

# Catalyst Biosciences

Nasdaq: CBIO



Essential Medicines for Hemophilia • Greater Convenience • Superior Outcomes

12 February 2018

# Forward Looking Statements

This presentation includes forward-looking statements that involve substantial risks and uncertainties. All statements, other than statement of historical facts, included in this presentation are forward-looking statements. Examples of such statements include, but are not limited to, the potential benefits of subcutaneous administration of CB 2679d and marzeptacog alfa (activated), the potential for long-term dosing of CB 2679d to maintain FIX activity in the high-mild hemophilia range, statements relating to Catalyst's clinical trial timelines, including plans for patient enrollment of the Phase 2/3 trial of marzeptacog alfa (activated) and the anticipated announcement of interim trial results in the first half of 2018, and plans for the initiation of a Phase 2b clinical trial of CB 2679/d, and the potential market opportunities for these products. Actual results or events could differ materially from the plans and expectations and projections disclosed in these forward-looking statements. Various important factors could cause actual results or events to differ materially from the forward-looking statements that Catalyst makes, including, but not limited to, the risk that trial initiation may be delayed and that trials and enrollment may be delayed and may not have satisfactory outcomes, that subsequent clinical trials will not replicate the results from initial clinical studies on small numbers of patients and that human clinical trials will not replicate the results from earlier animal trials, that subcutaneous dosing of marzeptacog alfa (activated) may not provide a therapeutic response, that potential adverse effects may arise from the testing or use of Catalyst's products, including the generation of antibodies or inhibitors, the risk that costs required to develop or manufacture Catalyst's products will be higher than anticipated, competition, our ability not to infringe third party intellectual property rights, and other factors described in the "Risk Factors" section of Catalyst's Annual Report on Form 10-K for the year ended December 31, 2016, and Quarterly Reports on Form 10-Q for the quarters ended March 31, 2017, June 30, 2017 and September 30, 2017. Forward-looking statements speak only as of the date the statements are made. Catalyst does not assume any obligation to update any forward-looking statements, except as required by law.

## Preventing Bleeding with Convenient Subcutaneous Dosing

### **Hemophilia is a large & growing market**

- Orphan hematology disease
- FVIIa & FIX products have \$3.4B in annual sales

### **Two novel clinical stage product candidates differentiated from IV market leaders**

- Simpler, less painful, small dose
- Potential to maintain continuous protective levels
- Disruptive to all current intravenous products
- Especially well suited for children, 40% of market

### **FIX: CB 2679d/ISU304**





- Phase 1/2 complete
- 22-fold more potent than BeneFIX®
- Daily SQ dosing achieved rising factor levels that correlate with reduced annual bleed rates
- **Corrected all 5 patients from severe to mild hemophilia with only 6 daily SQ doses**
- Less frequent dosing possible
- Phase 2b to initiate in 2018

### **FVIIa: Marzeptacog alfa (activated)**

- Phase 1/2 complete
- 9-fold more potent than NovoSeven®
- Phase 2/3 clinical trial enrolling
- Interim Phase 2 data in H1 2018

