# Catalyst Biosciences

- Essential Medicines for Hemophilia
- Greater Convenience
- Superior Outcomes

21 June 2018



#### catalystbiosciences.com

**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), cohort 6 of the Phase 1/2 trial of CB2679d and the anticipated announcement of trial results, plans for the initiation of a Phase 2b clinical trial of CB 2679d, the potential uses and benefits of Catalyst's anti-C3 protease, 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, 2017. Forwardlooking 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.



## **Catalyst Biosciences: CBIO**



### Preventing bleeding with convenient subcutaneous (SQ) dosing

#### Hemophilia is a large & growing market

- + Orphan hematology disease
- FVIIa & FIX products have ~\$3.5B in annual sales

### Two novel clinical stage SQ 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

- + 22-fold more potent than BeneFIX® in man
- All subjects in the P1/2 multi-dose cohort 5 corrected from severe to mild hemophilia with only 6 daily SQ doses, median of ~16%
- Two subjects In Cohort 6, IV loading + 9 daily
  SQ doses showed >30% activity levels
  - Less frequent dosing possible
  - nAbs detected
    - Source under investigation
  - Multiple backup constructs available

#### FVIIa: Marzeptacog alfa (activated)

- + Phase 1/2 complete
- + 9-fold more potent than NovoSeven®
- + Phase 2/3 clinical trial enrolling
  - No ADA or nAb detected to date

## **Catalyst Biosciences pipeline**



#### Next generation hemostasis programs:

#### FVIIa: Marzeptacog alfa (activated)

Hemophilia A&B with Inhibitors, surgical Bleeding, subcutaneous prophylaxis

FIX: CB 2679d/ISU304

Hemophilia B, subcutaneous prophylaxis, surgical bleeding, treatment of bleeding

#### FXa: CB 1965a

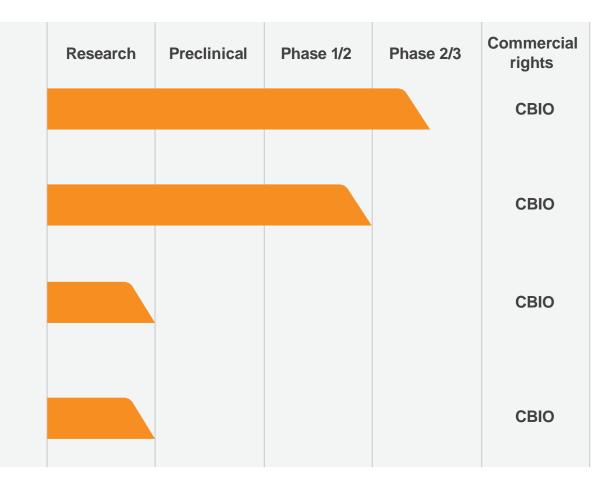
Universal pro-coagulant

#### Anti-complement programs:

Anti-C3 Protease: CB 2782

MOSAIC BIOSCIENCES

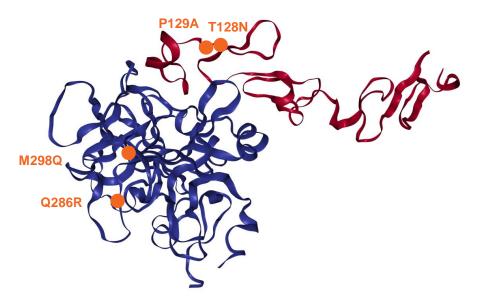
Dry age-related macular degeneration (dAMD)



### **Products & intellectual property**

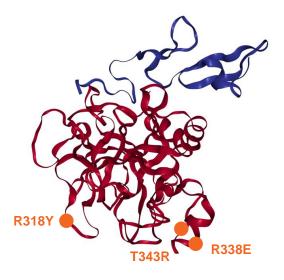


Factor VIIa: Marzeptacog alfa (activated)



- 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

## Advantages of subcutaneous prophylaxis



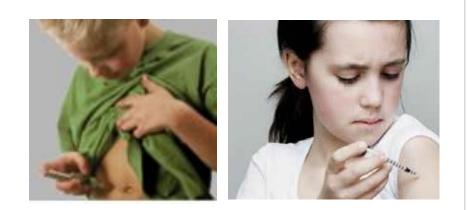
### Intravenous infusion



"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."

