Pharmacokinetic & Activity Levels Achieved with Daily Subcutaneously Administered CB 2679d/ISU304 in Hemophilia B Dogs

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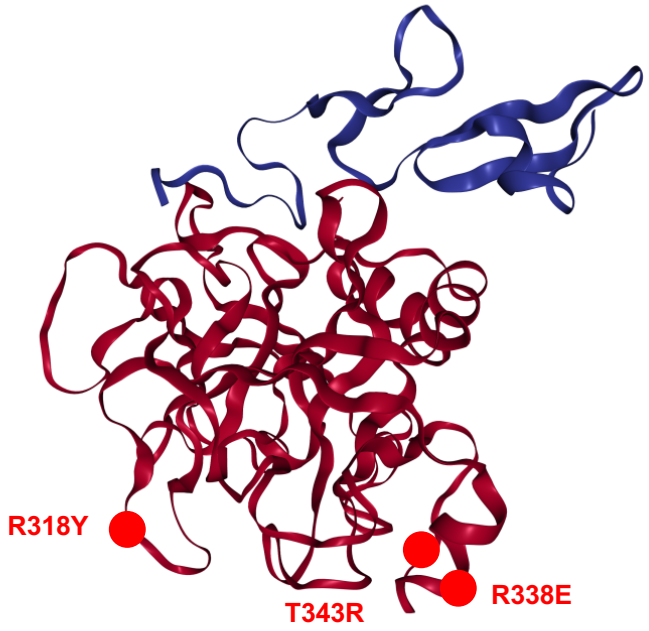
Disclosure

- Employee of Catalyst Biosciences

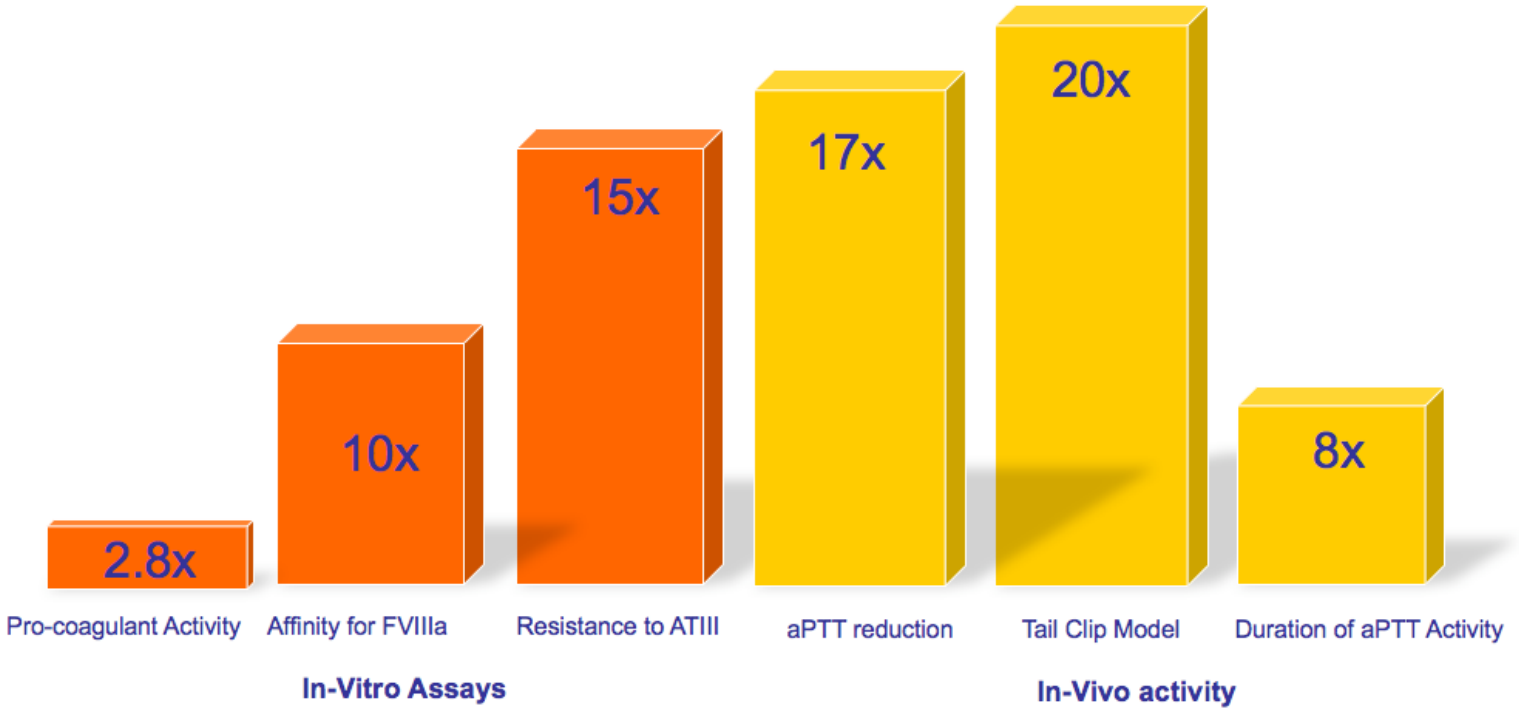
Factor IX Modified with 3 Point Mutations