# Catalyst Biosciences Pipeline

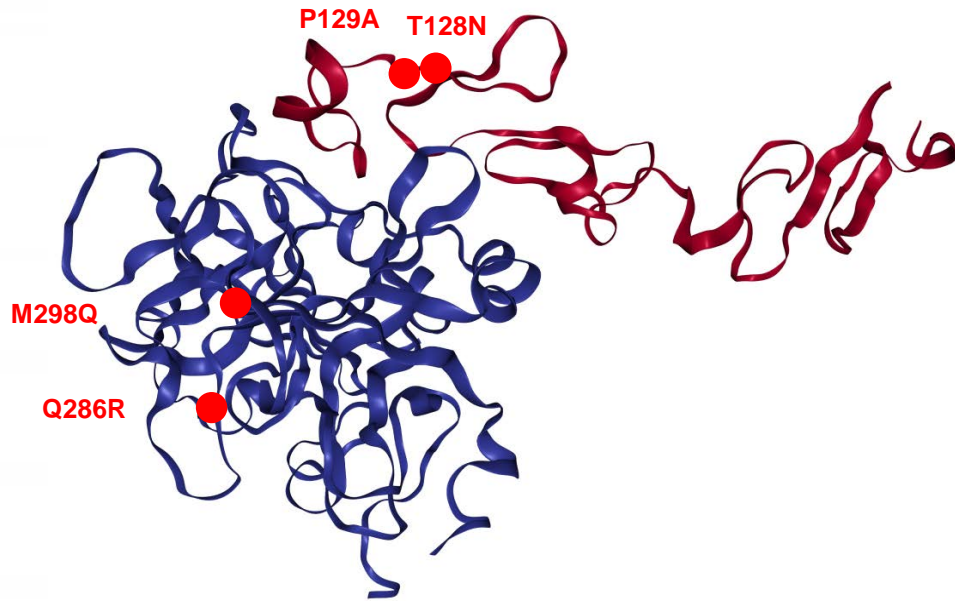
## Next Generation Hemostasis Programs

	Research	Preclinical	Phase 1/2	Phase 2/3	Commercial Rights
<b>FVIIa: Marzeptacog alfa (activated) - CB 813d</b> Hemophilia A&B with Inhibitors, Surgical Bleeding, Subcutaneous prophylaxis					
<b>FIX: CB 2679d/ISU304</b> Hemophilia B, Subcutaneous prophylaxis, Surgical bleeding, Treatment of bleeding					 
<b>FXa: CB 1965a</b> Universal Pro-coagulant					

## Anti-Complement Programs

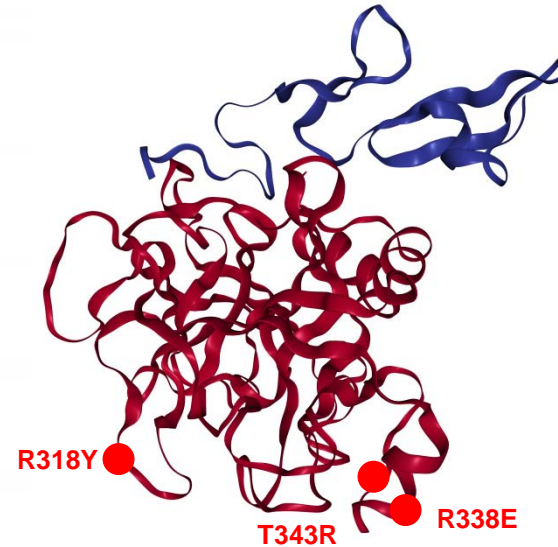
<b>Anti-C3 Protease: CB 2782</b> Dry Age-related Macular Degeneration (dAMD)					
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## Factor VIIa: Marzeptacog alfa (activated)



- Worldwide patents cover MarzAA and related molecules
- Granted and pending through **2029** without extensions
- Orphan Drug Designation in **US**

## Factor IX: CB 2679d/ISU304



- Worldwide patents cover CB 2679d and related molecules
- Granted and pending through **2031** without extensions
- Orphan Drug Designation in **US & EU**



# Experienced Leadership & Investors

## Leadership Team

### **Nassim Usman, Ph.D.**

President & Chief Executive Officer

- MIT, Ribozyme Pharma, Sirna Therapeutics, Morgenthaler Ventures

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

Chief Medical Officer

- Lilly, Novo Nordisk, Sangart, Inspiration, CSL

### **Fletcher Payne**

Chief Financial Officer

- IBM, Cell Genesys, Abgenix, Dynavax, Rinat, Plexxikon, CytomX

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

Sr. VP, Technical Operations

- GSK, Bayer, Novartis

### **Arwa Shurrab**

VP, Regulatory Affairs

- Baxter, Baxalta, Shire

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

VP, Business Development

- Jazz Pharmaceuticals, Orphan Medical, Eli Lilly, Onyx, Threshold

## Investors



# Advantages of Subcutaneous Prophylaxis

## Intravenous Delivery



*"I started helping Mom and Dad with the treatment...I don't want to try to get the needle in the vein yet. Maybe when I'm ten."*

- Intravenous infusion through painful needle stick
- Requires supervision and skilled insertion of needle into vein
- Challenging for patient, family, school
- Activity levels fluctuate, low trough levels