- Slow infusion through a 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



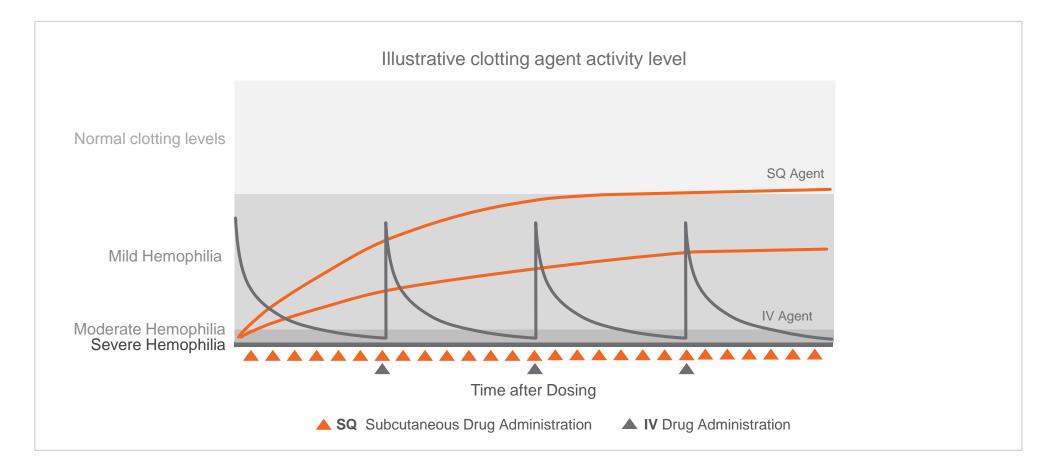
Pediatric use of subcutaneous delivery is common for diabetes & HGH deficiency, regularly self-administered

- + 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

### Advantages of subcutaneous prophylaxis



### Time in mild range predicts protection from spontaneous bleeds

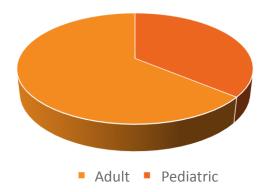


### ~40% of Individuals with hemophilia are children

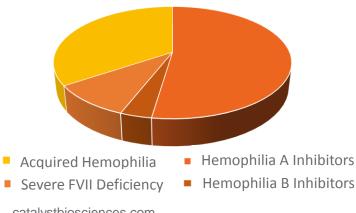


KOL's, individuals & treaters want a better dosing method & better efficacy

FIX \$1.2B market treatable population ~10,000



FVIIa \$2.2B market treatable population ~3,200



#### 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

#### 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"
- "There is a clear unmet need for a SQ therapy in acquired hemophilia and MarzAA could fill that need, I think it is an excellent idea

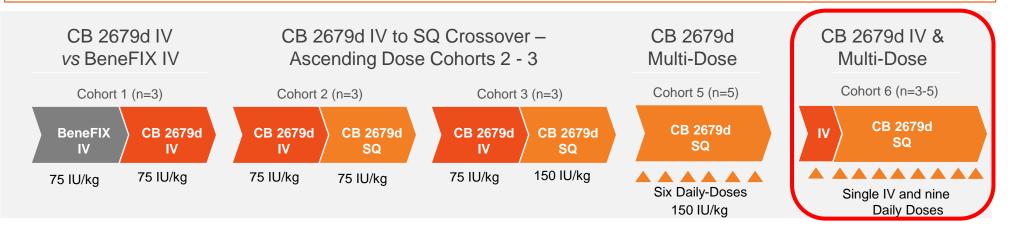
## Factor IX program: CB 2679d/ISU304



#### Phase 1/2 open label IV to SQ cross-over design

- Ascending dose Cohorts followed by Multi-dose SQ Cohorts
- N = 11 (5 subjects participated in 2 cohorts)
- + 22-fold higher potency vs BeneFIX in IV/IV Cohort 1

