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Data Readout: Open-Label Extension (OLE) of Phase 2a Study of SerpinPC for Hemophilia

December 10, 2022

AGENDA

Data Readout: Open-Label Extension (OLE) of Phase 2a Study of SerpinPC for Hemophilia

- Opening
  - Kristen K. Sheppard, Esq
    Senior Vice President, Investor Relations & Corporate Communications

- Introduction to SerpinPC
  - Antoine Yver, MD MSc
    Chairman of Development

- SerpinPC Phase 2a Open-Label Extension Data*
  - Trevor Baglin, MedScD PhD
    Vice President, Global Head for Hemophilia

- SerpinPC Pivotal Program Design for Hemophilia B
  - Antoine Yver, MD MSc
    Chairman of Development

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As presented in an oral presentation at the American Society of Hematology (ASH) Annual Meeting on December 10, 2022.

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SerpinPC Development Program

Antoine Yver, MD MSc

Chairman of Development

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SerpinPC in persons with severe hemophilia (PwH): long-term treatment from a multi-center, multi-part, first-in-human study

T Baglin*, A Koch[f], I Mocanu[+], L Makhaldiani[$], J Huntington*

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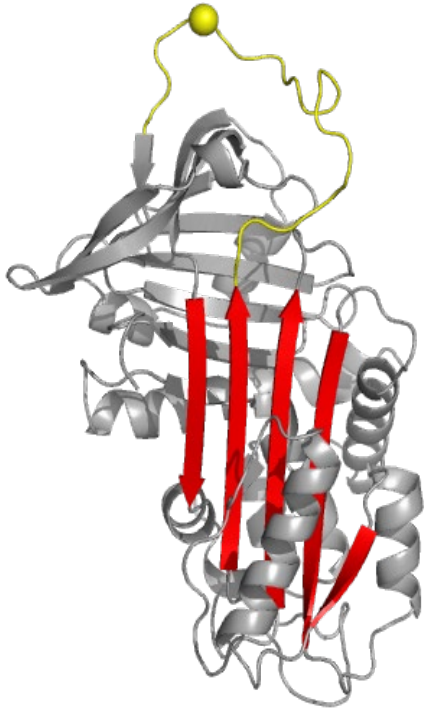
* Slides were presented at the American Society of Hematology (ASH) Annual Meeting on December 10, 2022.

SerpinPC: a subcutaneously administered biologic inhibitor of APC



3D-model of SerpinPC*

- Unprecedented biology with novel pharmacology
- Intended for subcutaneous prophylaxis across hemophilia subtypes
- Modified α1 anti-trypsin with 3 substitution mutations to confer selective inhibition of activated protein C (APC)
- Prevents bleeds by inhibiting APC to prolong prothrombinase activity and allow sufficient thrombin generation in the absence of intrinsic tenase

