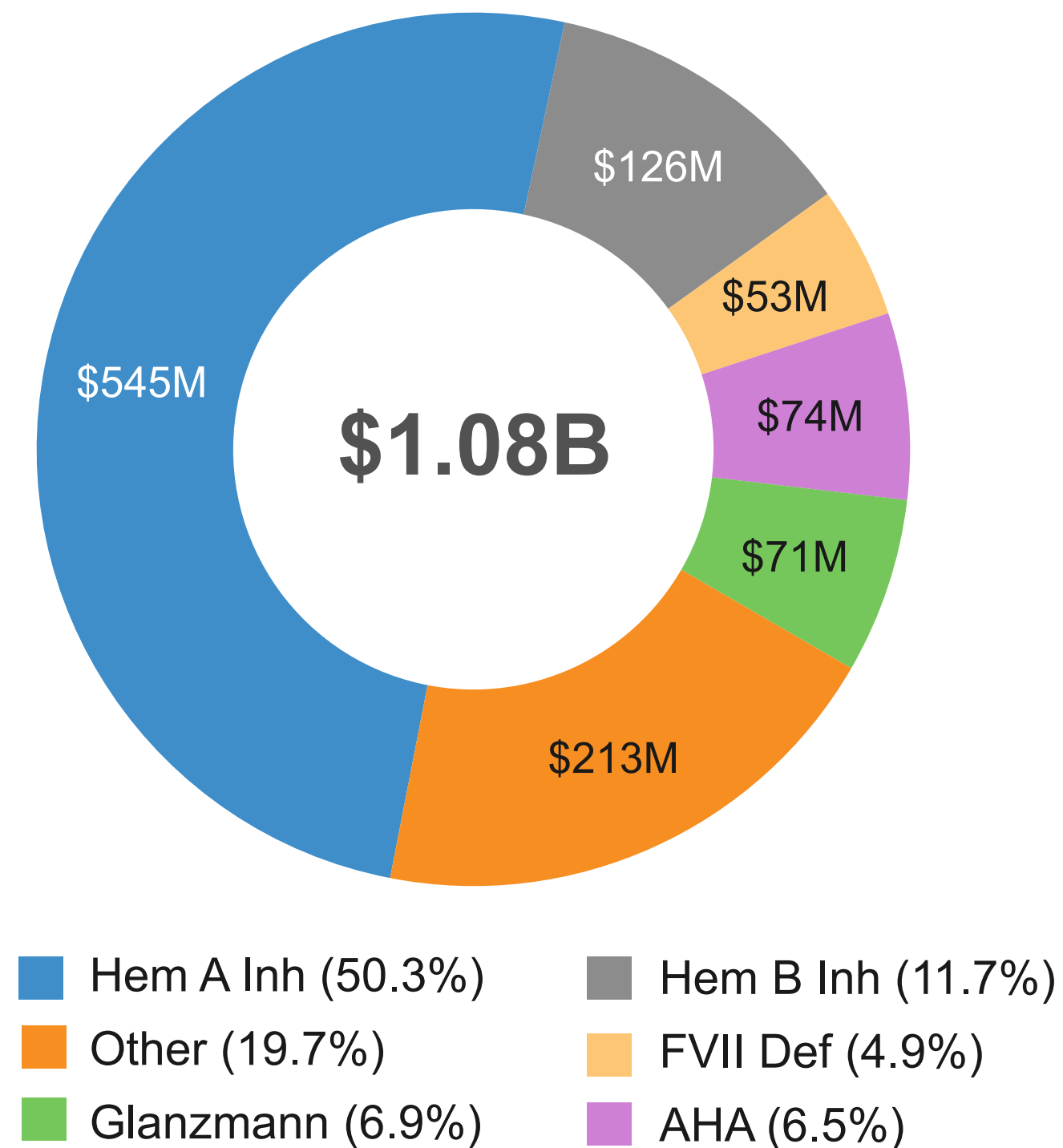
- + Granted on 2 December 2020





# SQ MarzAA is a large commercial opportunity

## Global NovoSeven sales breakdown by indication (2020)

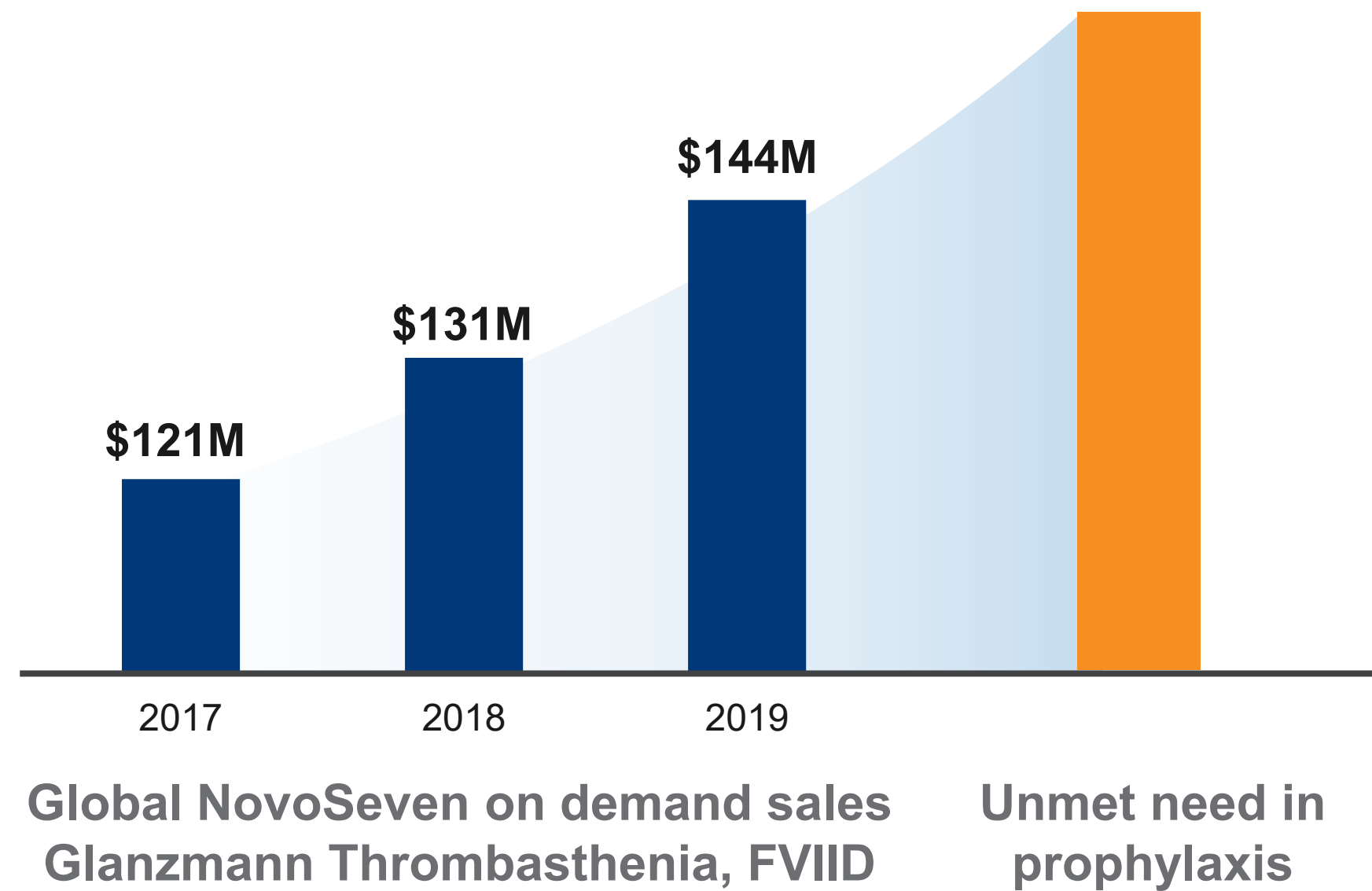


## SQ MarzAA has a superior profile

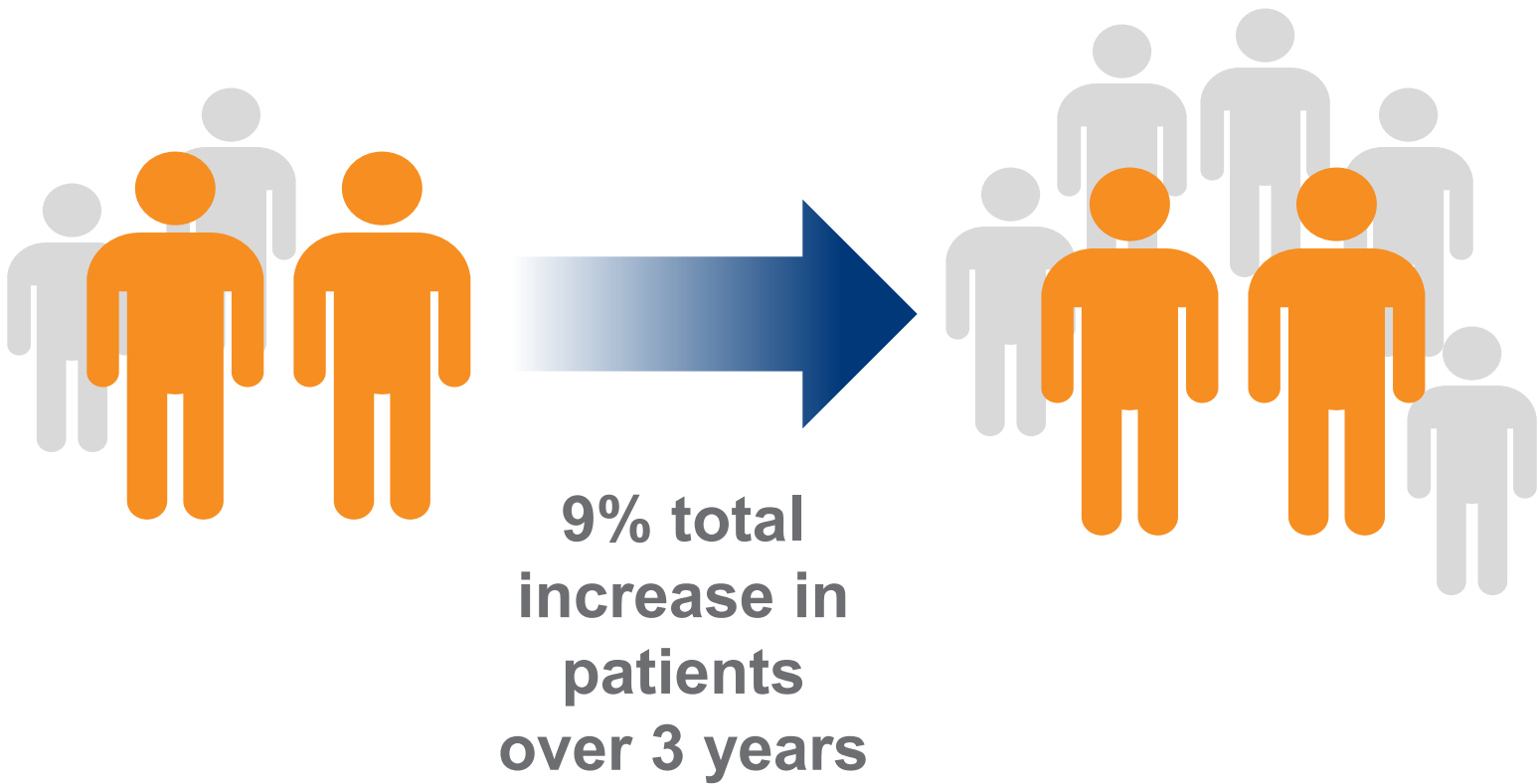
- ✓ Faster & easier to administer vs N7 dosed every 2 hours IV until hemostasis
- ✓ MarzAA SQ half-life ~8x longer than N7
- ✓ Potential to control rebleeding
- ✓ Can be combined with Hemlibra *in vitro* without increased thrombogenicity
- ✓ Ideal for pediatrics and patients with venous access issues
- ✓ Prophylaxis efficacy demonstrated in P2

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

# MarzAA could be the first prophylaxis for Glanzmann & FVIID



Growing number of Glanzmann Thrombasthenia and FVIID patients treated with NovoSeven



Source: Catalyst Biosciences, Adivo Associates Market Research, Data on file. \*Note: 2019 estimates Treated patients may be counted multiple times as patients may have multiple bleeding events per year needing factor treatment