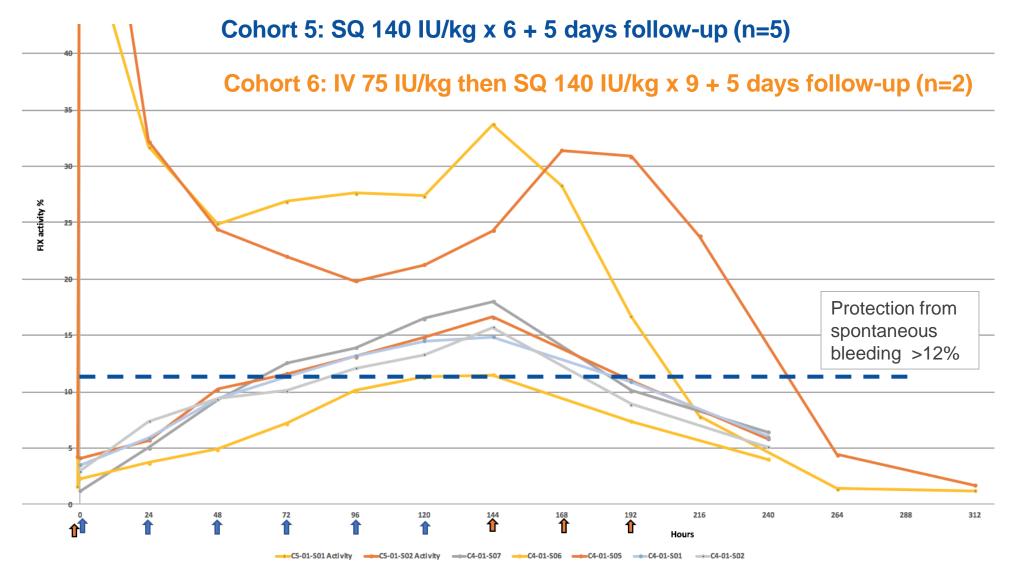
- 6 daily SQ doses corrects severe hemophilia to mild hemophilia with six daily doses<sup>1</sup>
- 9 daily SQ doses following a single IV loading dose corrects to >30%
- + Well tolerated
- + nAb detected in Cohort 6, cause to be determined
  - + Does not cross react with wt FIX



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

### Phase 1/2: Cohort 5 & 6 FIX activity results





## CB 2679d/ISU304 program summary

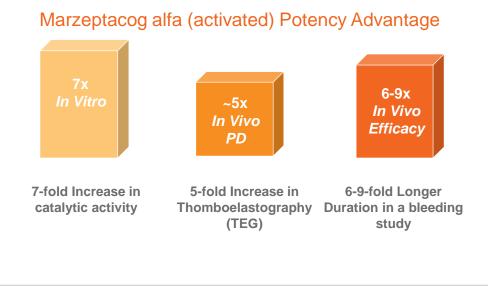
- CB 2679d/ISU304 was designed as a best-in-class high potency recombinant Factor IX
- 22-fold potency advantage vs BeneFIX allows subcutaneous administration
- SC SC
  - SQ delivery significantly increases half-life to 63.2 hours
- Daily SQ dosing of 150 IU/kg for 6 days resulted in median 15.7% FIX

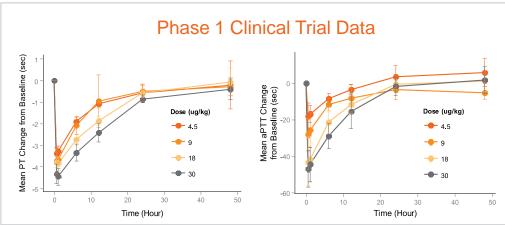
- Daily SQ dosing of 150 IU/kg for 9 days following an IV loading dose resulted in median >30% FIX
  - nAbs detected, one transient
  - Does not cross react with wt FIX
  - Analysis ongoing
- Decreased dosing frequency is feasible once target activity level achieved
- Phase 2b study will explore reduced frequency and longer-term dosing

### 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





### MarzAA Phase 2 part of P2/3 SQ trial

#### Phase 2 SQ multi-dose & dose escalation

- + Hemophilia A & B with Inhibitors
- + Open label SQ individual dose escalation study, only if a breakthrough bleed occurs
- + Up to 12 adult subjects with documented annualized bleeding rate (ABR) >12
- + Study enrolling