## Subcutaneous Prophylaxis Delivery

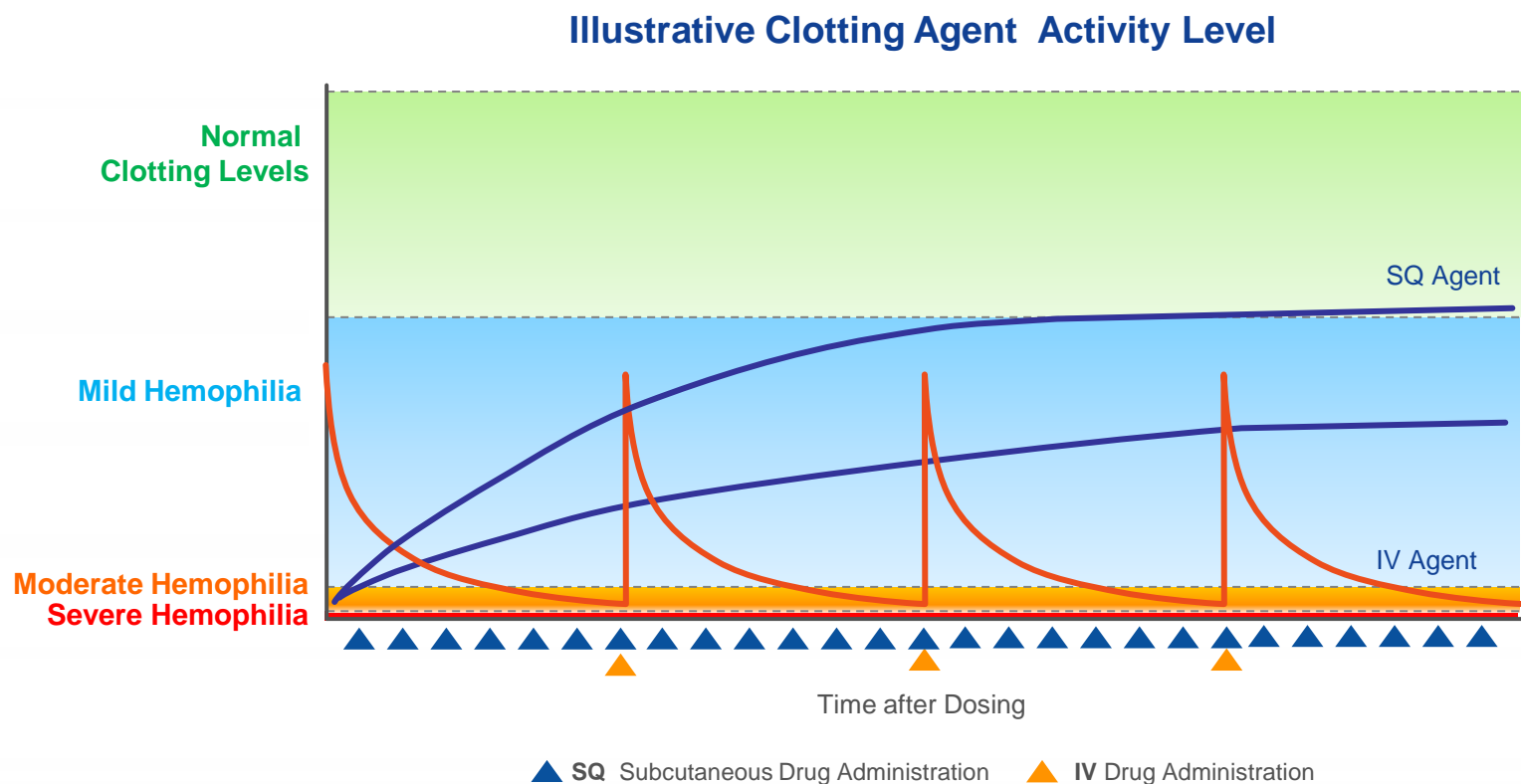


*Pediatric use of subcutaneous delivery is common for diabetes & HGH deficiency, regularly self-administered*

- Subcutaneous injections are easier
- Home therapy - family or patient
- Potential for:
  - Fewer bleeds, reduce joint and muscle damage
  - Fewer demands on healthcare system
  - Reduced hospital stays & outpatient visits

# Subcutaneous Administration may be a Superior Prophylaxis Regimen Compared with IV Agents

## Time in Mild Predicts Protection from Spontaneous Bleeds

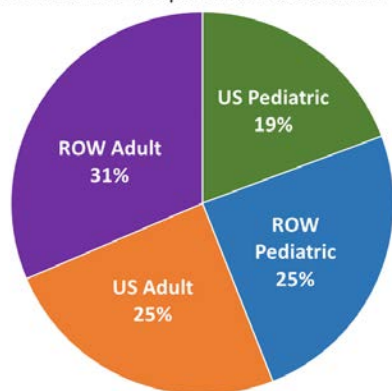




# ~40+% of Individuals with Hemophilia are Children: *KOL's, Individuals & Treeters Want a Better Dosing Method*

## FIX \$1.2B Market Treatable Population 9,700

2024 Patient Population Distribution



## What Do FIX Key Opinion Leaders Say...

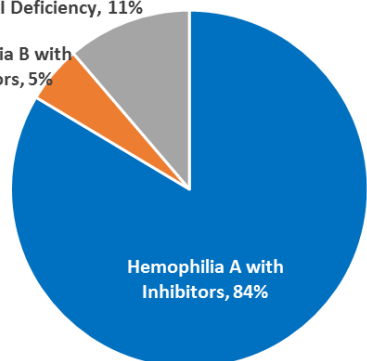
*"These exciting results demonstrate for the first time the feasibility of a subcutaneous FIX injection to provide meaningful protection from bleeding, even after only six doses,"*