- Rapid clearance of FIX necessitates frequent intravenous administrations to achieve effective prophylaxis
- Subcutaneous administration is the preferred route of administration but has been limited by low bioavailability and potency of the marketed FIX products
- Designed as best-in-class high potency recombinant FIX product
- Significantly more potent than currently available products
- Orphan Drug Designation in EU
- Open label, Phase 1/2 proof-of-concept trial underway in individuals with hemophilia B

Factor IX: CB 2679d/ISU304



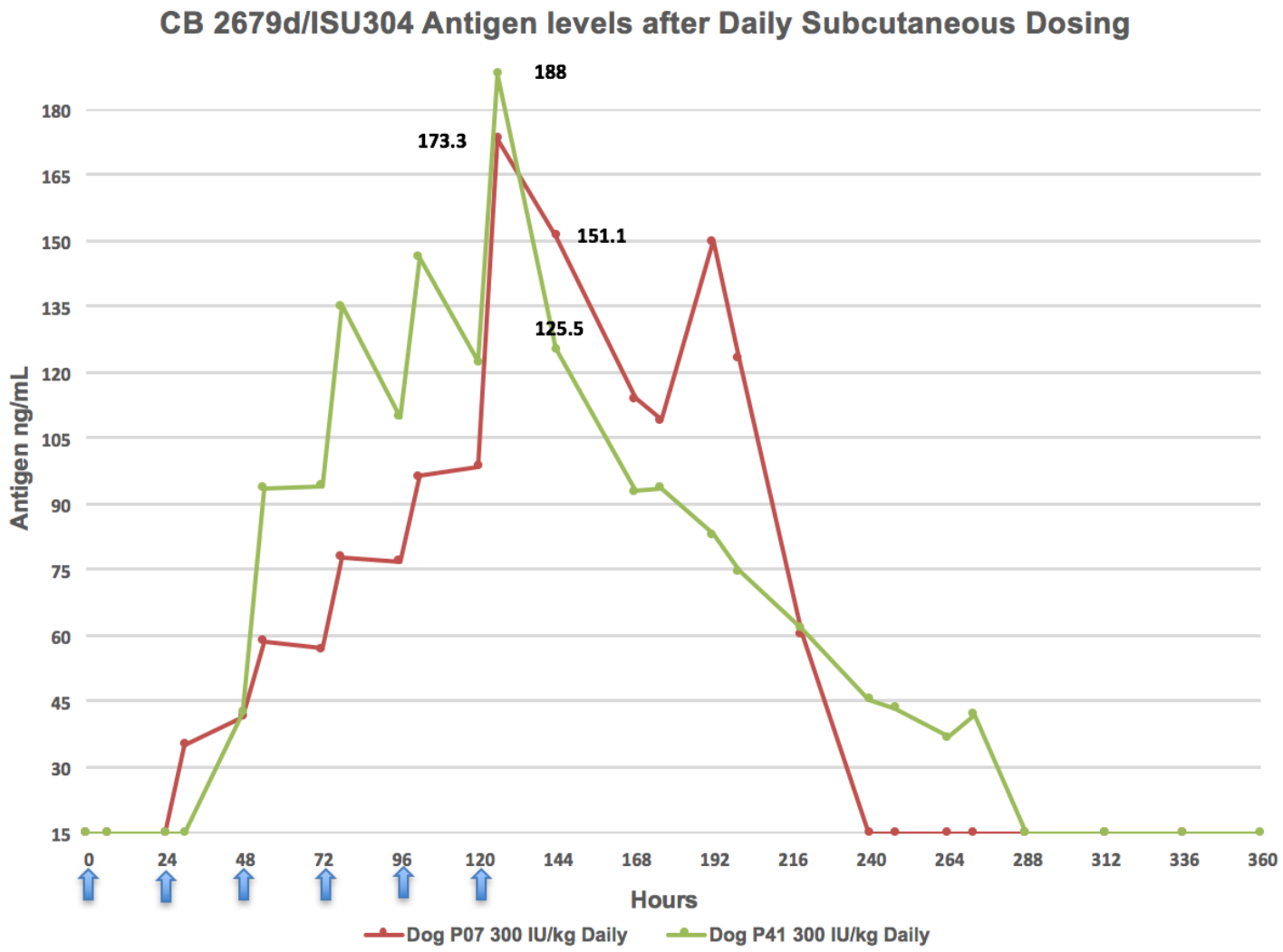
CB 2679d/ISU304 Potency Advantage over wt-FIX