# Unmet need in treatment of a bleed



## NovoSeven



- + Patients reported needing an average of **6 hours and 3 infusions** of NovoSeven to resolve bleeds
- + Some bleeds take longer than 72 hours to resolve<sup>1,2,3</sup>

**Current bypass agents require multiple infusions over the course of hours**

## MarzAA



- + MAA-102: PK MarzAA levels support SQ ToB
- + Target levels are **rapidly achieved**
- + Target levels can be maintained for 18 hours with a single SQ dose of 60 µg/kg

**Clinical PK MarzAA levels support SQ ToB**

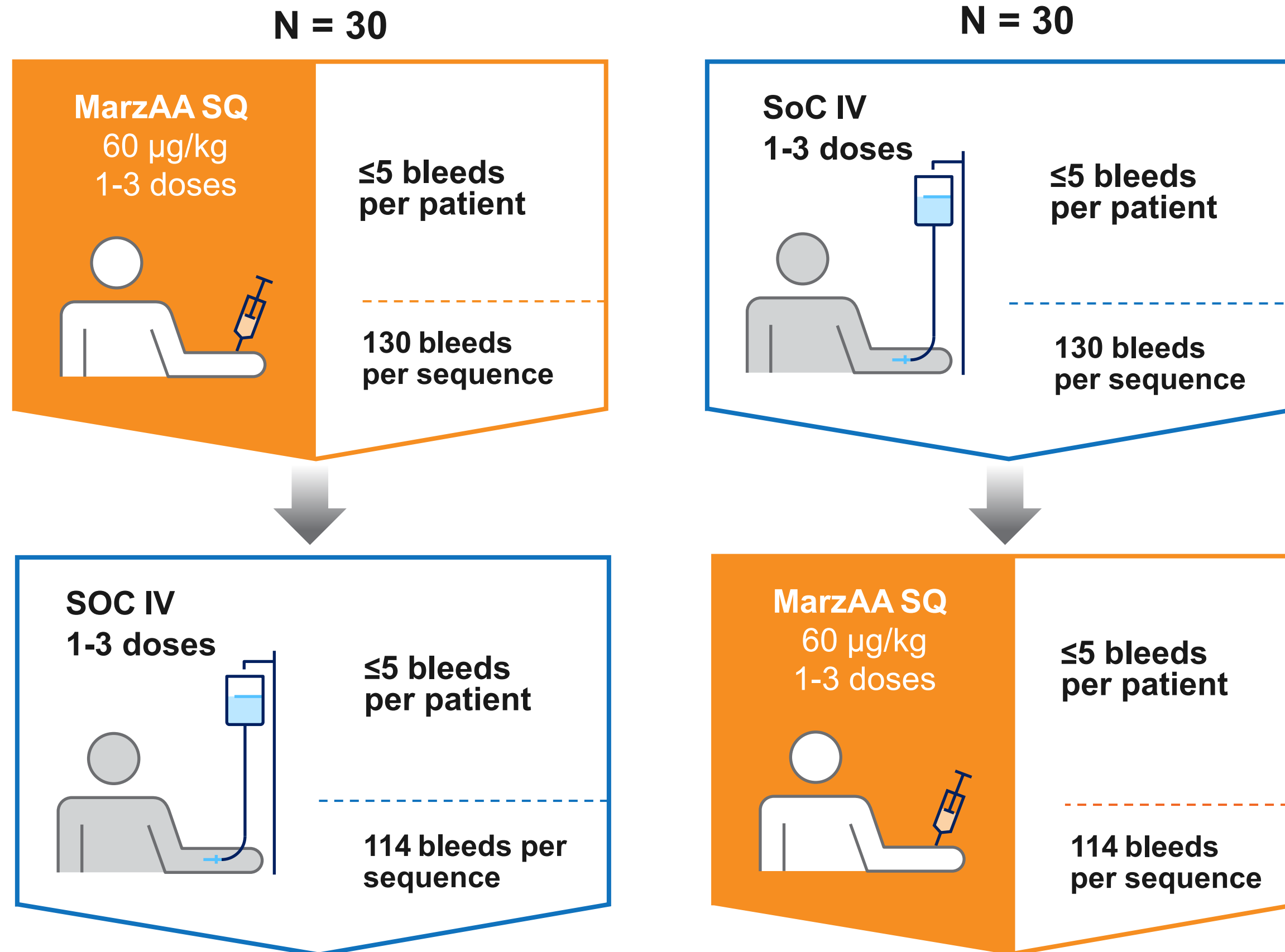
Source: <sup>1</sup>NovoSeven PI Rev 7/2020; <sup>2</sup>Adivo Associates market research; <sup>3</sup>Catalyst Biosciences market research; Data on file; Neuman *et al.* ISTH 2020