#### Phase 2 clinical data

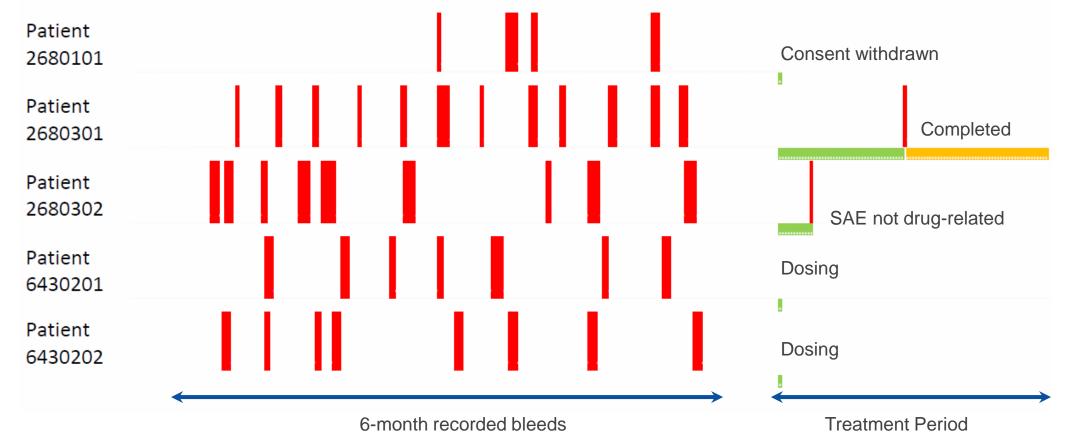
- + Interim data at ISTH 18 July 2018
- + Study end points
  - Safety & tolerability of daily SQ dosing
  - Monitoring of potential inhibitor formation
  - ABR vs recorded historical ABR
  - After 50 exposure days with no bleeds, individuals will move to safety follow-up





## Bleeding History Prior to and During Treatment with MarzAA

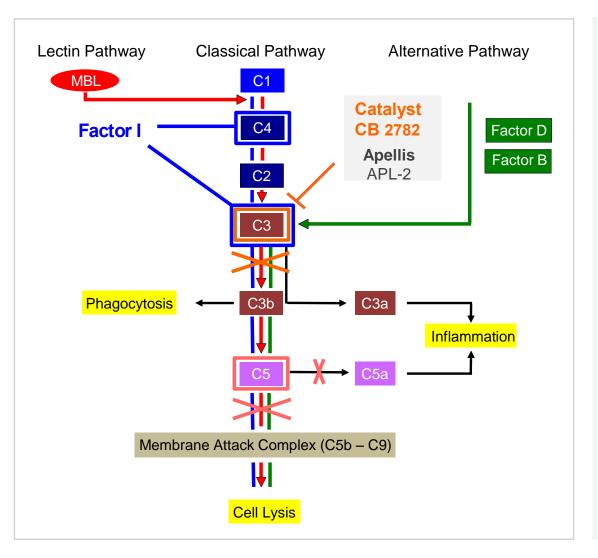




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Nasdag: CBIO

## 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

Nasdag: CBI

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 intravitreal injection [IVT]), randomized P2 (n=246):
- Q1mo 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

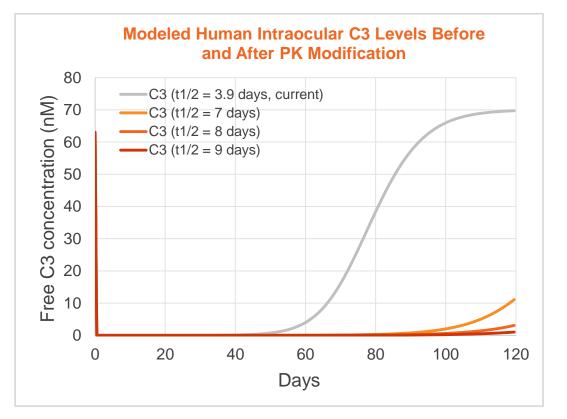
 May provide superior efficacy with every 3 months (or less frequent) dosing, fewer IVT AEs