**Dr. John Pasi**, Professor of Haemostasis & Thrombosis at Barts and The London School of Medicine

## \$2.2B FVIIa Market, Treatable Population ~3,000

Severe FVII Deficiency, 11%

Hemophilia B with Inhibitors, 5%



## What Do Inhibitor Key Opinion Leaders Say...

*"(MarzAA) would become 1st line treatment for all hemophilia B inhibitor patients."*

*"(MarzAA) would conservatively capture >10% hemophilia A inhibitor patients, not every patient will go on, or stay on ACE910."*

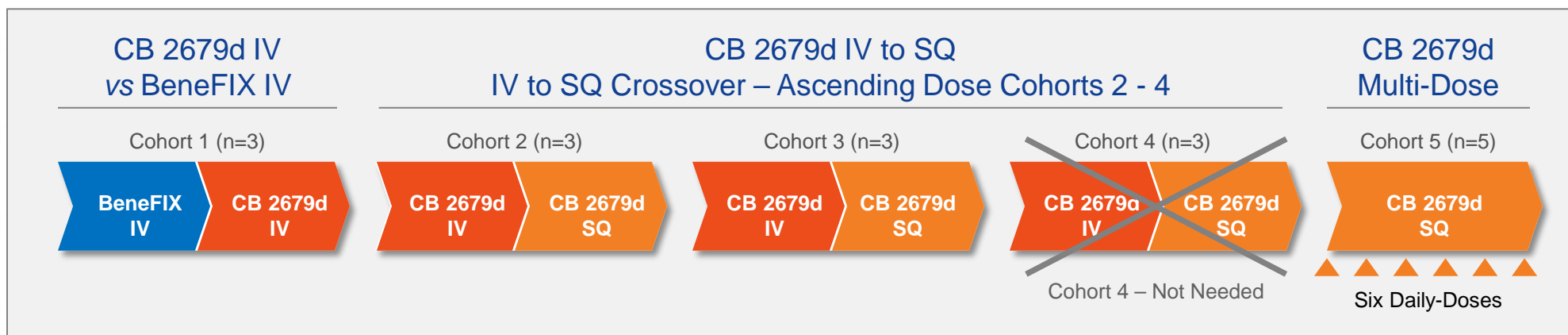
*"Severe FVII deficient patients would want to switch to MarzAA... a daily SQ could 'normalize' them"*