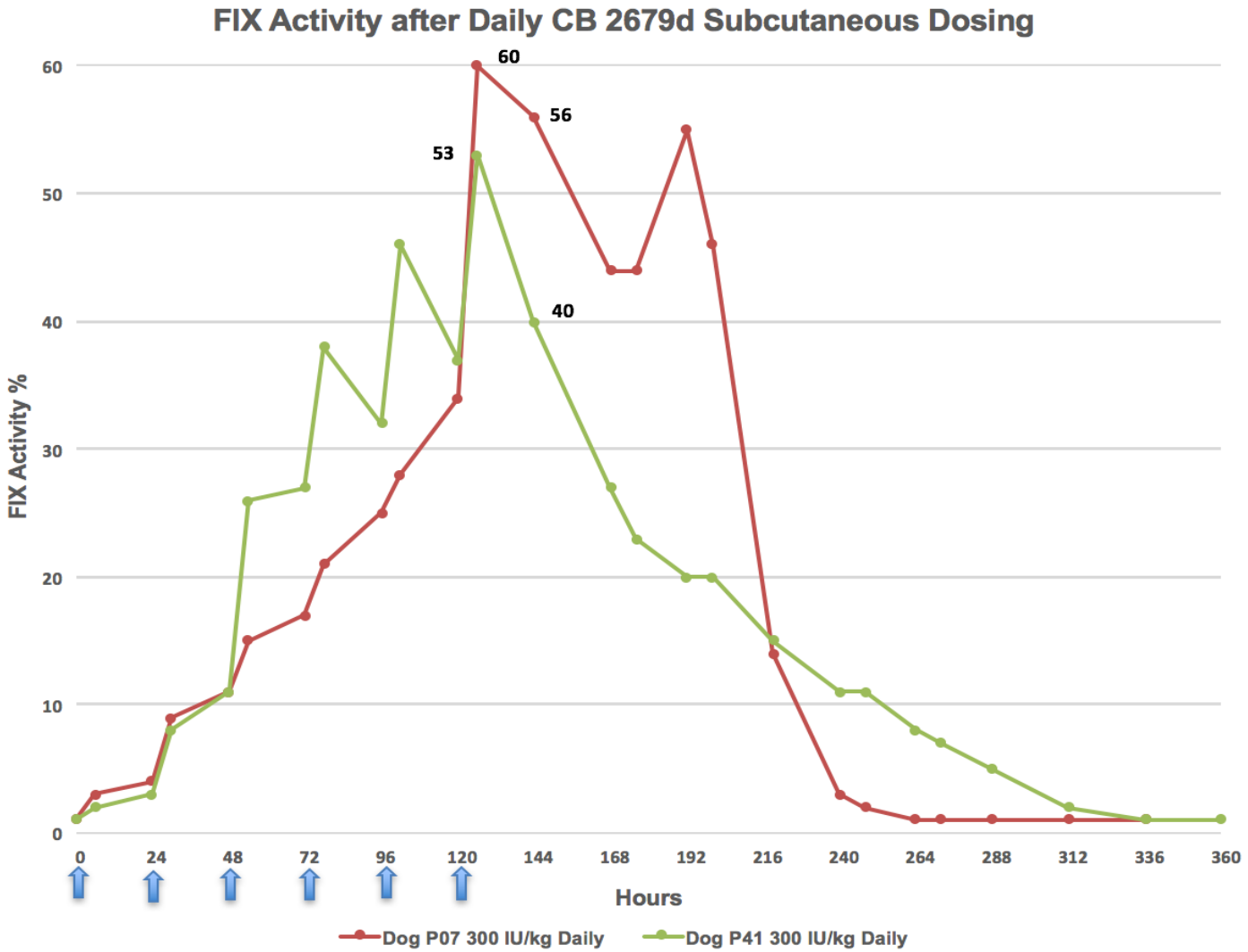
Aims & Methods

- Determine pharmacokinetics of daily subcutaneous CB 2679d
- CB 2679d 300 IU/kg was injected SQ daily for 6 days in hemophilia B dogs
- Sampled at 0, 6, 24, 30, 48, 54, 72, 78, 96, 102, 120, 126, 144, 168, 176, 192, 200, 219, 240, 248, 264, 272, 288, 312, 336 and 360 hours