# 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 at 24 h

- **Secondary endpoints**

Time to bleed resolution;  
number of doses; rescue meds

- **Safety**

Adverse events, anti-drug  
antibodies (ADA); thrombosis

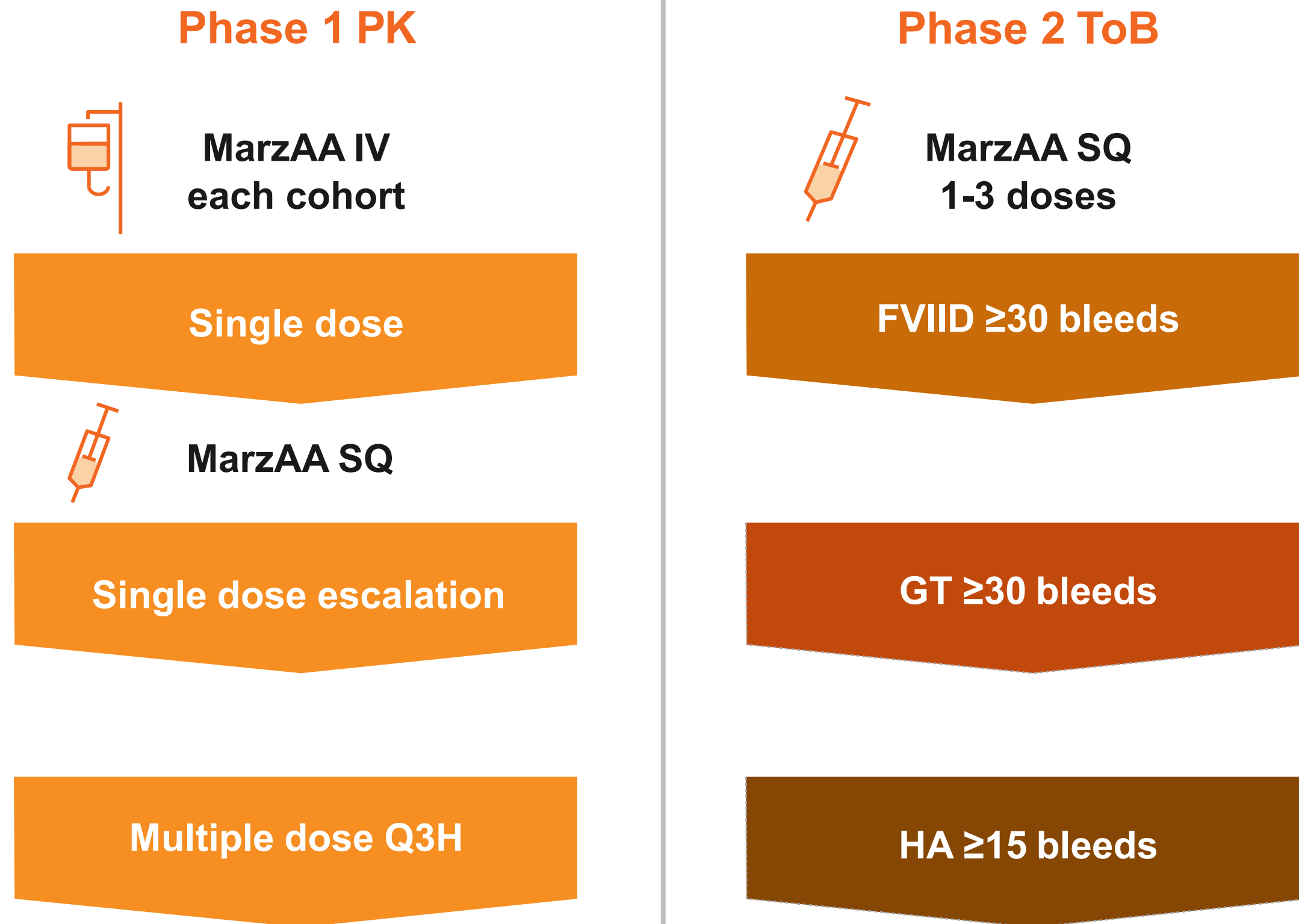
- **Statistics**

- + **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 endpoint:**

Pharmacokinetics

**Secondary endpoint:**

Pharmacodynamics

- **Phase 2 ToB**

**Primary endpoint:**

Hemostatic efficacy at 24 hours

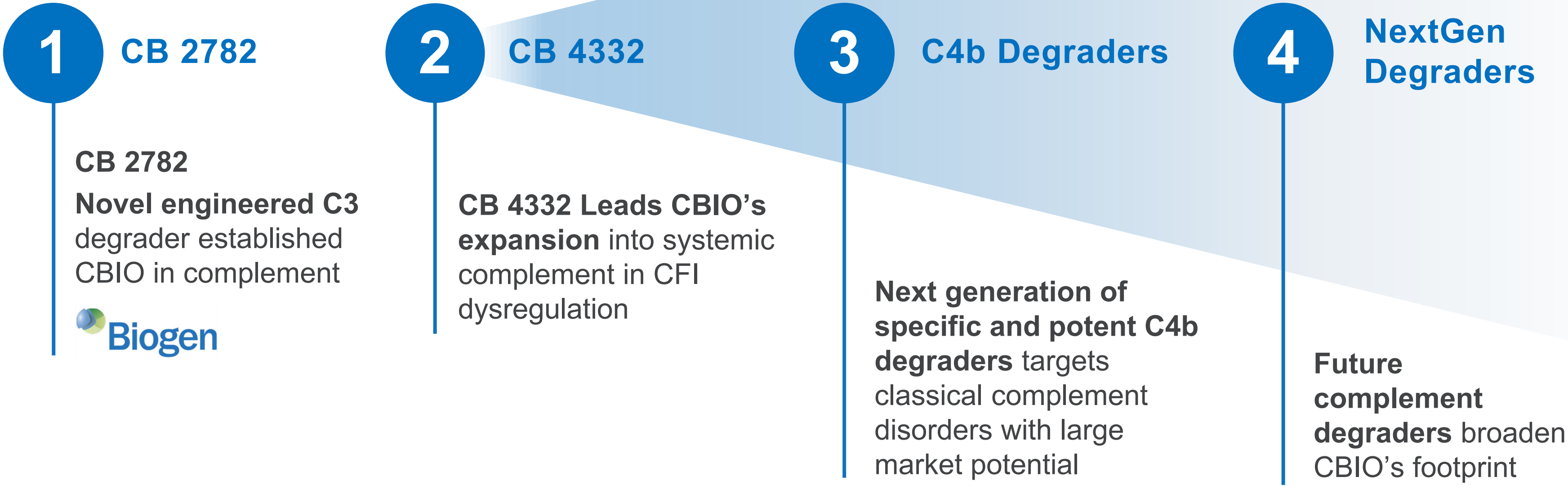
**Secondary endpoints:**

Effective hemostasis at successive timepoints; doses needed; rescue meds

**Safety:**

Adverse events and ADA

# CBIO's complement pipeline

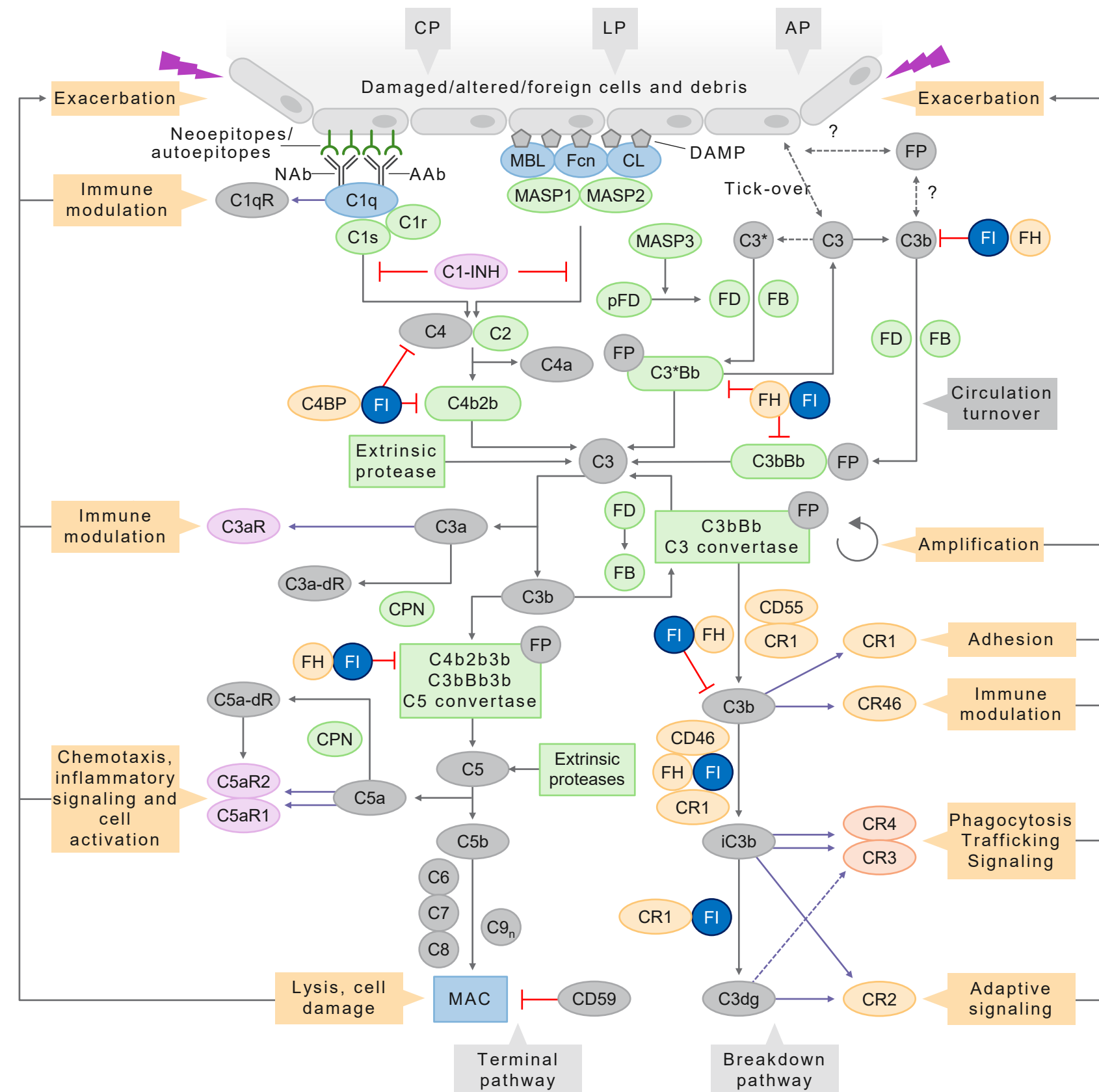






# Complement is a perfect fit to develop protease therapeutics

## The complement pathway is driven by a protease cascade



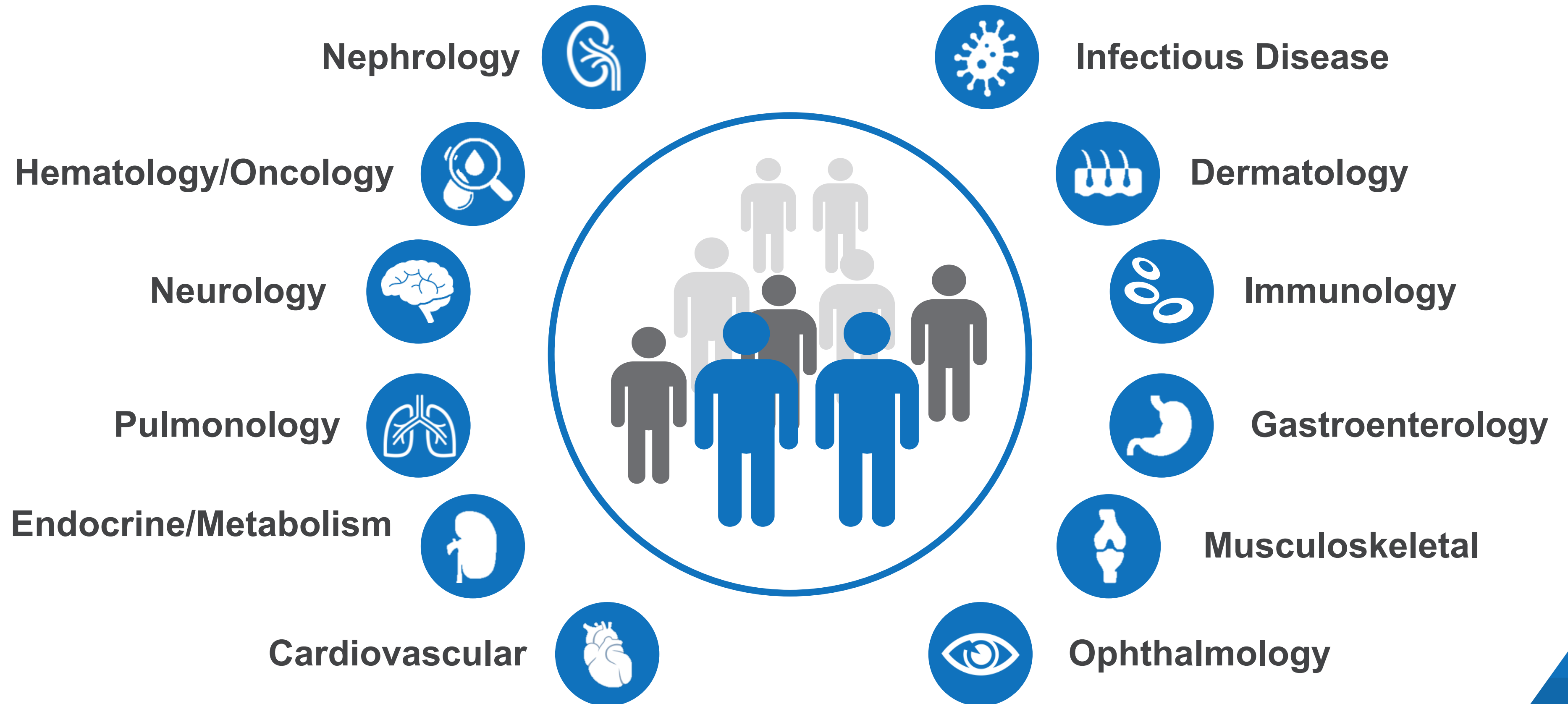
**80%**  
of the complement  
cascade is regulated  
by proteases

Reference: Figure adapted from Mastellos *et al.*,  
Clinical promise of next-generation complement  
therapeutics. Nature Reviews. 2019



# Complement plays a critical role in many diseases

**Late-stage complement therapies projected to achieve net sales over \$12B by 2026**

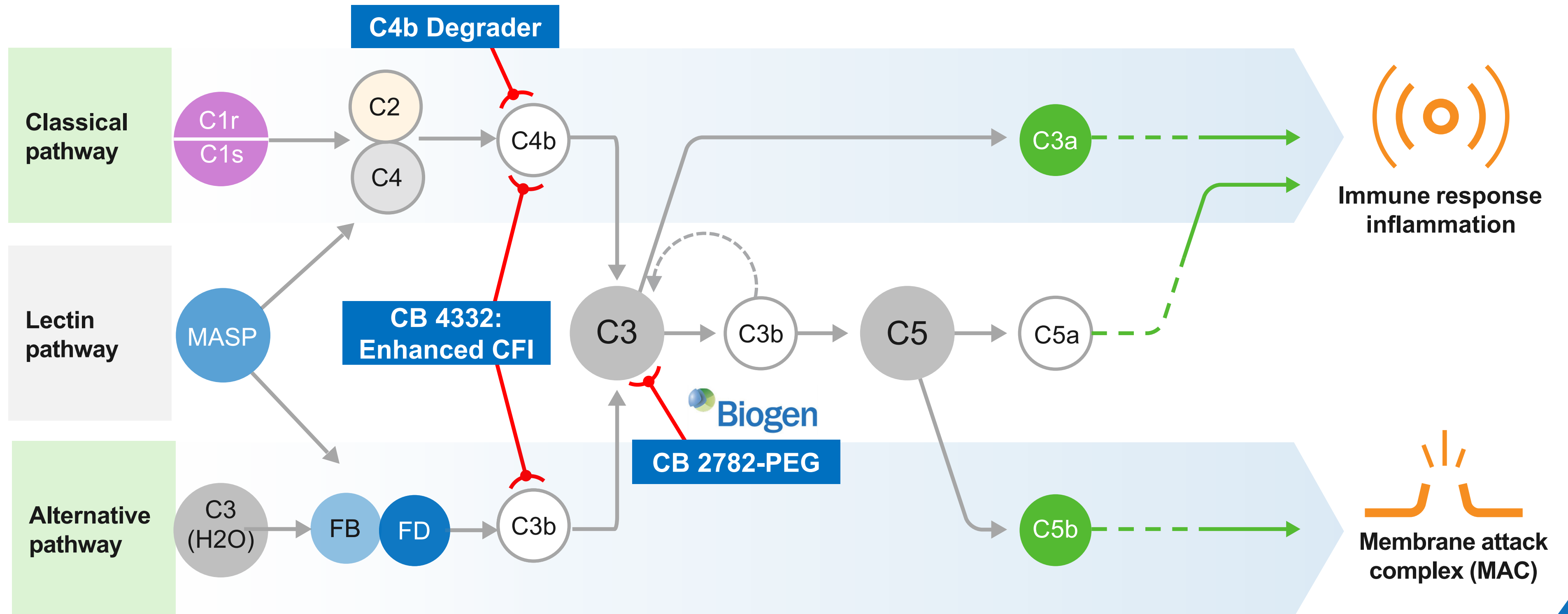


References: Globaldata consensus net sales forecast 2020

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# CBIO is taking a targeted approach to complement regulation

## Engineered proteases address the root cause of the pathology



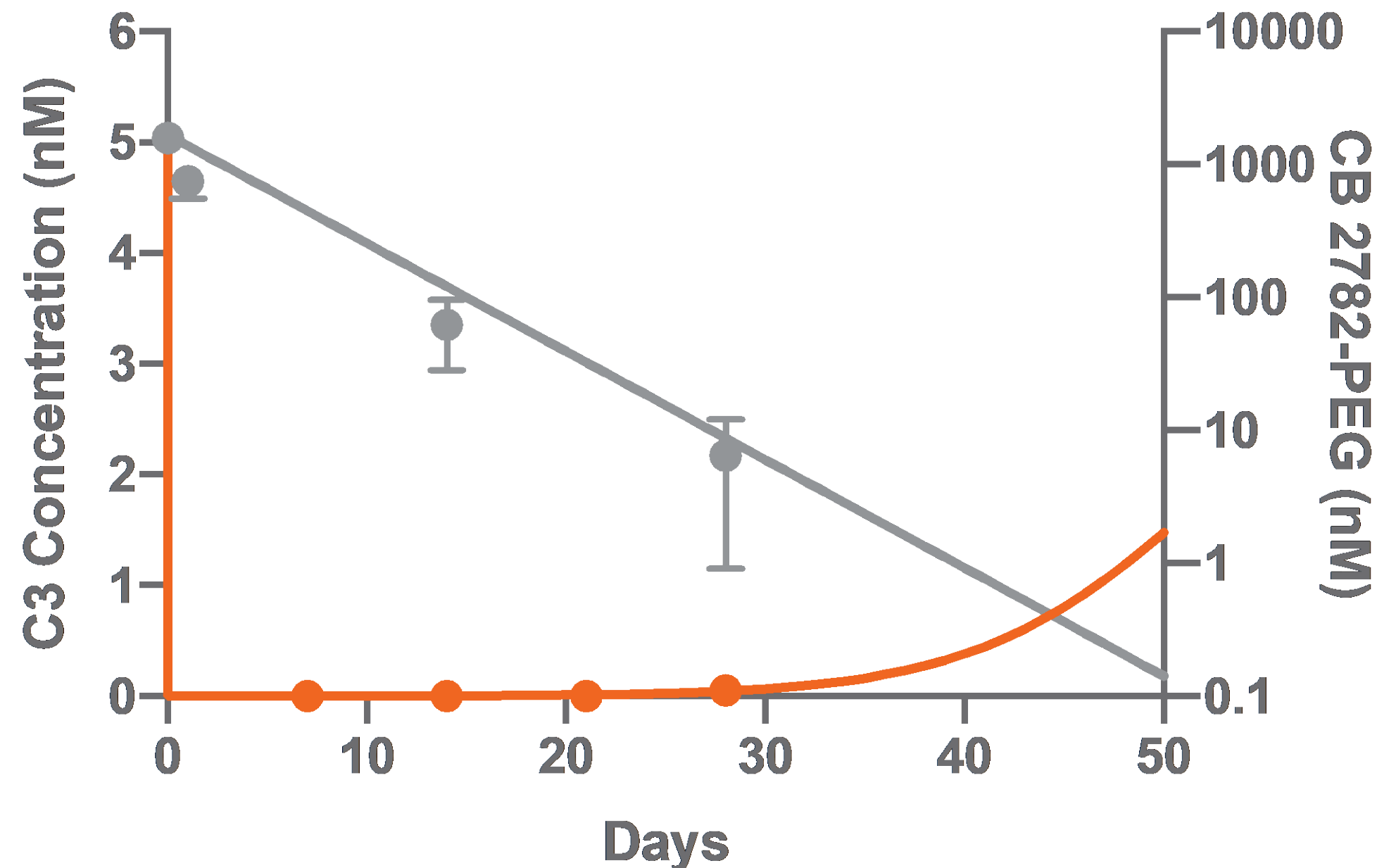
- + Current C5 blockade therapies do not address disease root cause leading to inadequate disease control
- + The catalytic power of proteases provides advantages over small molecules and antibodies