Sources: GlobalData, WFH 2015 Survey, CBIO market Research

# Factor IX Program: CB 2679d/ISU304

## Phase 1/2 Open Label IV to SQ Cross-Over Design

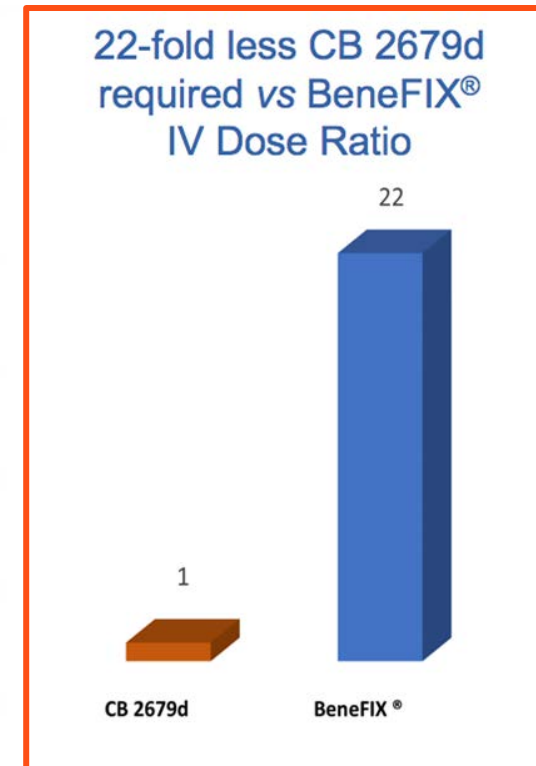
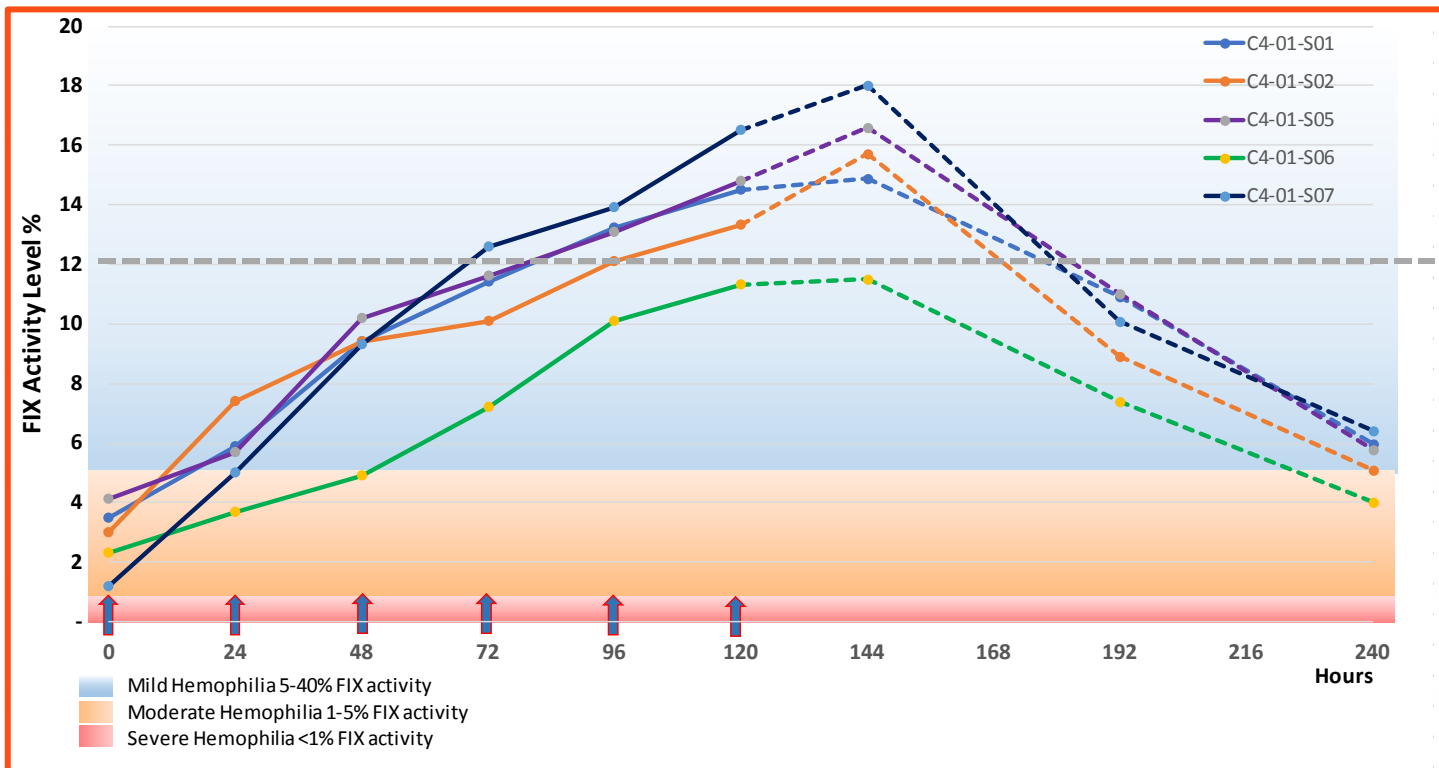
- N = 11
- Ascending Dose Cohorts followed by Multi-dose SQ Cohort
- Cohorts 1-3 & 5 completed
- 6 daily SQ doses corrects severe hemophilia to mild hemophilia with six daily doses<sup>1</sup>
- Well tolerated
- No inhibitors detected



<sup>1</sup>You, Levy *et al.* EAHAD 2018

# Cohort 5 FIX Activity Results (140 IU/kg daily SQ)

## Six Days of Dosing With Five Days Follow-up (n=5)



- 4/5 subjects had trough levels >12%, sufficient to protect from spontaneous hemarthrosis
- Median 15.7% FIX activity levels [IQR 14.9-16.6%] reached after 6 daily doses
- Median half-life is 63.2 hours [IQR 60.2-64.0]

- Cohort 5
  - Mild injection site adverse events that resolved without sequelae were reported
    - Pain
    - Erythema
    - Redness
  - One subject reported these AEs as moderately severe for the first and second injection and mild for subsequent injections
  - Injection site bruising was seen with initial SQ injections in 2 subjects and did not occur with subsequent injections when FIX activity levels increased to mild hemophilia range
- Entire study:
  - No inhibitory antibodies to CB 2679d/ISU304 or FIX were detected

# CB 2679d/ISU304 Program Conclusions

- CB 2679d/ISU304 was designed as a best-in-class high potency recombinant Factor IX
- 22-fold potency advantage vs BeneFIX allows subcutaneous administration
- SQ delivery significantly increases half-life to 63.2 hours
- Daily SQ dosing of 140 IU/kg for 6 days resulted in median 15.7% FIX activity and is more convenient compared with all IV FIX approved products
- At the observed rate of increase, higher levels may potentially be achieved over time
- Decreased frequency may be feasible once target activity level achieved
- No inhibitory antibodies to CB 2679d/ISU304 or FIX were detected
- Phase 2b study will explore:
  - Reduced frequency of dosing
  - IV loading dose to increase collagen IV saturation more rapidly and increase bioavailability