### **Anti-C3 Protease for Dry dAMD**



### **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 randomized P2 efficacy with Q1mo and potentially Q2mo dosing
- Catalyst's proprietary potent and selective anti-C3 protease leads have demonstrated <u>complete</u> intravitreal C3 inhibition *in vivo* in NHPs
- Current CBIO lead suggests Q1-2 month dosing frequency in man at 2 mg IVT
- Modifying the PK could extend human dosing to at most every three months with superior efficacy
- Preclinical data with longer acting proteases in 2018



## Experienced leadership & investors<sup>1</sup>



#### 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.

SVP, Technical Operations – GSK, Bayer, Novartis

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

VP, Business Development – Jazz Pharmaceuticals, Eli Lilly, Onyx, Threshold



### Milestones & planned data presentations



	2017			2018			
	Q2	Q3	Q4	Q1	Q2	Q3	Q4
CB 2679d (FIX)	Phase 1/2 Cohort 1 completed	ISTH Preclin data 22x potency Cohort 2 (SQ) Asia patents US ODD	ASH Interim SQ clinical data (oral)	EAHAD Top-line multidose clinical data (oral)	WFH Final Cohorts 1-5 data Initiate Cohort 6	ISTH Cohort 6 interim data	<b>ASH</b> Final P1/2 data Initiate P2b
MarzAA (FVIIa)	Started INC, P2 clinical CRO	ISTH Preclinical data	Initiate P2			<b>ISTH</b> Interim P2 data	<b>ASH</b> Final P2 data



#### **Financial Strength**

Cash & Cash Equivalents Q1/2018.....\$143.5M April 2017 follow-on financing at \$5.00/share.....\$18.6M Dec 2017 follow-on financing at \$9.50/share.....\$10.5M Feb 2018 follow-on financing at \$34.00/share.....\$115M 2018 Warrant proceeds at \$5.50/share.....\$9.6M

#### **Capitalization Table Simplification**

No Debt

Converted all Series A Preferred to Common Stock 🗸

1

Called \$5.50 Warrants or exercised for Common Stock  $\checkmark$ 

#### First Quarter 2018 Share Data

Common Stock Outstanding	11,935,081
Fully Diluted Shares	14,743,688
Average Volume	
Market Capitalization (19 June 2018)	\$124.8M

#### **First Quarter 2018 Operating Results**

Operating Expense First Quarter 2018	\$6.7M
Net Loss First Quarter 2018(	(\$5.0 M)
Net Loss per share First Quarter 2018	(\$0.56)

### **Investment highlights**





#### Disruptive approach to a \$3.5 billion market

Subcutaneous Prophylactic dosing designed to be less painful and much more convenient, especially for children

Stable & high 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 >30% activity levels seen in multiple dose cohorts with daily dosing

nAb cause under investigation

Potential to maintain FIX activity in the mild hemophilia range with less frequent dosing to be explored in P2b



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

Phase 2 of a Phase 2/3 program enrolling

No ADA or nAb observed to date

Interim Phase 2 Data at ISTH 2018



#### Anti-C3 for Dry AMD: multi-billion market opportunity

C3 is a clinically validated target, potential to generate a best-in-class molecule Pre-clinical proof-of-concept in 2018



## Cash runway allows independent development of lead programs

Strengthened balance sheet & simplified our capitalization structure

# Thank you

Nassim Usman, Ph.D. President & CEO



### Phase 1/2 safety



### Cohort 5 and 6

- Mild injection site adverse events that resolved without sequelae were reported
  - Pain
  - Erythema
  - Redness

- Two subjects reported these AEs as moderately severe for the initial injections and mild for subsequent injections
- - Injection site bruising was seen with initial SQ injections in 2 subjects and did not occur when FIX activity levels were in the mild hemophilia range



DSMB had no safety concerns and approved cohort 6

**V** I

Inhibitory antibodies to CB 2679d/ISU304 but not FIX were detected

## Factor IX program: Phase 2b



### Phase 2b open label IV load and SQ dosing daily, alternate day and third day dosing



- + All subjects proceed through every dosing level
- + Final design will be based on cohort 6 results
- + Time above 12% will be determined
- + Initiate study in Q4 2018