# Protease advantage demonstrated *in vivo*

## CB 2782-PEG – designed as a best-in-class C3 degrader in dry AMD

CB 2782-PEG degrades C3 levels in the eye for at least 28 days in a non-human primate model



### Catalytic advantage of proteases

- + One therapeutic molecule neutralizes 1000s
- + Fast & potent response
- + Extended pharmacodynamic effect
- + Can activate or degrade therapeutic targets
- + Engineered novel protein degraders “sweep away” difficult to drug targets



# CB 2782-PEG long acting anti-C3 protease

## Geographic atrophy in dry AMD can result in blindness

- + Advanced stage of dry age-related macular degeneration (dAMD)
- + dAMD affects ~1M people in the US & >5M WW, no currently approved therapy
- + Global market ~ >\$5B
- + C3 is a clinically validated target (randomized P2) for the treatment of dAMD



## Best-in-class C3 degrader for dry AMD

- + Generated from Catalyst's proprietary **protease engineering platform**
- + Potent, selective & long acting, degrades C3 into inactive fragments
- + Preclinical NHP PK & PD data\* predict **best-in-class** human intravitreal **dosing 3 or 4 times a year**

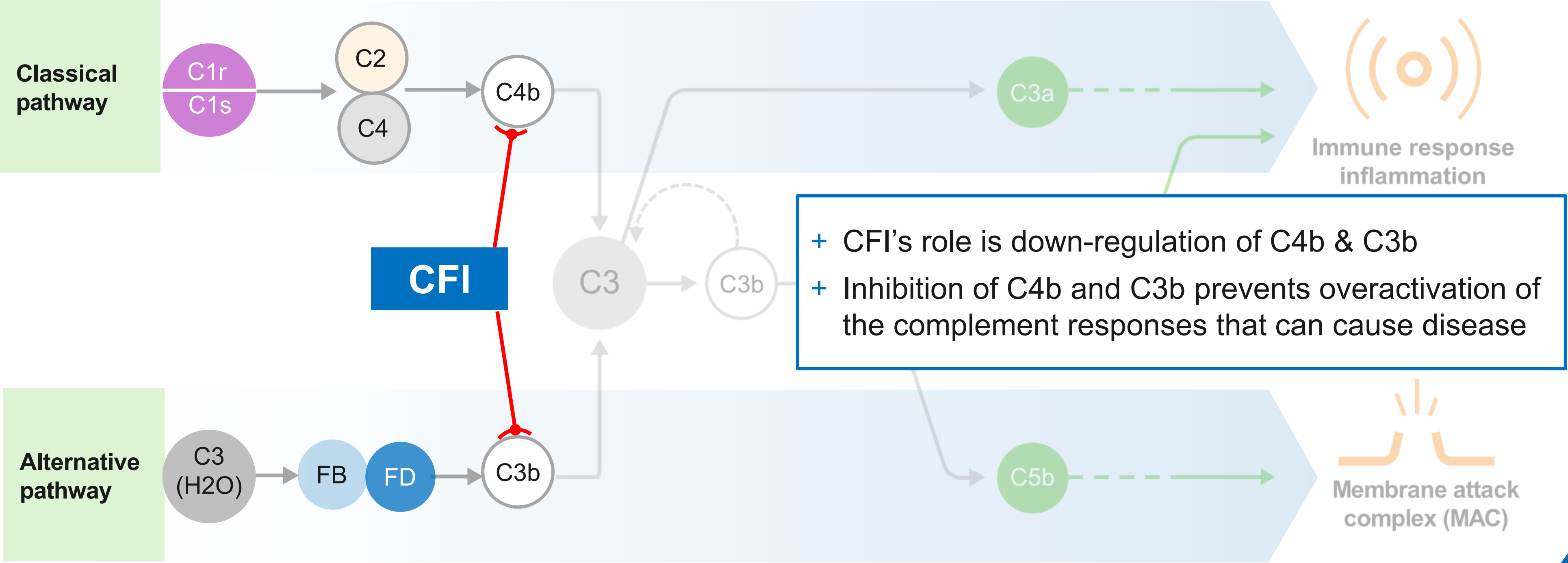
## Biogen collaboration

- + \$15M upfront, up to \$340M in milestones and tiered royalties up to low double digits
- + Catalyst: fully funded pre-clinical and manufacturing activities
- + Biogen: IND-enabling activities, WW clinical development & commercialization



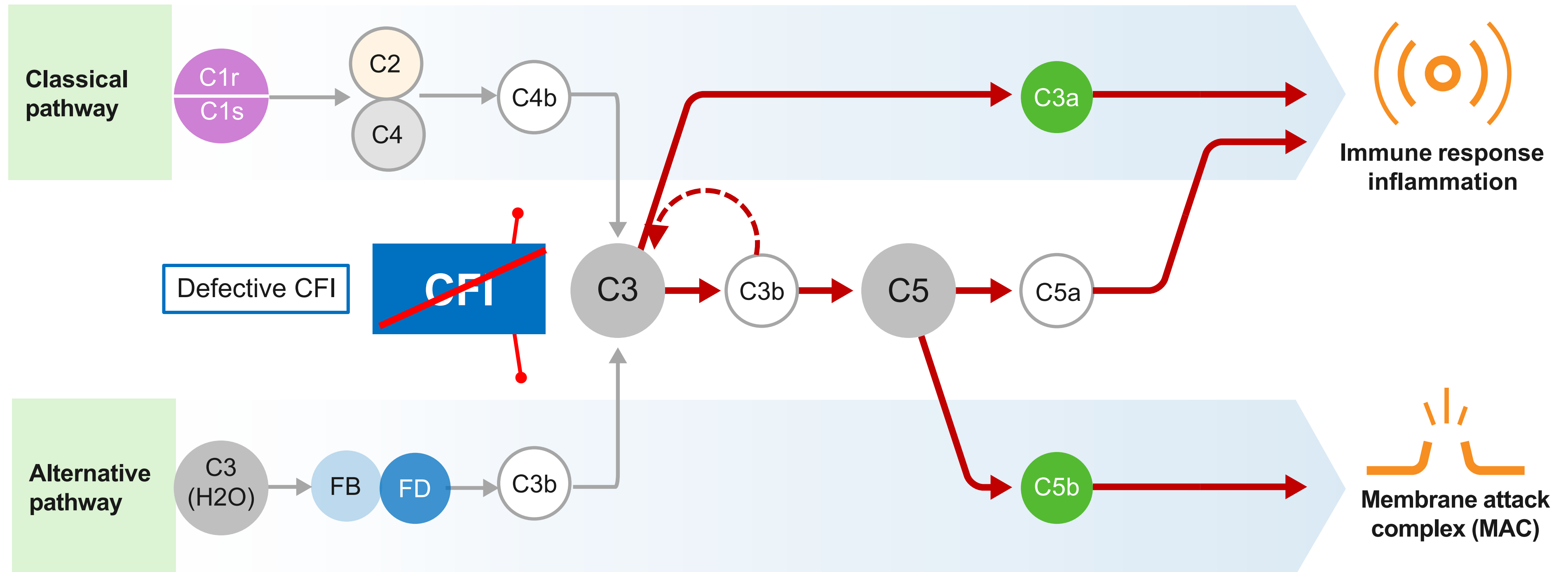
\*Furfin *et al.* ARVO 2019

# Normal CFI: Key central regulator of complement activation





# CFI dysregulation: Lack of proteolytic CFI activity causes disease

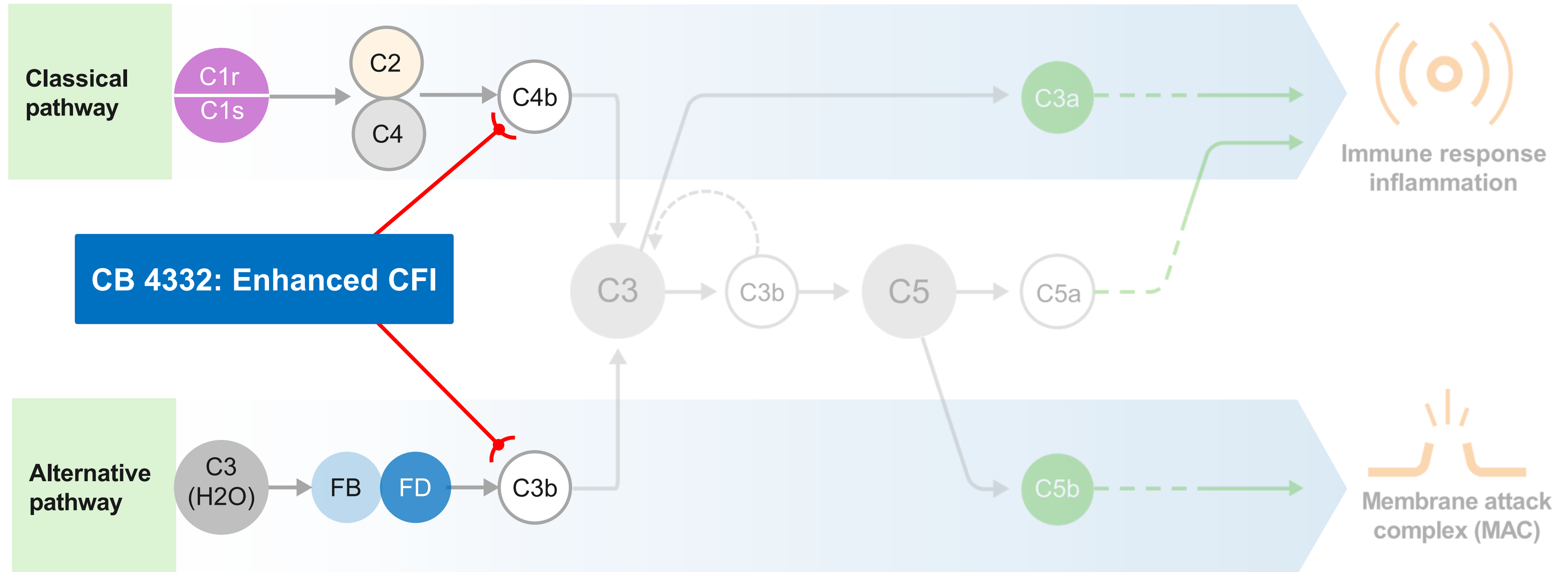


- + In patients with CFI mutations, C4b and C3b cannot be sufficiently regulated
- + Dysregulation leads to overactivation of the complement pathway and damaging immune responses