# Factor VIIa: Marzeptacog alfa (activated) – MarzAA

- Leading next-generation FVIIa with prophylaxis & subcutaneous delivery potential
- 6-9 fold improvements in potency and duration of effect vs NovoSeven
- Phase 1 intravenous clinical trial results
  - 25 severe hemophilia patients with and without inhibitors
  - Demonstrated Proof-of-Mechanism
  - Excellent safety and tolerability\*\*
  - No serious drug-related AEs
  - Good correction of PT and aPTT for ~12 h

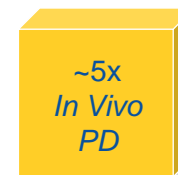
\*\*<http://clinicaltrials.gov/ct2/show/NCT01439971?term=FVIIa&rank=2>

## Marzeptacog alfa (activated) Potency Advantage



### 7-fold Increase in Catalytic Activity

Measured by the rate of Factor Xa generation *in vitro*, both in the presence and absence of tissue factor



### 5-fold Increase in TEG

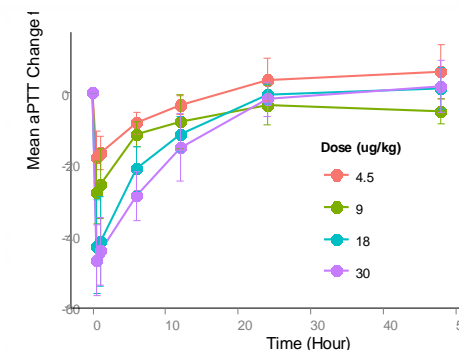
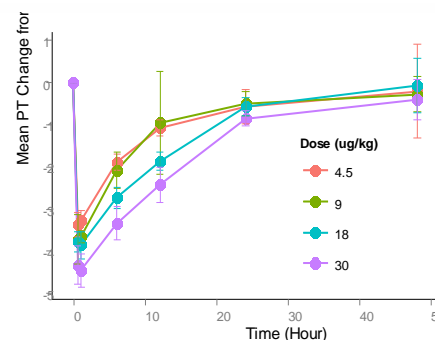
(Thromboelastography)\* Acute peak effect parameters for marzeptacog alfa (activated) 10 µg/kg, were similar to 50 µg/kg wt-FVIIa



### 6-9-fold Longer Duration of Effect in bleeding study

Single injection of marzeptacog alfa (activated) maintains 50% inhibition of bleeding after tail clip injury for 6-9-fold longer than NovoSeven in hemophilia A mouse

## Phase 1 Clinical Trial Data



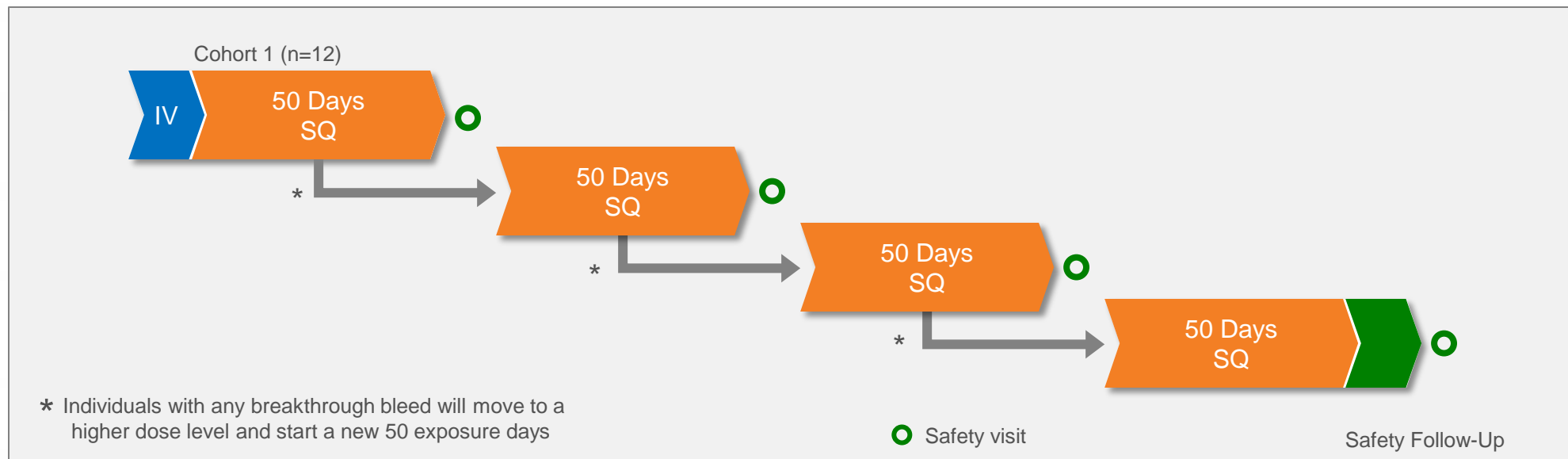
# MarzAA Phase 2 Part of Phase 2/3 SQ Trial