- rhFIX antigen in canine plasma was determined by ELISA using an Affinity Biologicals kit
- FIX activity was measured in duplicate, using a single-stage aPTT-based FIX clotting assay performed on an ACL-TOP instrument using Instrumentation Laboratories reagents

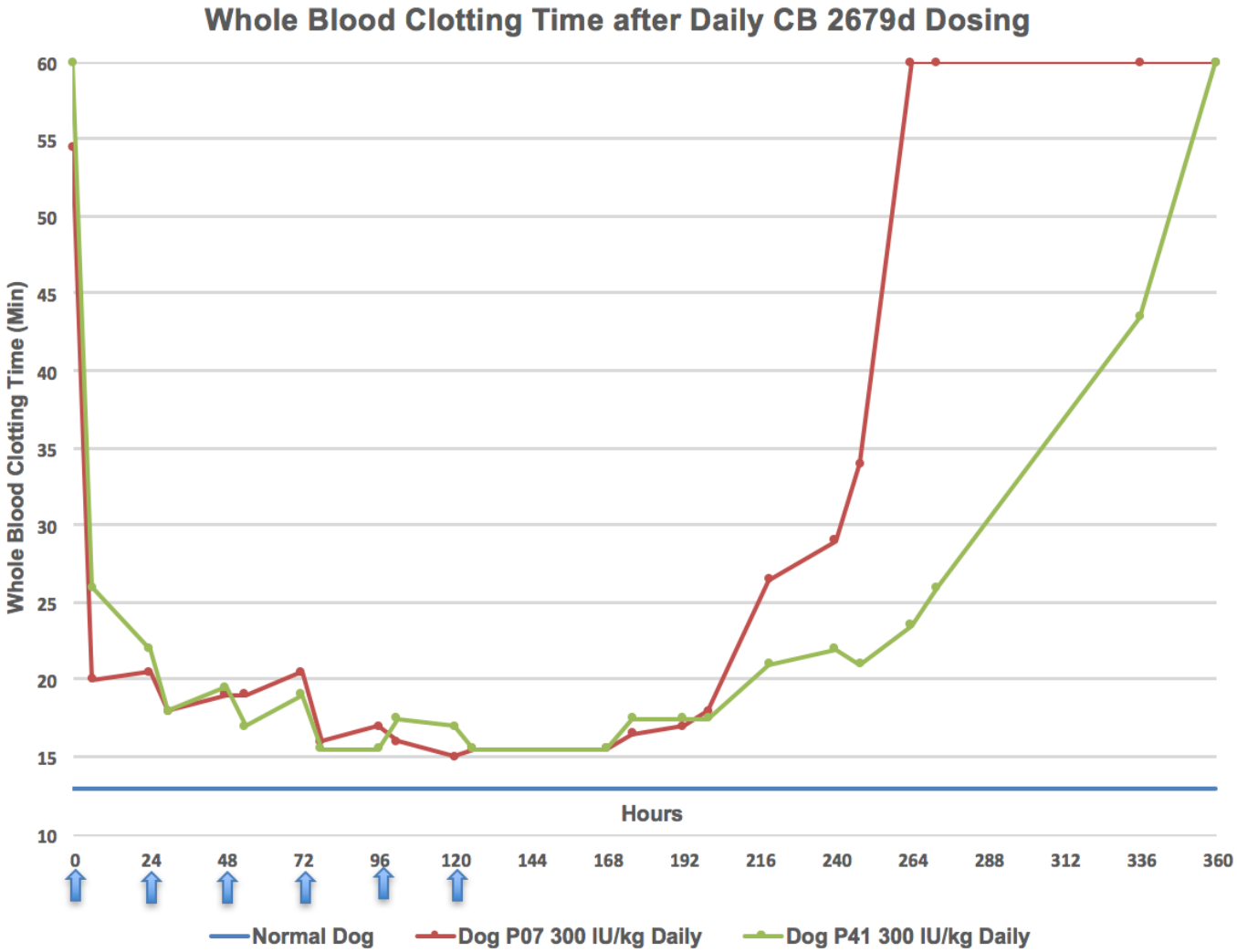
Progressive Increase in Peak and Trough FIX Antigen Levels with Daily Subcutaneous Dosing in Hemophilia B Dogs