# CB 4332 – CBIO's enhanced CFI

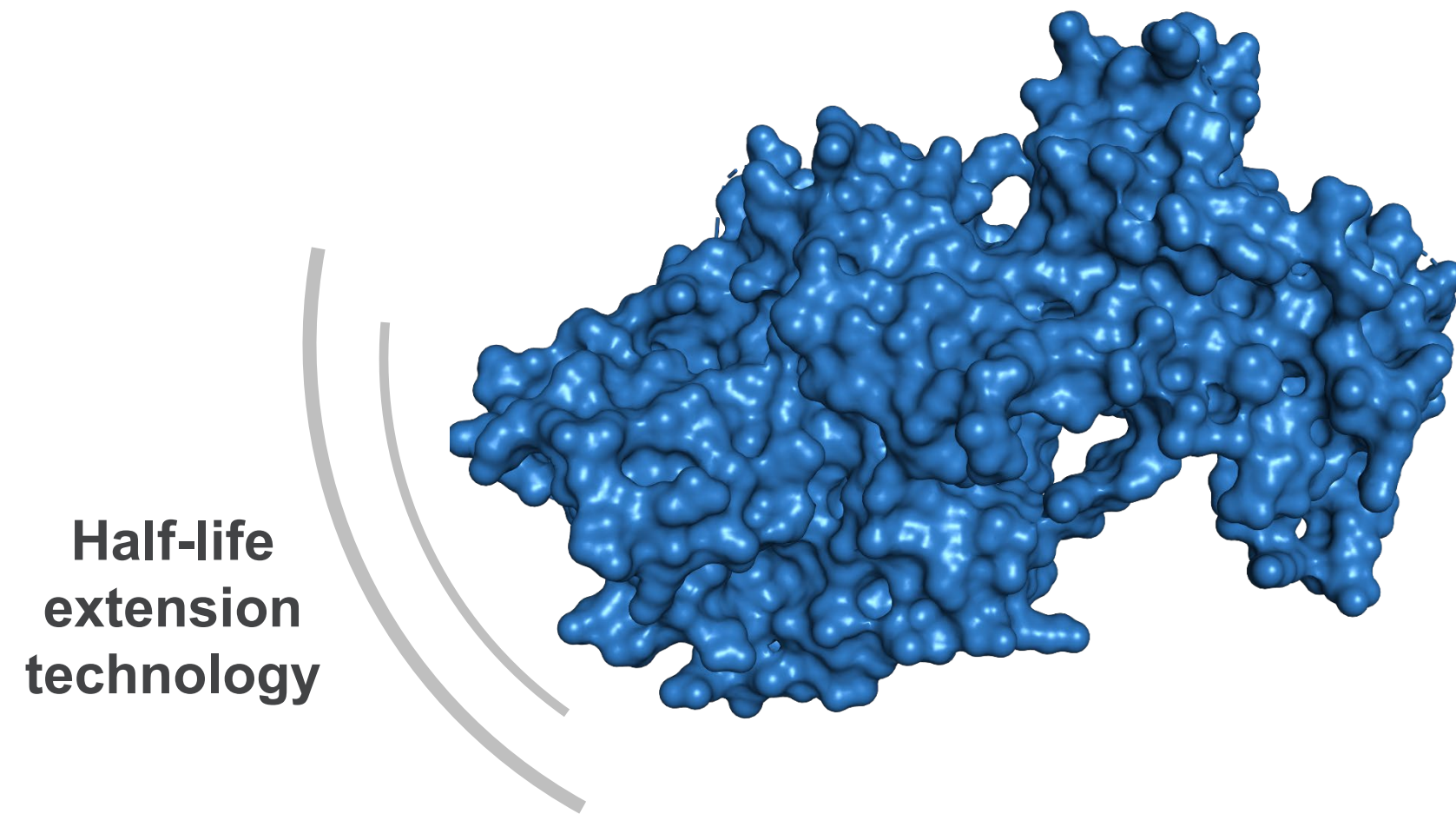
Specifically addresses the problem by restoring CFI regulation





# CB 4332: Enhanced Complement Factor I

## CBIO's next SQ development candidate to restore CFI regulation



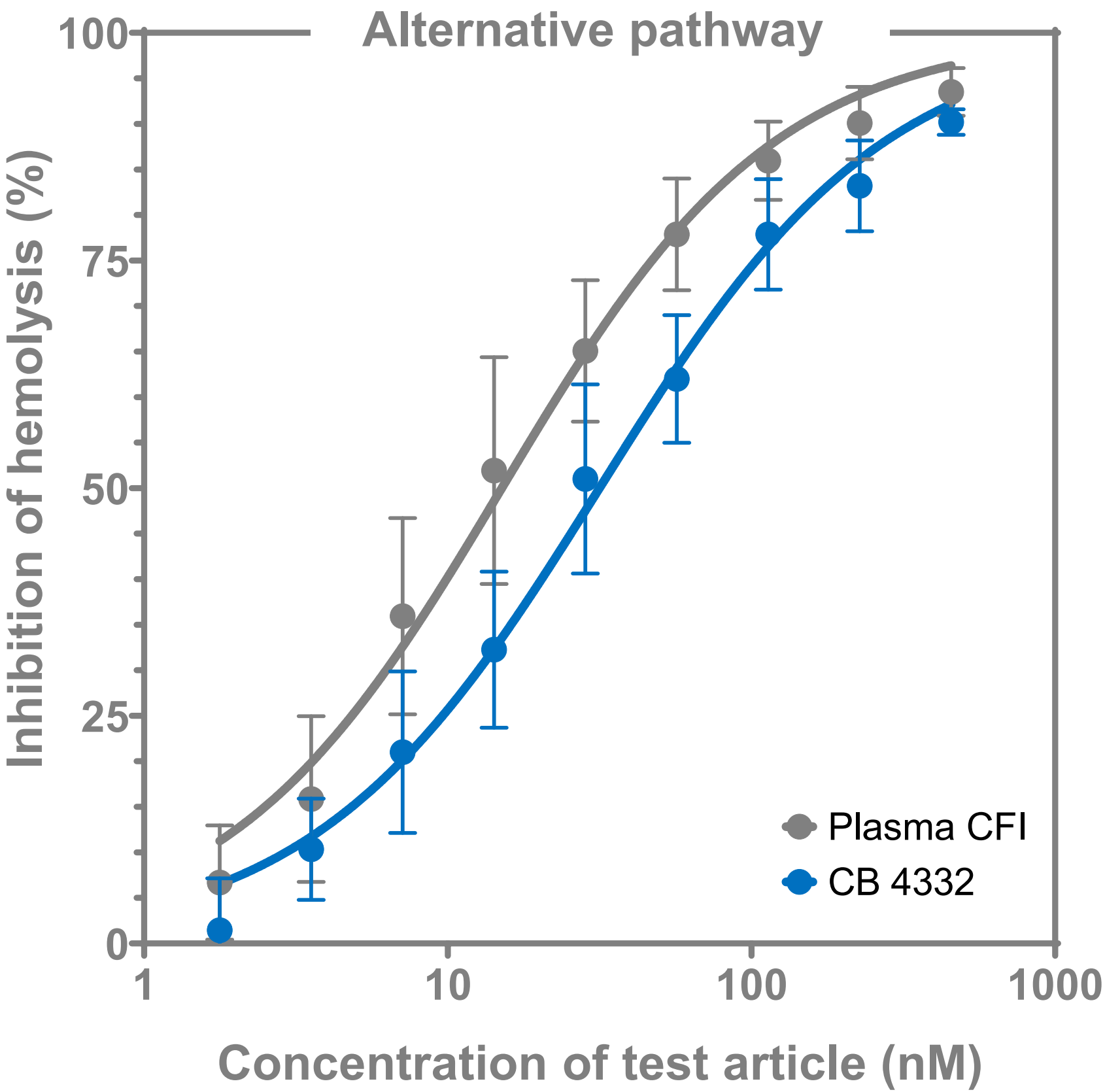
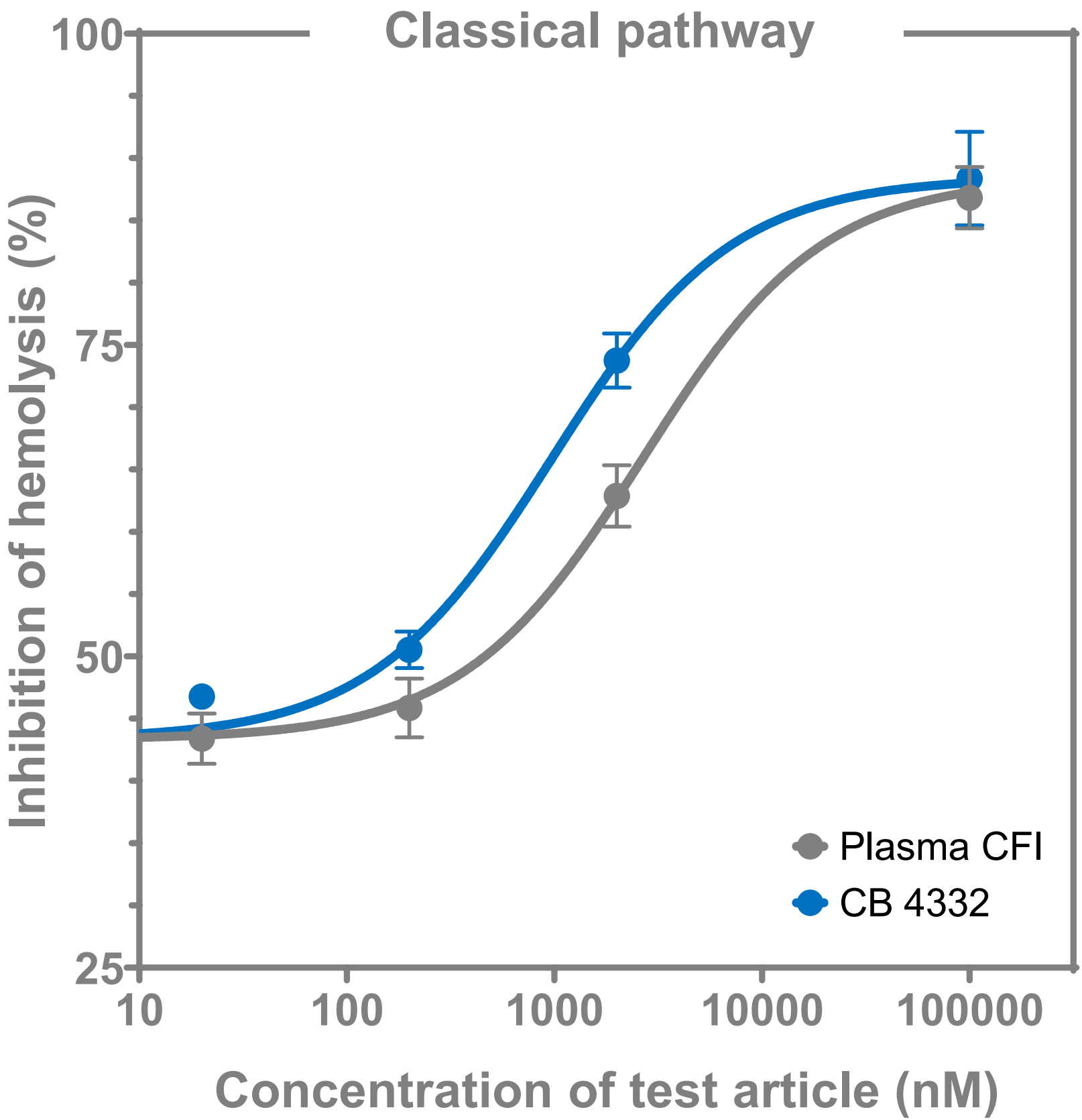
- + **Engineered for an extended half-life**
  - Once weekly SQ therapy – no PEG
- + **Full activity comparable to native CFI**
  - Classical and alternative pathway regulation
- + **Efficient high yield production process**

### Rationale & unmet need

- + **Restores normal complement system** in patients with dysregulated CFI
- + **No specific therapies exist** to correct CFI dysregulation
- + Targets population with **no treatment or who respond poorly to current treatments**<sup>1,2</sup>
- + **Genetically defined patient population**

