

# Phase 1/2 Trial of Single and Multiple Dose Subcutaneously Administered Factor IX Variant CB 2679d/ISU304: Pharmacokinetics, Activity and Safety

Chur Woo You MD PhD, **Howard Levy** MBBCh PhD, Ho-Jin Shin MD, Jin Kim MD, Jung Han MD, Soo-Jeung Kim MD, Martin Lee PhD, June Young Park PhD, Seung-Beom Hong PhD, and Jamie Ellen Siegel MD



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# Disclosure for Howard Levy

In compliance with COI policy, EAHAD requires the following disclosures to the session audience:

| Shareholder              | Catalyst Biosciences                         |
|--------------------------|--|
| Grant / Research Support | No relevant conflicts of interest to declare |
| Consultant               | No relevant conflicts of interest to declare |
| Employee                 | Catalyst Biosciences                         |
| Paid Instructor          | No relevant conflicts of interest to declare |
| Speaker bureau           | No relevant conflicts of interest to declare |
| Other                    | No relevant conflicts of interest to declare |

Presentation includes discussion of the following off-label use of a drug or medical device:

N/A

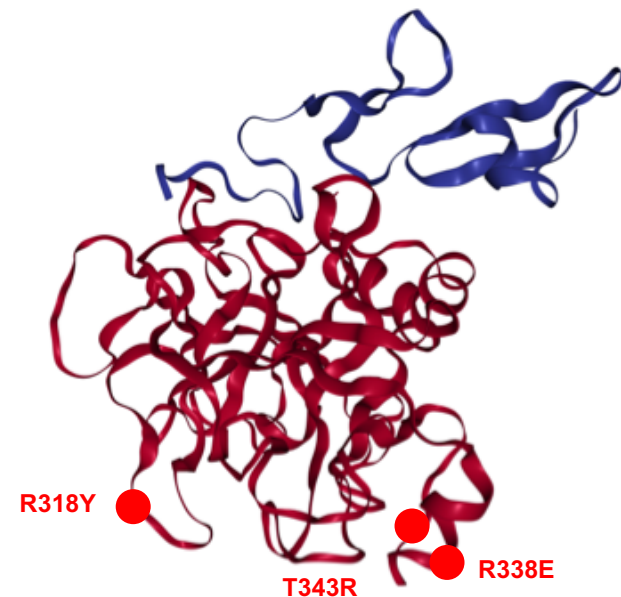
# Factor IX Modified with 3 Point Mutations



## CB 2679d/ISU304

- Designed as a best-in-class high potency recombinant Factor IX product
- 22-fold potency advantage over wt-FIX allows subcutaneous administration
- IV half-life 27.0 hours is significantly longer than 21.0 hours for BeneFIX® ( $p=0.0014$ )
- SQ delivery significantly increases half-life
- Orphan drug designations have been granted in the US and EU