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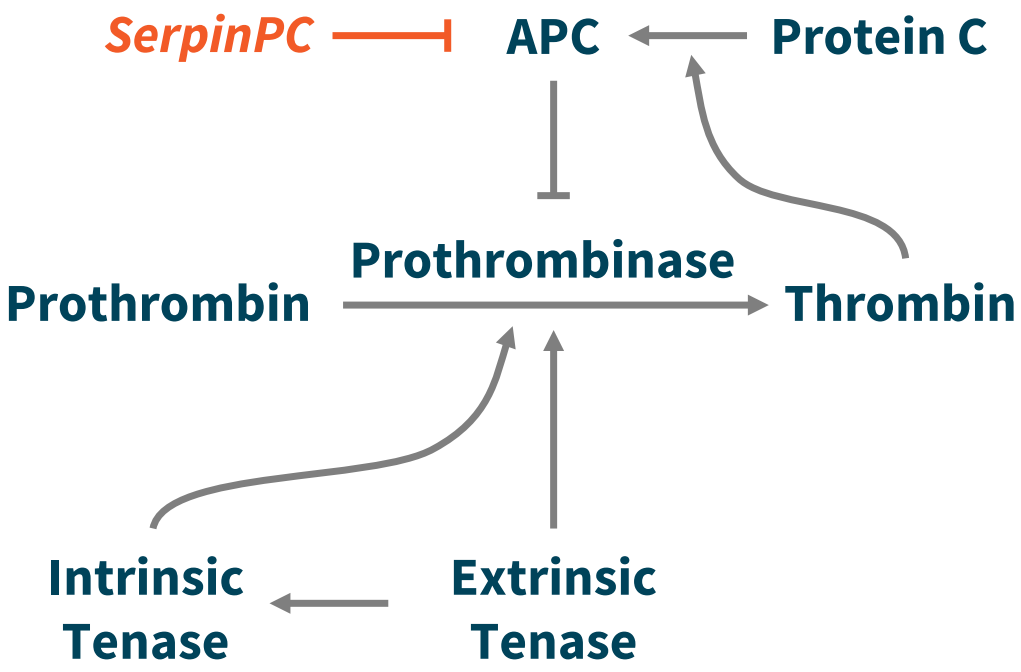
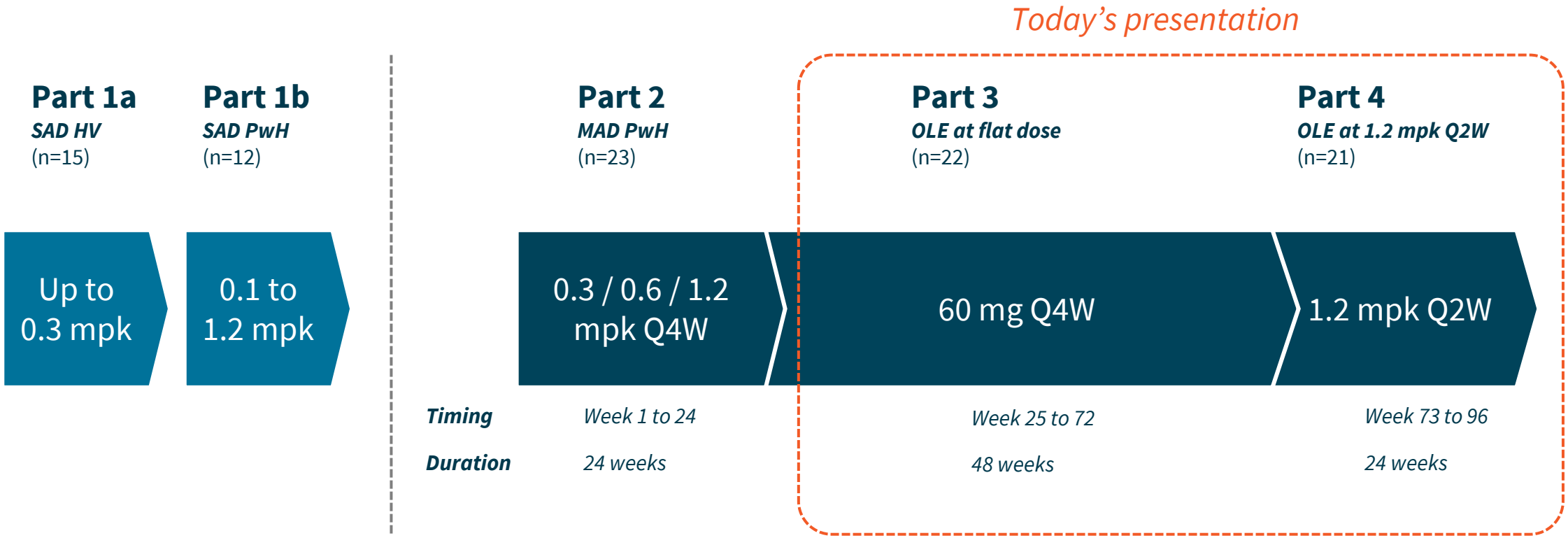
* SerpinPC is an investigational agent that has not been approved by the FDA or any other regulatory authority

SerpinPC and thrombin generation



AP-0101 study design: adaptive first-in-human study to investigate the safety, tolerability, efficacy and PK of SerpinPC



AP-0101 Parts 2-4: demographics, baseline characteristics and early terminations

Demographics and baseline characteristics

Characteristic	Value
Age, median (min to max)	**39** (21 to 56)
Number of subjects	**23** (including 12 from Part 1b SAD)
Prospective baseline Annualized Bleed Rate (ABR)[1], median (min to max)	**34.1** (22.8 to 53.0)
% subjects receiving previous prophylaxis	**0%**
% subjects with target joints[2]	**100%**
No. of target joints, median (min. to max.)	**2.5** (1 to 4)

Early terminations

Part	Early termination
Part 2	**1 subject** due to skin-rash – treatment-related[3]
Part 3	**1 subject** due to emigration to another country
Part 4	**1 subject** due to recto-sigmoid cancer – not related to treatment[3]

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[1] Values for Part 3 subjects

[2] "Target joint" = joint with >3 bleeds in any 6-month period

[3] Determined by Safety Review Group

AP-0101 Parts 3 and 4: no observations of treatment-related adverse events

	Part 3 (n=22)		**Part 4** (n=21)	
Treatment Emergent Adverse Events	**Subjects with event** No. (%)	**Treatment-related***	**Subjects with event** No. (%)	**Treatment-related***
Elevated ALT	3 (14%)	0	3 (14%)	0
Elevated gamma-GT	0	NA	2 (10%)	0
COVID-19 infection	2 (9%)	0	1	0
Hepatic fibrosis	1	0	1	0
Chronic hepatitis C	0	NA	1	0
Fever	0	NA	1	0
Urinary tract infection	0	NA	1	0
Fracture	1	0	1	0
Radiculopathy	1	0	1	0
Elevated creatinine phosphokinase	1	0	0	NA
Anemia	1	0	1	0
Elevated sodium	0	NA	1	0
Rectosigmoid cancer	0	NA	1	0
Low neutrophil count	1	0	0	NA