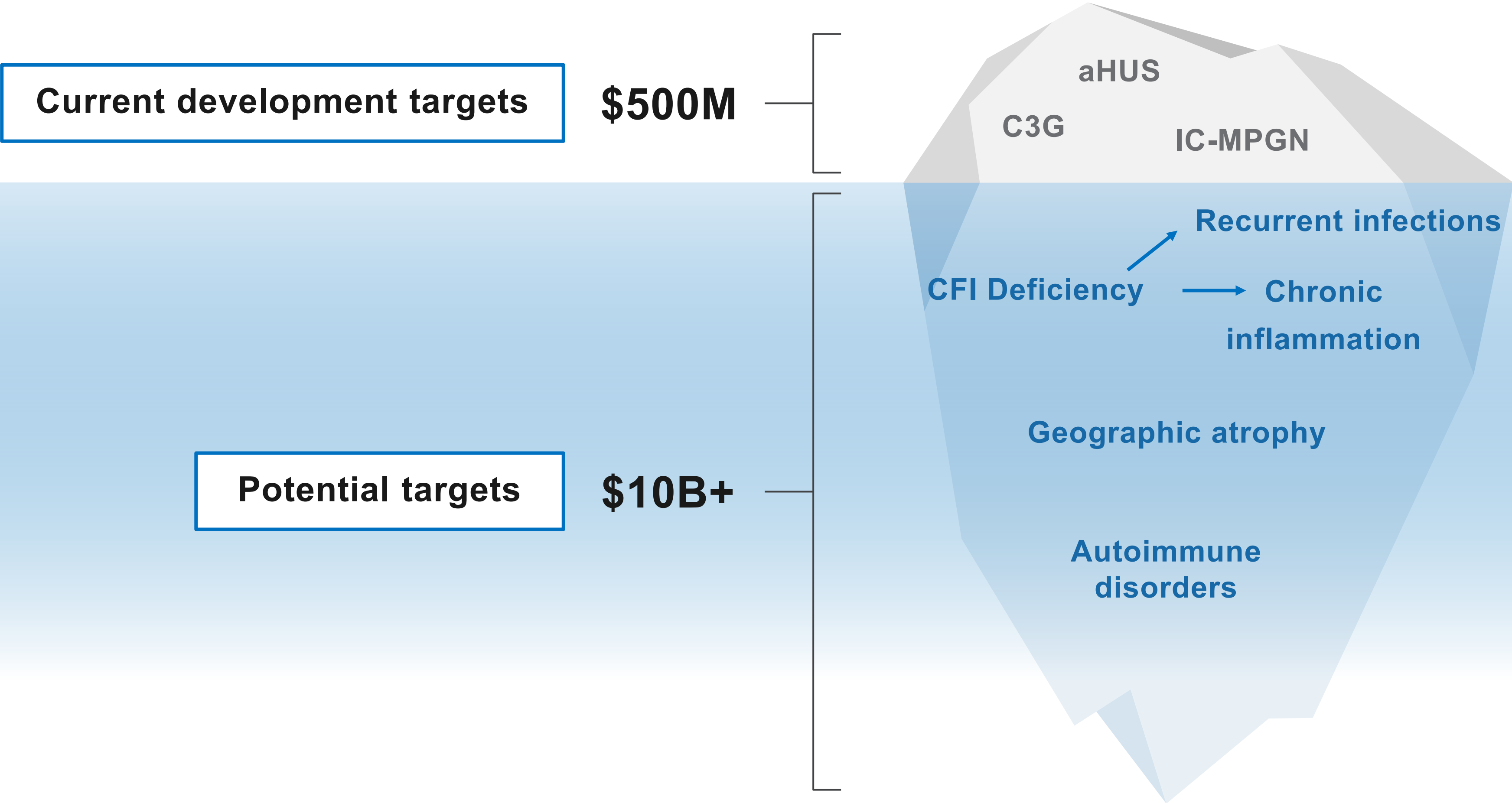
References: <sup>1</sup>Bienaimé *et al.* Kidney Int. 2010; <sup>2</sup>Ferreira *et al.* Nefrologia. 2016; Note: CFH = Complement factor H; Structural model based on PDB 2XRC.

# CB 4332 & plasma CFI perform similarly in human serum





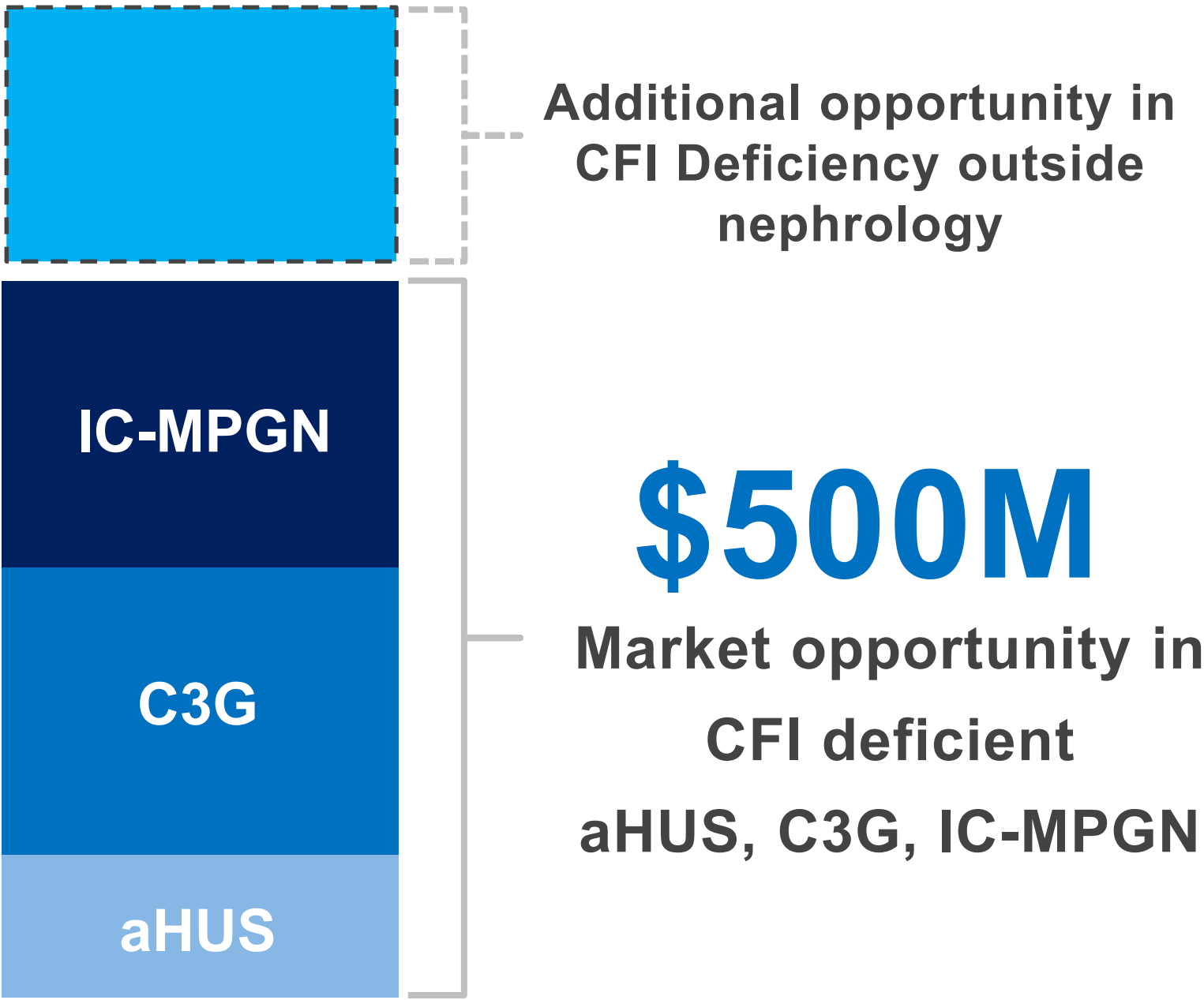
# Diseases with CFI mutations have tremendous potential



# CB 4332 initial market opportunity



## US / EU5 market opportunity



## Unmet needs

Significant opportunity for patients with CFI mutations

- 0 Specific systemic therapies in development for patients with dysregulated CFI
- 0 Therapies addressing the root cause of disease
- 0 Approved treatments for C3G, IC-MPGN, CFID

**CFI mutations are significant drivers of disease**

Note: aHUS = atypical Hemolytic Uremic Syndrome, C3G = Complement 3 Glomerulopathy, IC-MPGN = Immune-Complex Membranoproliferative Glomerulonephritis, CFID = Complement Factor I Deficiency

References: Bresin *et al.* JASN. 2013; Fremeaux-Bacchi *et al.* ASN. 2013; Rui-Ru *et al.* Jour Rare Dis Res. 2018; Servais *et al.* Kidney Int. 2012; Iatropoulos *et al.* Mol Immunol. 2016; Hou *et al.* Kidney Int. 2014; Alba-Domiguez *et al.* J rare Dis. 2012. El Sissy *et al.* Front. Immunol. 2019; Shields *et al.* Front Immunol. 2019; Naesens *et al.* Jour Allergy & Clin Immunol. 2020. Yan *et al.* Clin Epi 2020; Smith *et al.* Nature Reviews. 2019; Noris *et al.* Clin J Am Soc Nephrol. 2010; CBIO KOL interviews



# CB 4332 – CFI dysregulation observational study

## Natural history of CFI deficient patients for subsequent CB 4332 treatment

### Screen

**Patients with recurrent bacterial infection, autoimmune, immune complex-mediated disease**

**Study / Observational Period (6 m)**

**≥ 24 Subjects (male/female)  
≥ 12 years of age identified in screening study**

### Follow-up

**End of Study**

**Planned Phase 1/2 Study**

- **Primary Objective**

Demonstrate the phenotypic manifestation of CFI deficiency in recurrent bacterial infection, autoimmune, immune complex-mediated disease as a prelude to a Phase 1/2 study

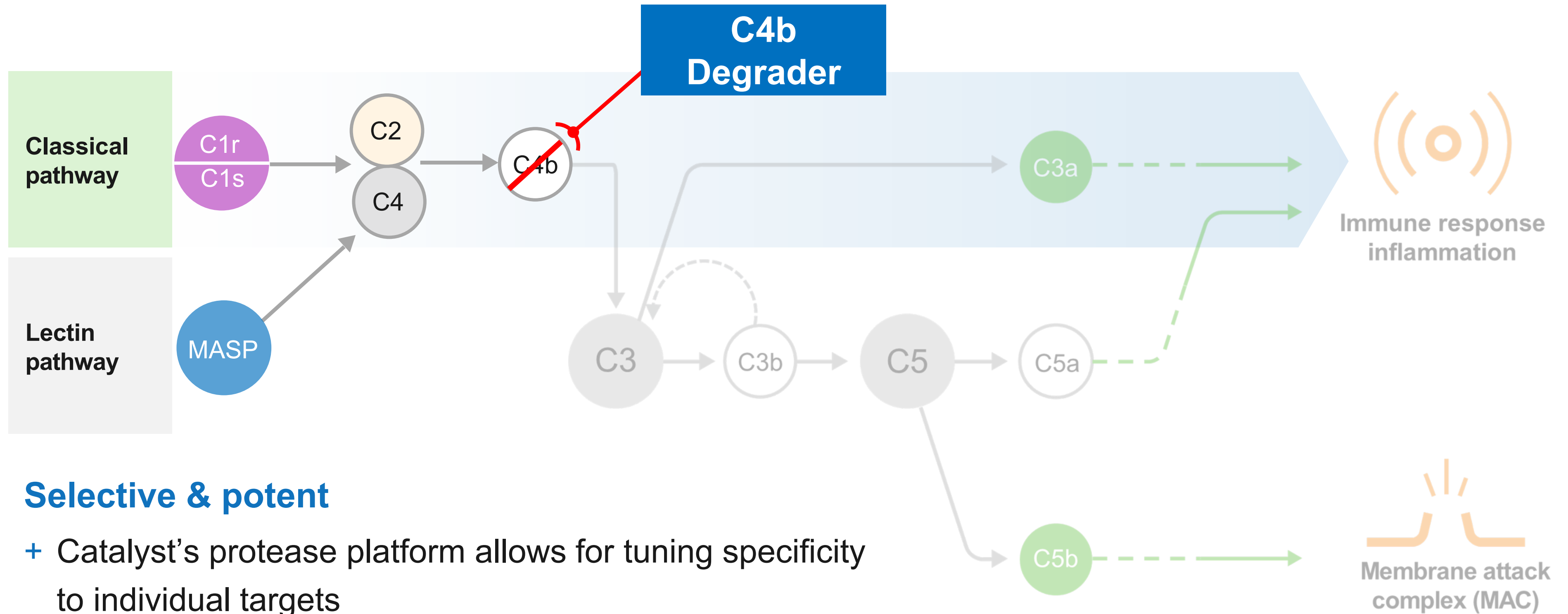
- **Secondary Objectives**

Monitor efficacy / disease status over time during SoC  
Monitor safety and tolerability of SoC  
Record dosing and compliance with SoC  
Monitor QoL measures