## Factor IX: CB 2679d/ISU304

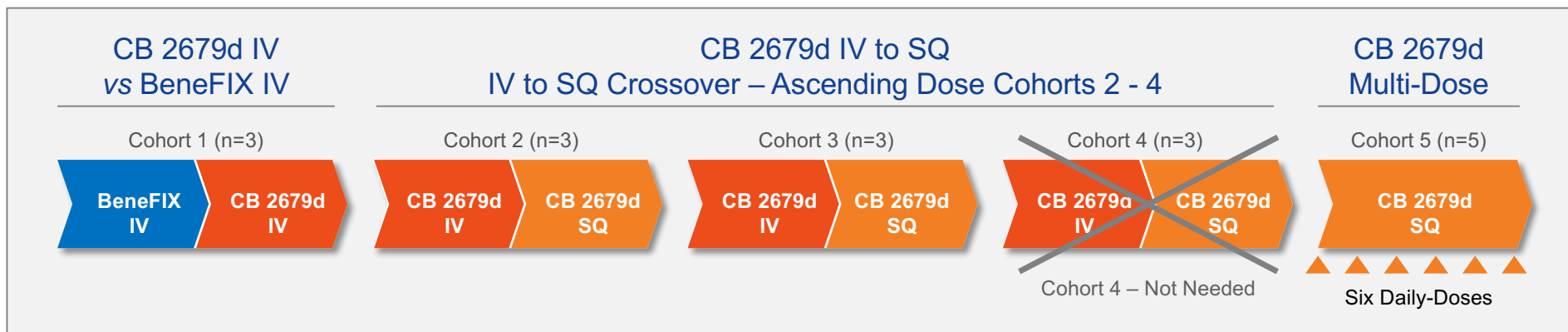


# Design and Results of Phase 1/2 Trial



## Phase 1/2 Multi-Dose Study

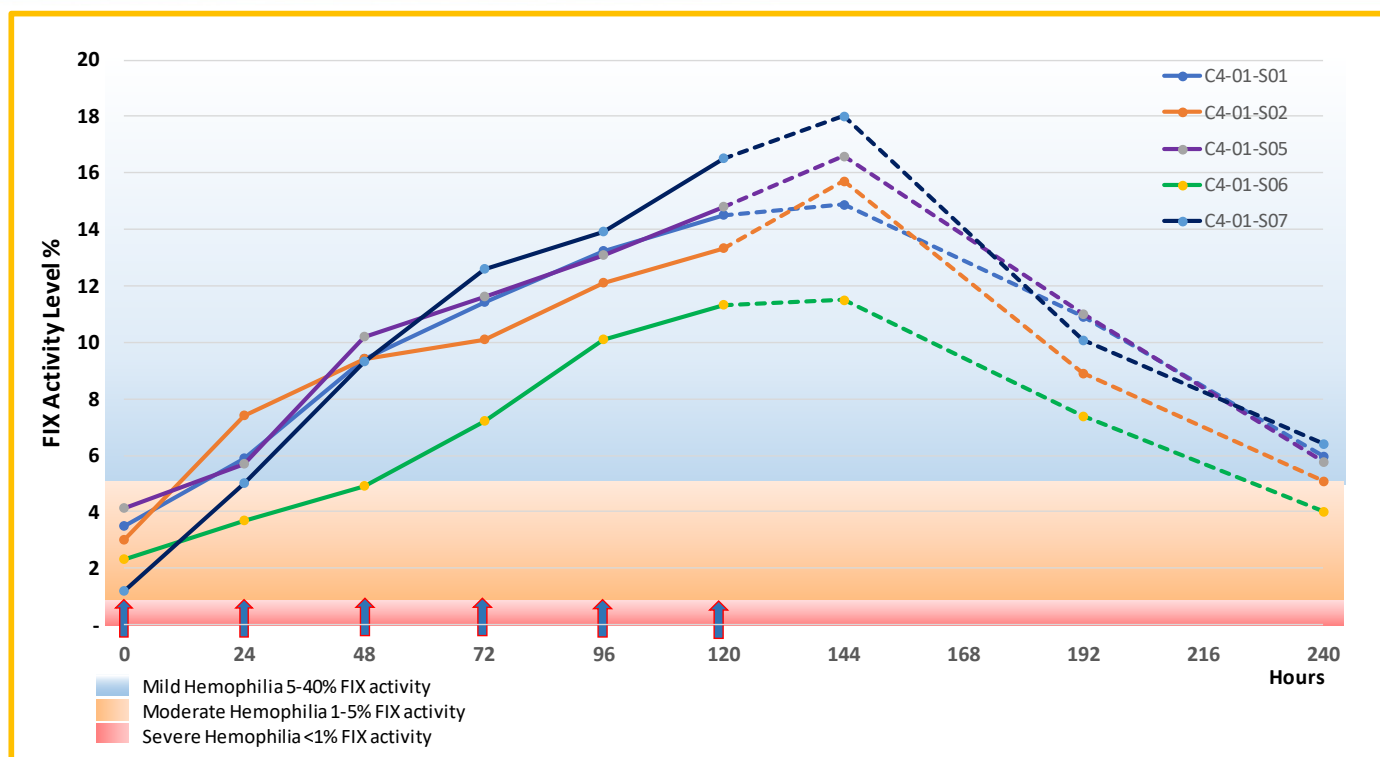
- N = 11
- Ascending Dose Cohorts followed by Multi-dose SQ Cohort



## Previously reported results

- Cohort 1: 22-fold greater potency vs BeneFIX®; Half-life 27.0 vs 21.0 hours
- Cohorts 2 & 3: Bioavailability 18.5%; Half-life 98.7 h similar to IV agents dosed biweekly or weekly
- Cohort 4 dropped as not needed

## Cohort 5 FIX Activity Results (140 IU/kg daily SQ) Six Days of Dosing With Five Days Follow-up (n=5)



- 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]
- FIX factor levels above ( $\geq 12\%$ ) are required to eliminate spontaneous hemarthrosis
- Results suggest that long-term dosing of CB 2679d/ISU304 has the potential to maintain FIX activity in the high-mild hemophilia to normal range

# Phase 1/2 (ISU-304-001) Safety



- 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 induced to date

# CB 2679d/ISU304 Program Conclusions



- CB 2679d/ISU304 was designed as a best-in-class high potency recombinant Factor IX
- 22-fold potency advantage 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
- At the observed rate of increase, higher levels may potentially be achieved over time
  - Collagen saturation may increase bioavailability and result in shortening of the time required to reach target activity levels
  - Lower dose or decreased frequency may be required once target activity level achieved
- SQ dosing may provide superior prophylaxis to IV extended half-life agents
- Phase 2b study will explore:
  - Reduced frequency of dosing
  - IV loading dose to increase collagen IV saturation more rapidly and increase bioavailability

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