## Phase 2 Multi-Dose SQ/ Dose Escalation

- Hemophilia A and B with Inhibitors
- Open label Subcutaneous (SQ) individual dose escalation study, only if a breakthrough bleed occurs
- Up to 12 adult subjects
- **Study initiated**

## Phase 2 Clinical Data

- Interim data expected in H1 2018
- Study end points
  - Safety & tolerability of daily SQ dosing
  - Monitoring of potential inhibitor formation
  - Annualized bleed rate (ABR) vs recorded historical ABR
  - After 50 exposure days with no bleeds, individuals will move to safety follow-up



# Milestones & Planned Data Presentations

2017

2018

	Q2	Q3	Q4	Q1	Q2	Q3	Q4
<b>CB 2679d (FIX)</b>	<b>Phase 1/2</b> Cohort 1 Completed  ✓	<b>ISTH</b> Preclin Data 22x Potency Cohort 2 (SQ) Asia Patents US ODD  ✓✓✓✓✓	<b>ASH</b> Interim SQ Clinical Data (Oral)  ✓	<b>EAHAD</b> Top-line multi- dose Clinical Data  ✓		<b>ISTH</b> Final P1/2 Clinical Data  <b>Initiate P2b</b>	
<b>MarzAA (FVIIa)</b>	<b>Started</b> INC, P2 Clinical CRO  ✓	<b>ISTH</b> Preclinical Data  ✓	<b>Initiate</b> Phase 2  ✓		<b>Report</b> Early P2 Clinical Data	<b>ISTH</b> Interim P2 Clinical Data	<b>ASH</b> Final Clinical Data

# Select Financial Data

## Financial Data

Cash as of Sep. 30, 2017 <sup>1</sup>	\$27.5M
Financing Activity since Sep. 30, 2017:	
- Financing proceeds from December 2017	\$9.7M
- Warrants exercised during 2017	\$1.3M
Revenue YTD <sup>2</sup>	\$0.7M
Operating Expense YTD <sup>2</sup>	\$16.7M

## Share Data

Shares Outstanding <sup>3</sup>	6,366,604 shares
Series A Preferred <sup>3</sup> (common equivalents)	736,000 shares
Warrants <sup>3</sup> ; represents ~\$8.0M of proceeds	1,454,295 shares
Average Volume <sup>4</sup>	439,000 shares
Market Capitalization <sup>4</sup>	\$205M

1. As of September 30, 2017

2. For the nine months ended September 30, 2017

3. Based upon S-3 Filed January 22, 2018

4. Based on February 9, 2018 \$32.15 closing price and Average Nasdaq Volume

## CBIO Stock Chart



## Stock Price Range

52 week range \$3.11 - \$33.81

## Disruptive approach to a \$3.4 Billion market

- **Subcutaneous (SQ) Prophylactic** dosing designed to be less painful and much more convenient, especially for children
- **Stable clotting activity** could dramatically reduce spontaneous bleeding and improve quality of life

## FIX: CB 2679d/ISU304 ~\$1.2 Billion market

- Confirmed 22-fold potency advantage vs BeneFIX
- Median 15.7% FIX activity levels [IQR 14.9-16.6%] reached after 6 daily doses
  - 5/5 severe hemophilia B patients converted to mild hemophilia
- Potential to maintain FIX activity in the mild hemophilia range with less frequent dosing

## FVIIa: Marzeptacog alfa (activated) ~\$2.2 Billion market

- Phase 2 of a Phase 2/3 program enrolling
- Interim Phase 2 data in 1H 2018

## Anti-C3 for Dry AMD: Multi-Billion market opportunity

- C3 is a clinically validated target, potential to generate a best-in-class molecule
- Plan to partner asset