- **Timeline**

Observational stage to start enrollment mid-2021  
Global phase 1/2 in patients with CFI deficiency expected in 2022  
Intend to pursue an accelerated approval regulatory path

# CBIO C4b degrader complement therapy



## Selective & potent

- + Catalyst's protease platform allows for tuning specificity to individual targets
- + Leverages CB 4332 protease scaffold & efficient high yield production process
- + No competitors specifically targeting C4b or planning a weekly SQ injection
  - Approaches targeting C1q and C1s with antibodies require substantial & frequent IV dosing



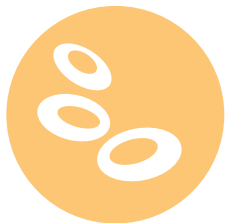


# C4b degraders target multiple high unmet need diseases

## US & EU5 patient opportunity



Nephrology



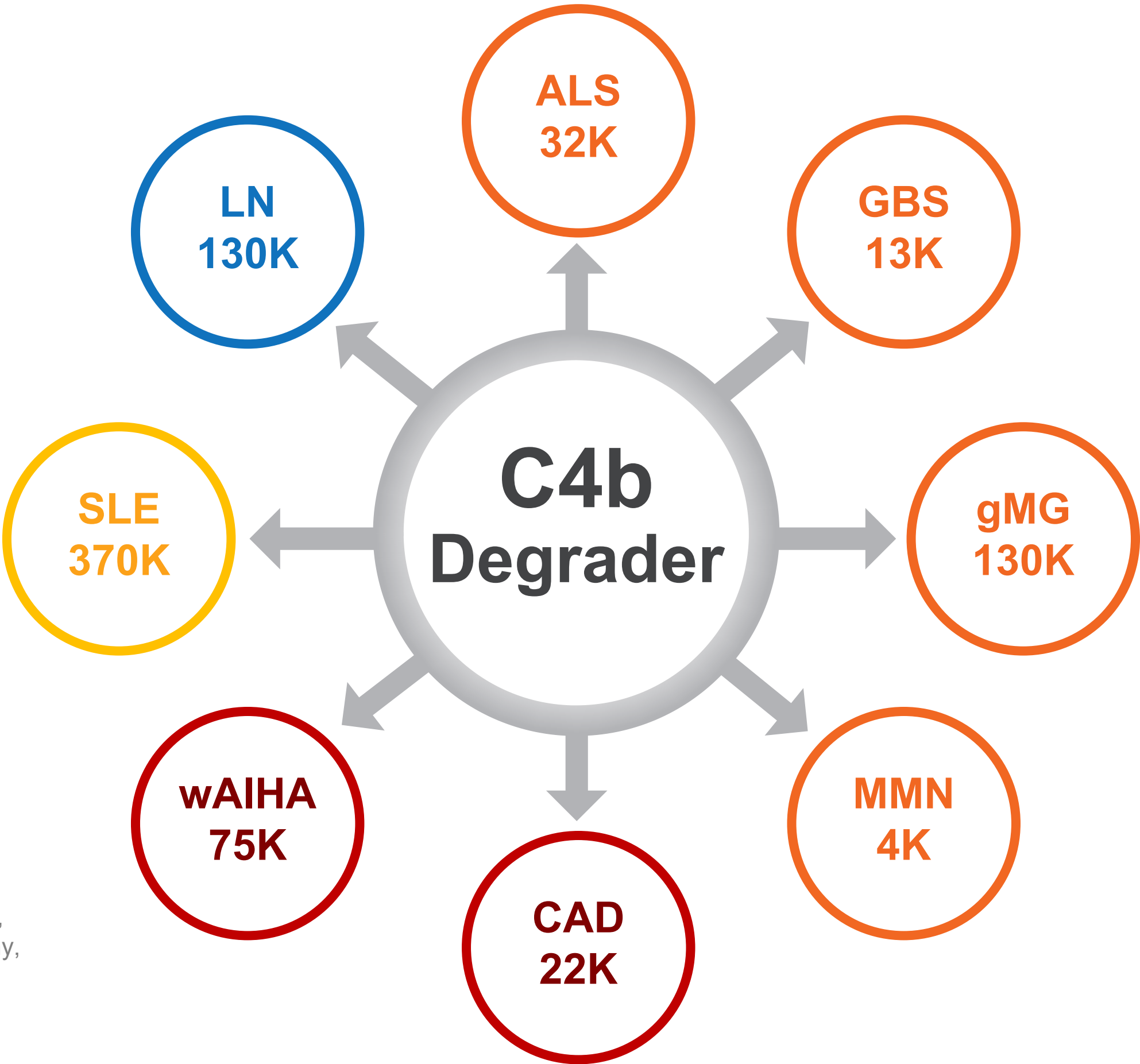
Immunology



Hematology

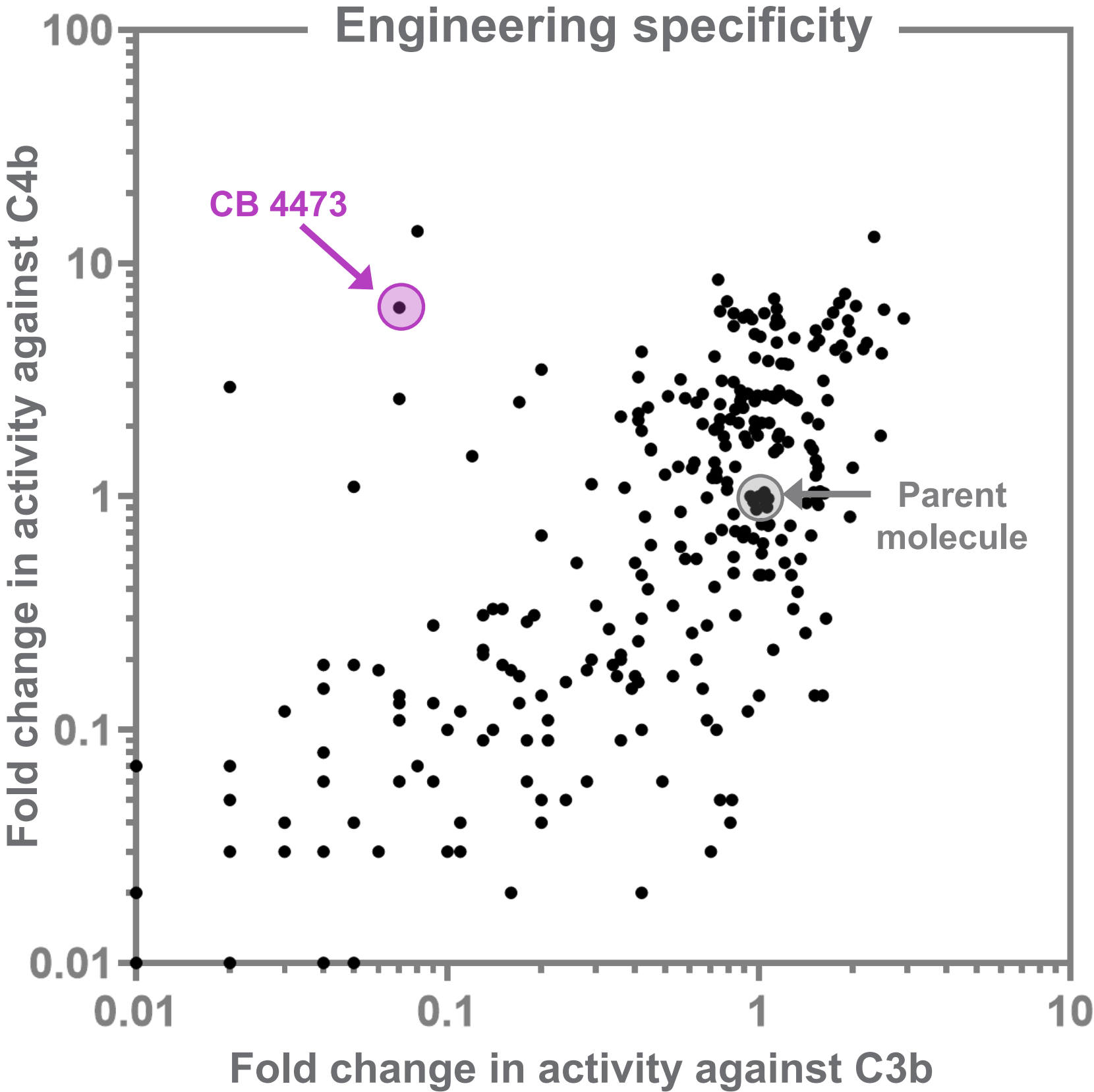
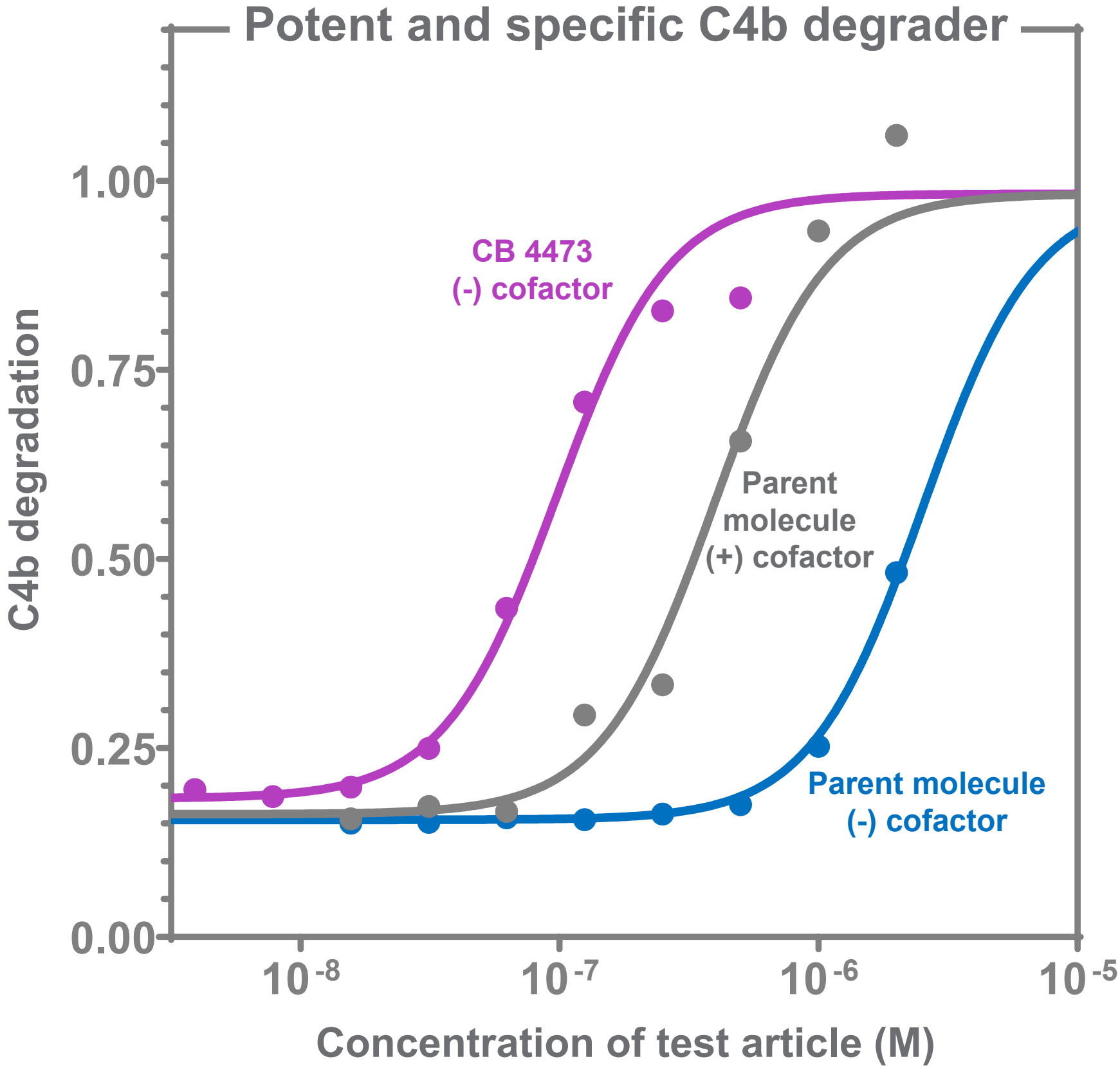