FIX Activity is in the Normal Range after 6 Daily Subcutaneous Doses in Hemophilia B Dogs



Rapid & Sustained Correction of Whole Blood Clotting Time in Hemophilia B Dogs with Daily Subcutaneous Dosing



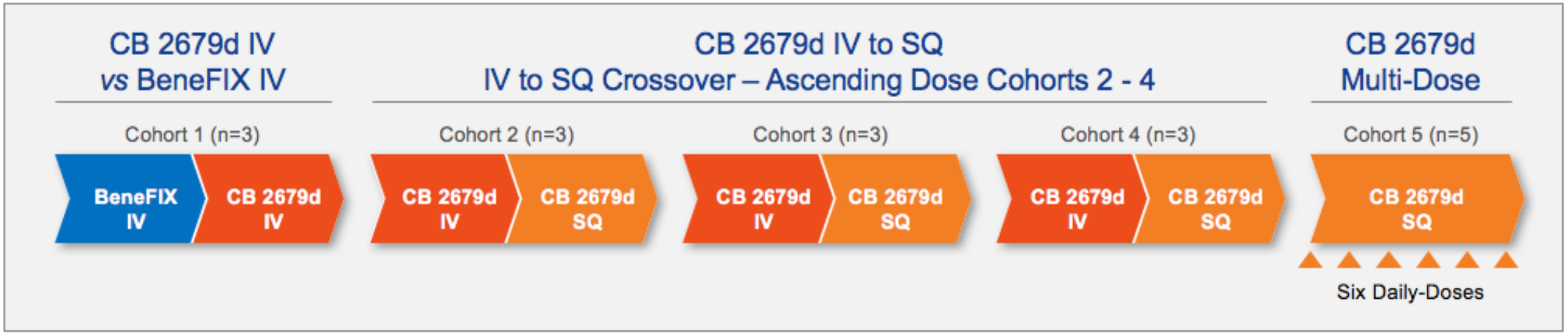
*Levy *et al*. EAHAD 2017 Haemophilia (2017), 23 (Suppl. 2), 29-140

Results

- Stable normal factor IX blood levels achieved with subcutaneous dosing
  - Daily SQ dosing of CB 2679d after 6 doses had peak FIX activity levels of 60% and 53% at 126 hours
  - Trough activity levels 24 hours after 6th daily dose were 56% and 40% respectively
- No emergent clinical adverse events or laboratory test abnormalities
- No skin reactions recorded