## Cash runway through Q2 2019



# Catalyst Biosciences

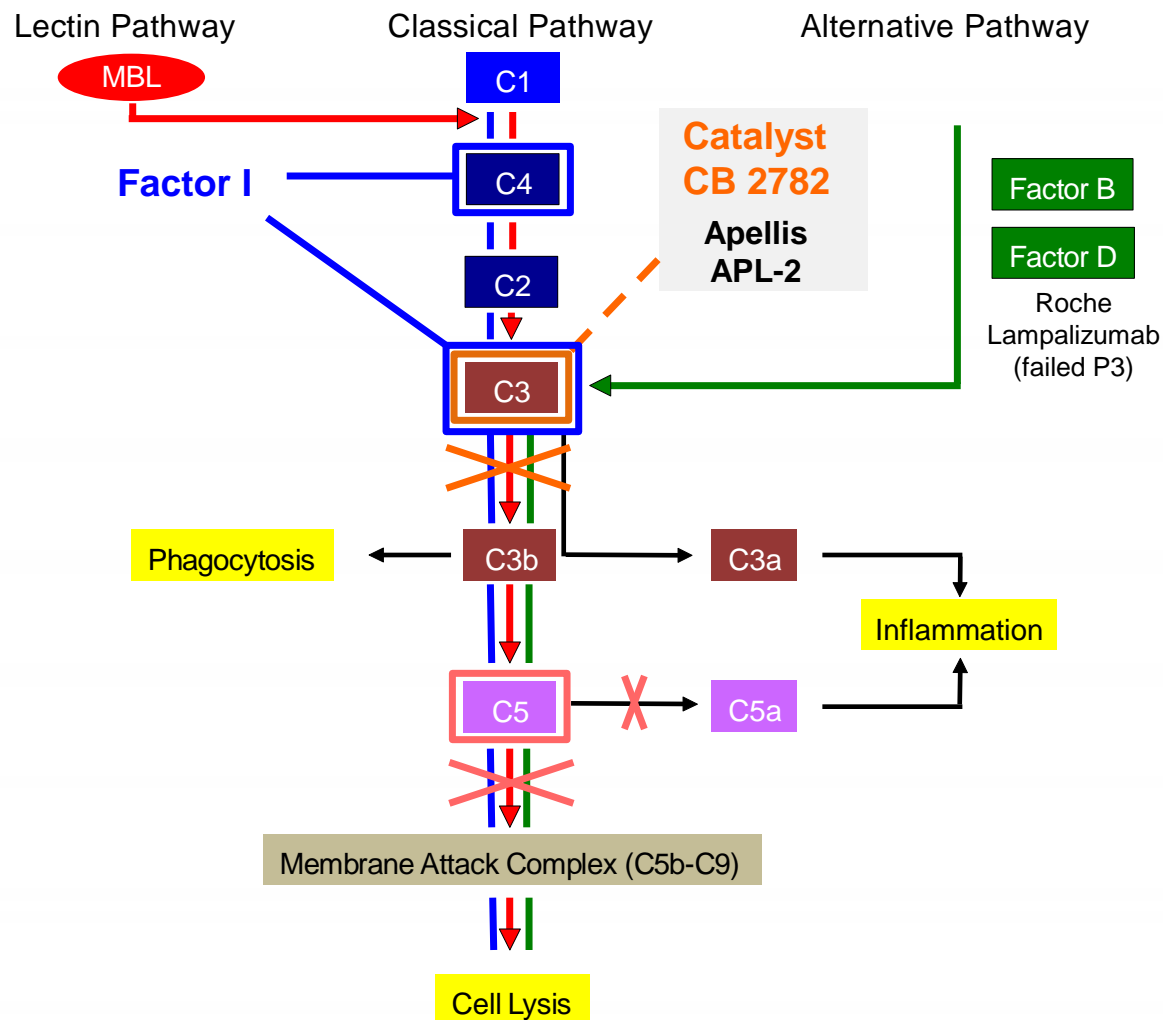
Nasdaq: CBIO



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# Anti-C3 for GA Dry AMD (dAMD)



- Advanced dAMD, or geographic atrophy (GA), leads to loss of RPE photoreceptors and blindness with no approved drugs
- Global dAMD market is >\$5 billion
- C3 is the “best target” in the complement cascade and clinically validated in GA\*
  - Apellis’ APL-2 (anti-C3 cyclic peptide, 15 mg IVT), rP2 (n=246):  
Qmo 29% (p=0.008) inhibition of GA  
Q2mo 20% (p=0.067) inhibition of GA
- **Catalyst’s anti-C3 protease program has the potential for best-in-class profile**
  - **May provide superior efficacy with every 3 months (or less frequent) dosing, fewer IVT AEs**

\*P. Rosenfeld AAO 2015, Apellis Inc

## Best-in-class Potential

- Catalytic mechanism of action of a protease to inhibit C3 is superior to antibodies and peptides
- Apellis' APL-2 (anti-C3 cyclic peptide, IVT) demonstrated rP2 efficacy with Qmo and potentially Q2mo dosing
- Catalyst's proprietary potent and selective anti-C3 protease leads have demonstrated complete intravitreal C3 inhibition *in vivo* in NHP
- Current CBIO lead suggests Q1-2 month dosing frequency in man at 2 mg IVT
- Modifying the PK could extend human dosing to at least every three months with superior efficacy