Neurology

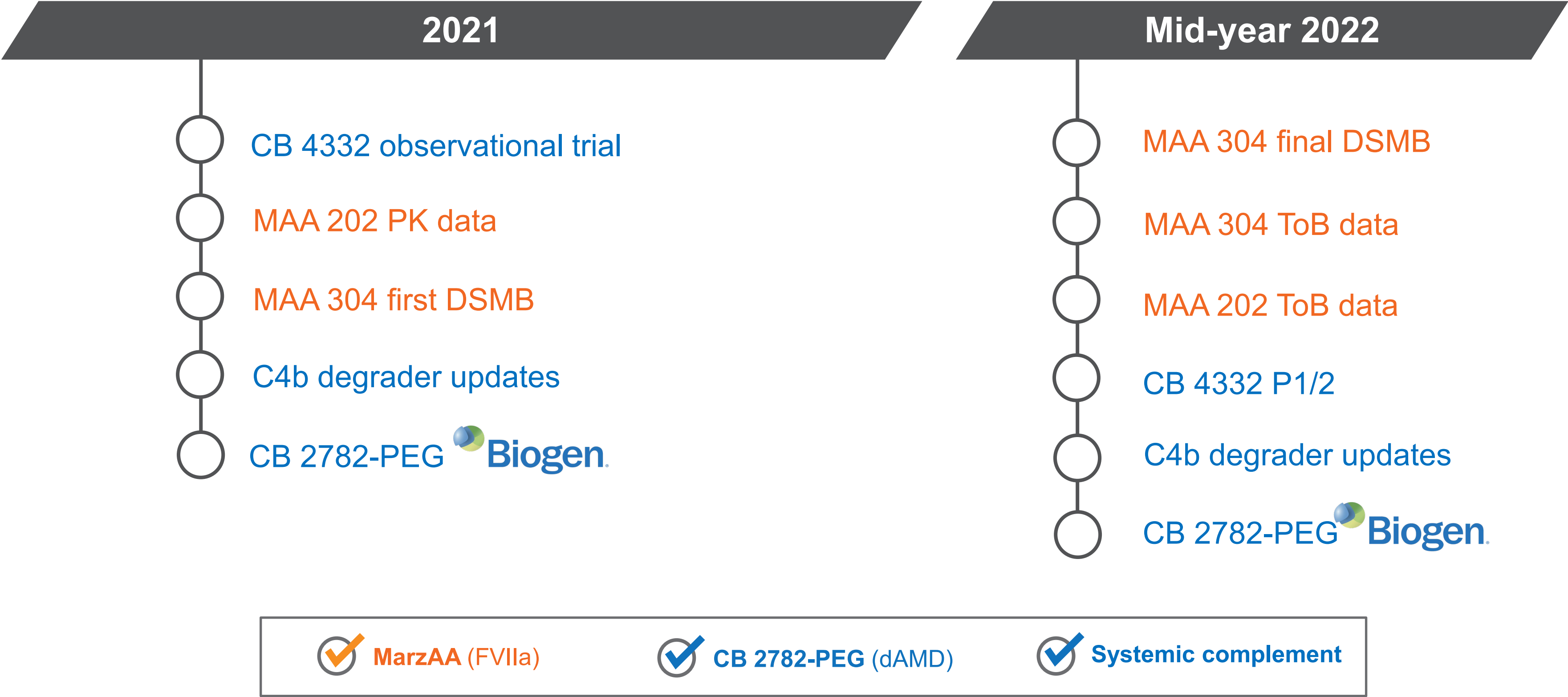


Note: ALS = Amyotrophic lateral sclerosis, GBS = Guillain-Barré syndrome, gMG = Generalized Myasthenia Gravis, MMN = multifocal motor neuropathy, CAD = Cold agglutinin disease, wAIHA = warm Autoimmune hemolytic anemia, SLE = Systemic lupus erythematosus, LN = Lupus Nephritis, References: Data on file

# CB 4473 demonstrates engineered C4b potency & specificity



# Milestones



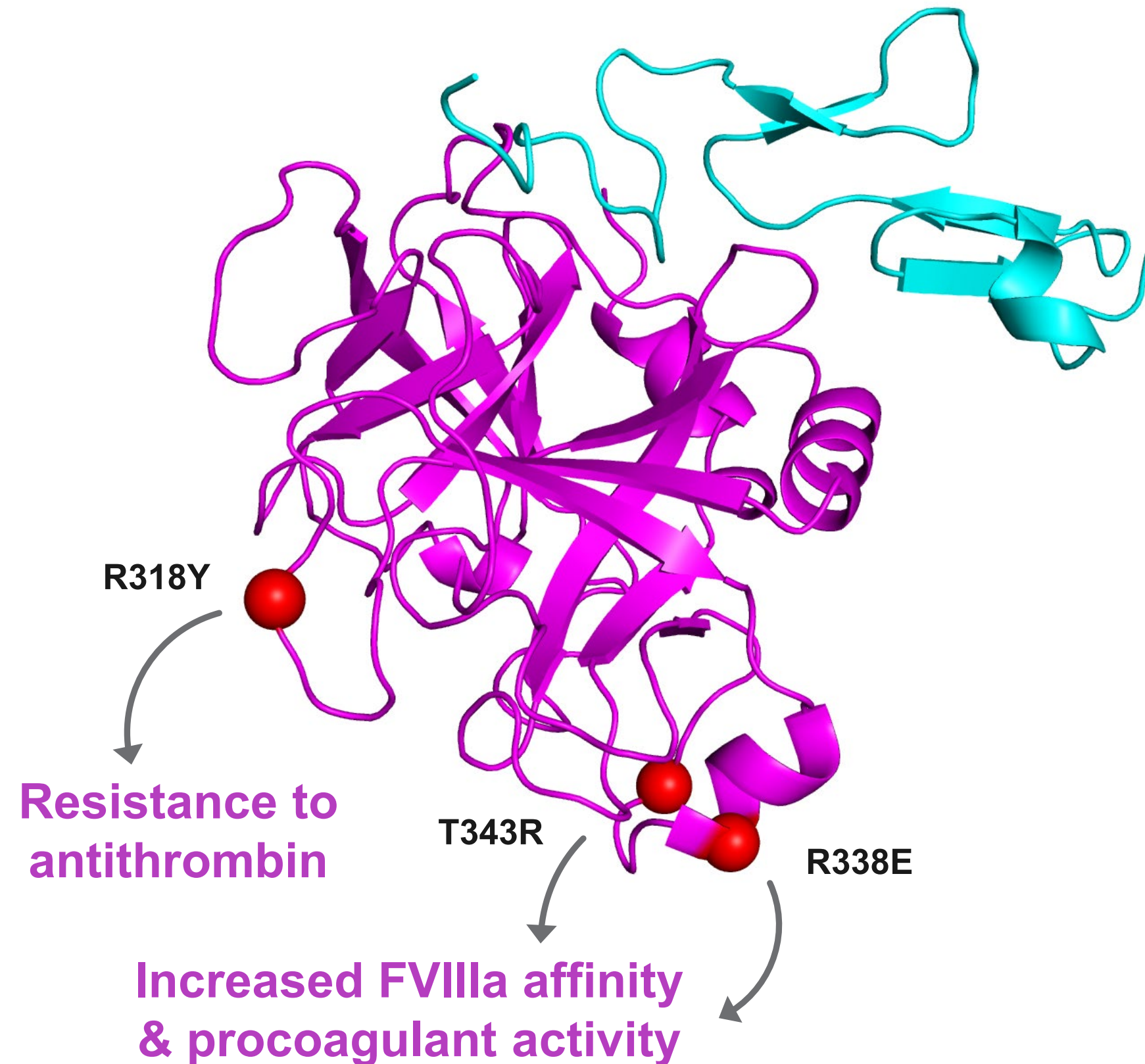
# THANK YOU

**Nasdaq: CBIO**

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

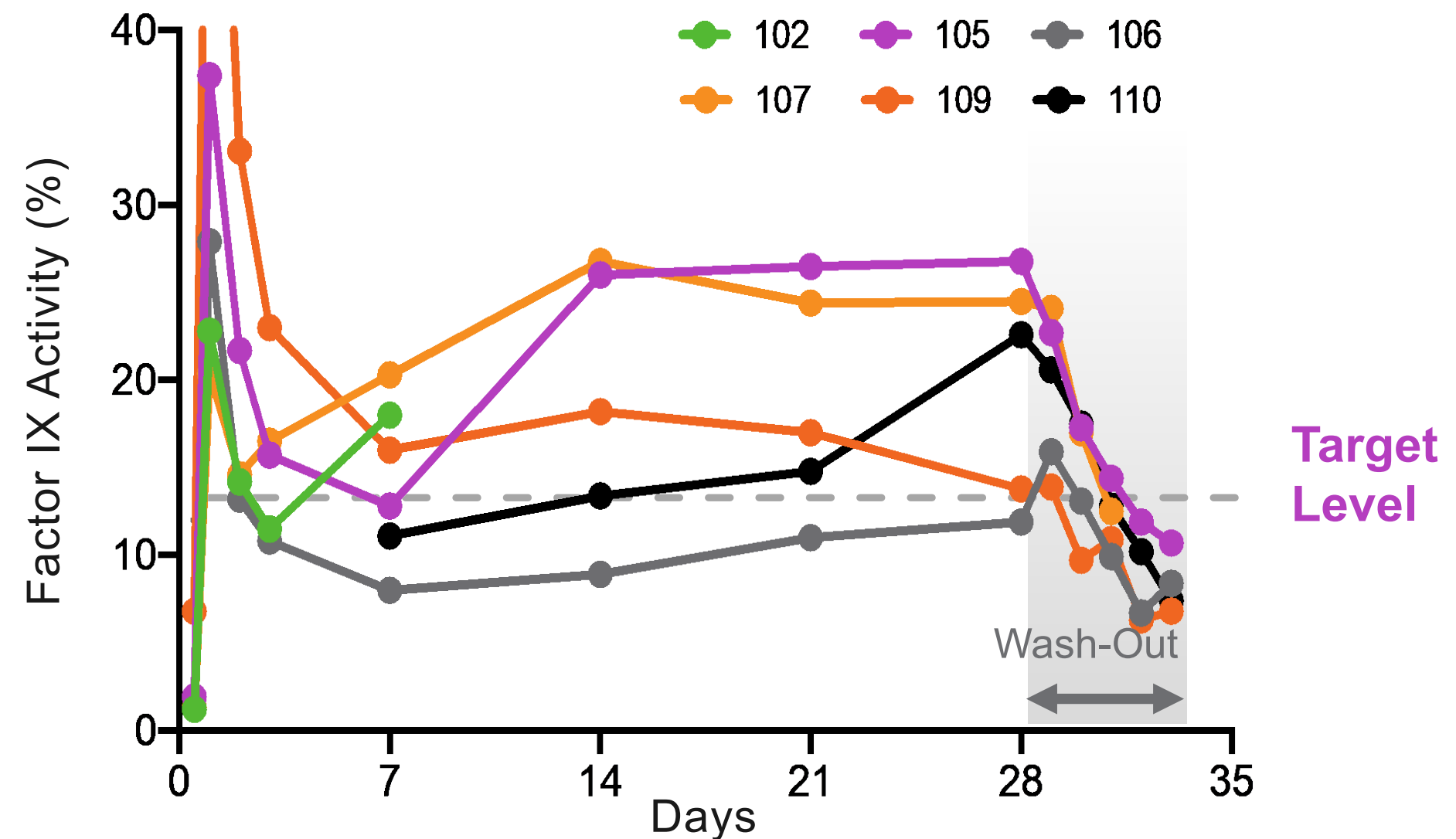


# DalcA P2b demonstrated efficacy & safety



## Differentiated from marketed IV FIXs

- + Small volume SQ administration
- + Enhanced pharmacokinetics with prolonged half-life
- + Excellent extravascular distribution
- + **Target levels >12% achieved with daily SQ 100 IU/kg dosing for 28 days**



# Catalyst's CB 2679d gene therapy 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 1/10th vector dose in mouse model
- + 4 to 5-fold reduction in bleeding time when compared to the Padua
- + Potential for improved efficacy & safety at 1-2 log reduced dose

## ✓ Achieved high initial FIX levels in NHP

- + Presented at World Federation of Hemophilia Virtual Summit 2020
- + Additional vector optimization & dose ranging studies ongoing

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