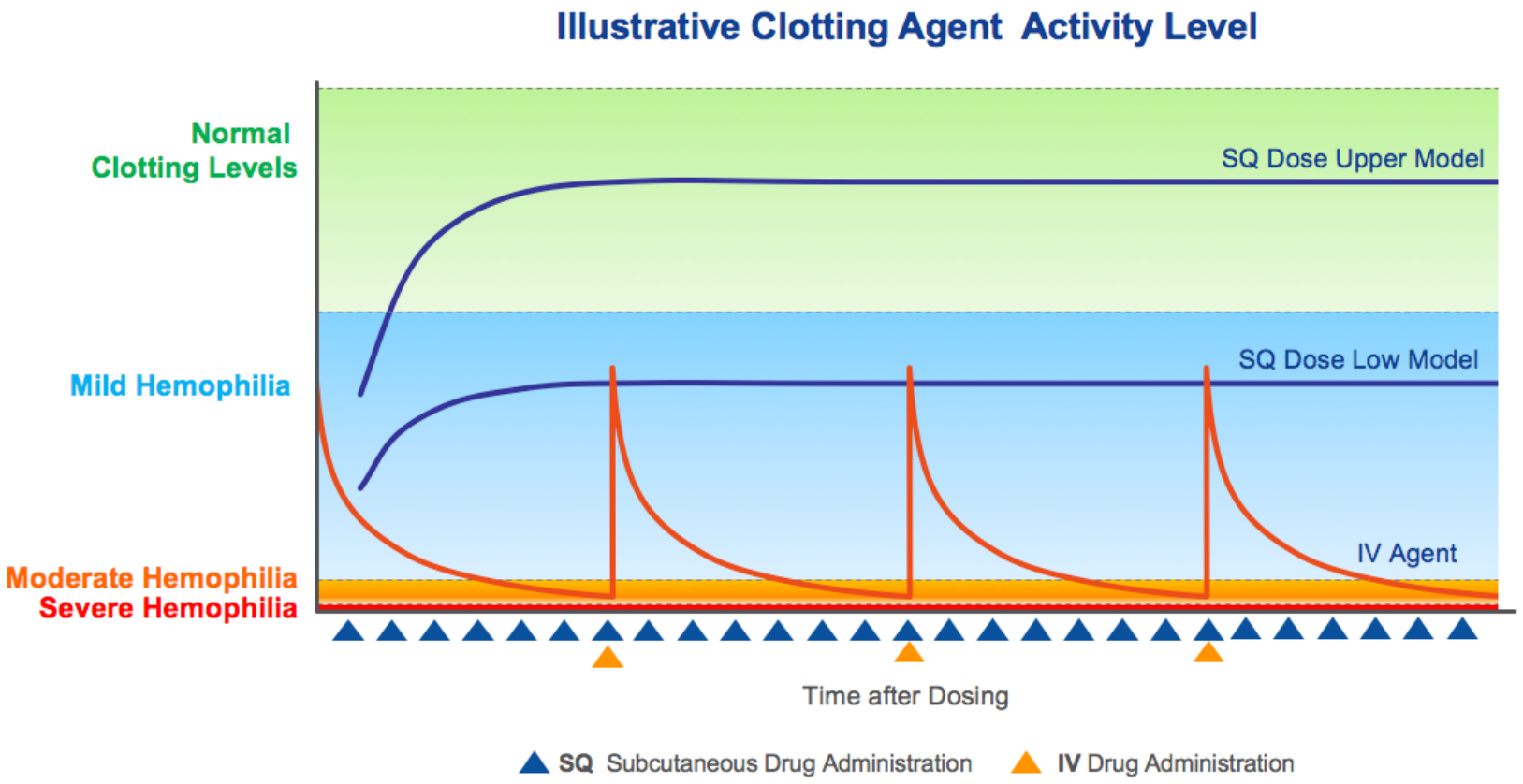
Dog Results Facilitated Ongoing Phase 1/2 Trial

- ISU Abxis is executing the Phase 1/2 trial
- Cohort 1 has been completed



Subcutaneous Dosing May Provide Superior Prophylaxis *vs.* Extended Half-life Agents

Time in Mild to Normal Levels Predicts Protection from Spontaneous Bleeds



CB 2679d/ISU304 Program Conclusions

- CB 2679d is designed as best-in-class high potency recombinant Factor IX product
- Potency advantage allows subcutaneous administration
- Hemophilia B dogs had daily subcutaneous dosing for 6 days
- Stable normal trough factor IX blood levels achieved after 6 daily subcutaneous doses
- Phase 1/2 subcutaneous trial is ongoing
  - Cohort 1 has been completed
  - Cohort 2 in screening
- Subcutaneous dosing may provide superior prophylaxis to intravenous extended half-life agents
- Orphan drug designation has been granted in EU