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* Determined by Safety Review Group

AP-0101 Parts 3 and 4: no observations of treatment-related, non-transient elevations in D-dimer

Result	Subjects in Part 3 (n=22) No. (%)	Subjects in Part 4 (n=21) No. (%)
Any result ≥ 500 ng/ml	5 (23%)	3 (14%)
2 consecutive results ≥ 500 ng/ml	2 of 5*	1 of 3**
Unexplained sustained elevation of D-dimer	**0 of 5**	**0 of 3**

>96% of D-dimer measurements were ≤ 500 ng/ml
(384 of 398 measurements)

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* For Part 3, one subject with rectosigmoid cancer and one subject with traumatic hip bleed

**For Part 4, one subject with rectosigmoid cancer

AP-0101: Anti-drug Antibodies (ADAs) and Pharmacokinetics (PK)

- Samples for ADA characterization including neutralizing capacity and cross-reactivity ongoing
- PK analysis ongoing, including exposure-response modeling

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AP-0101 Parts 3 and 4: reduction in Annualized Bleed Rate (ABR)

All bleed ABR

Part	Median ABR from prospective baseline	Median ABR observed in this part	Median % change from baseline
Part 3 (n=22)	34.1	6.2	-83%
Part 4 (n=21)	35.5	2.2	-93%

Spontaneous joint bleed ABR

Part	Median ABR from prospective baseline	Median ABR observed in this part	Median % change from baseline
Part 3 (n=22)	27.5	4.3	-86%
Part 4 (n=21)	28.3	2.2	-93%

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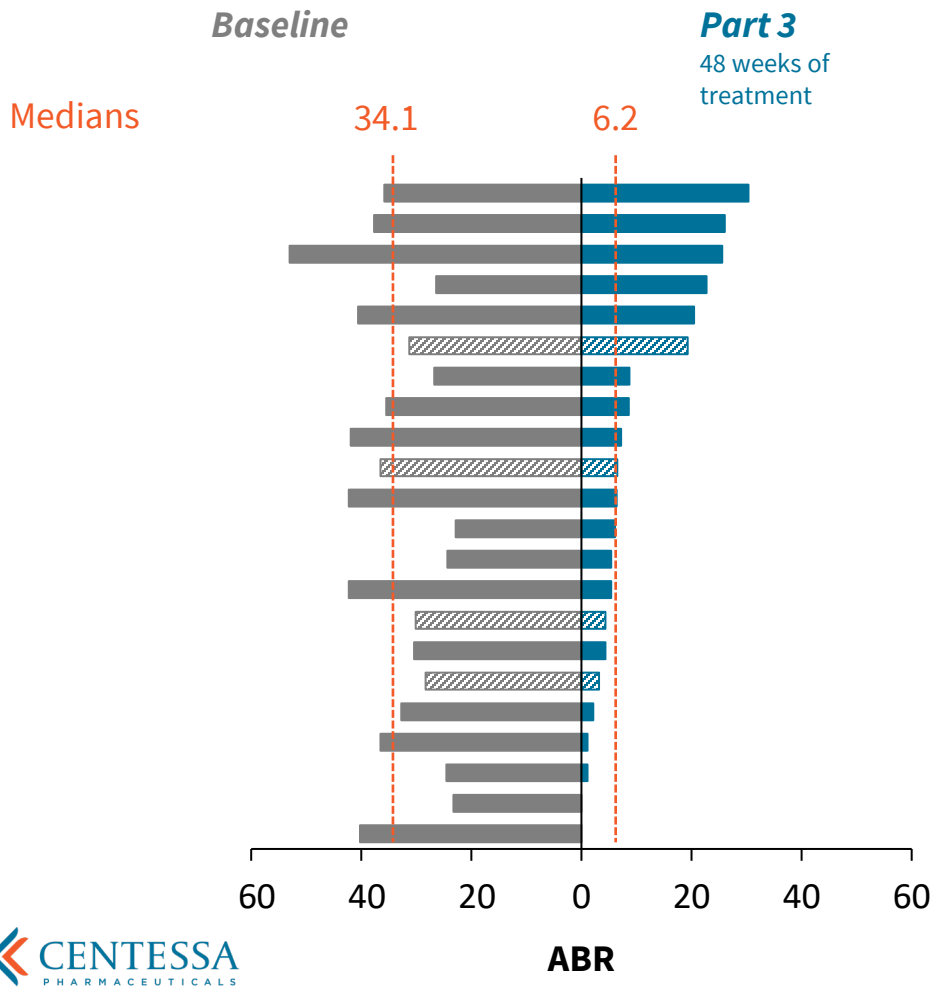
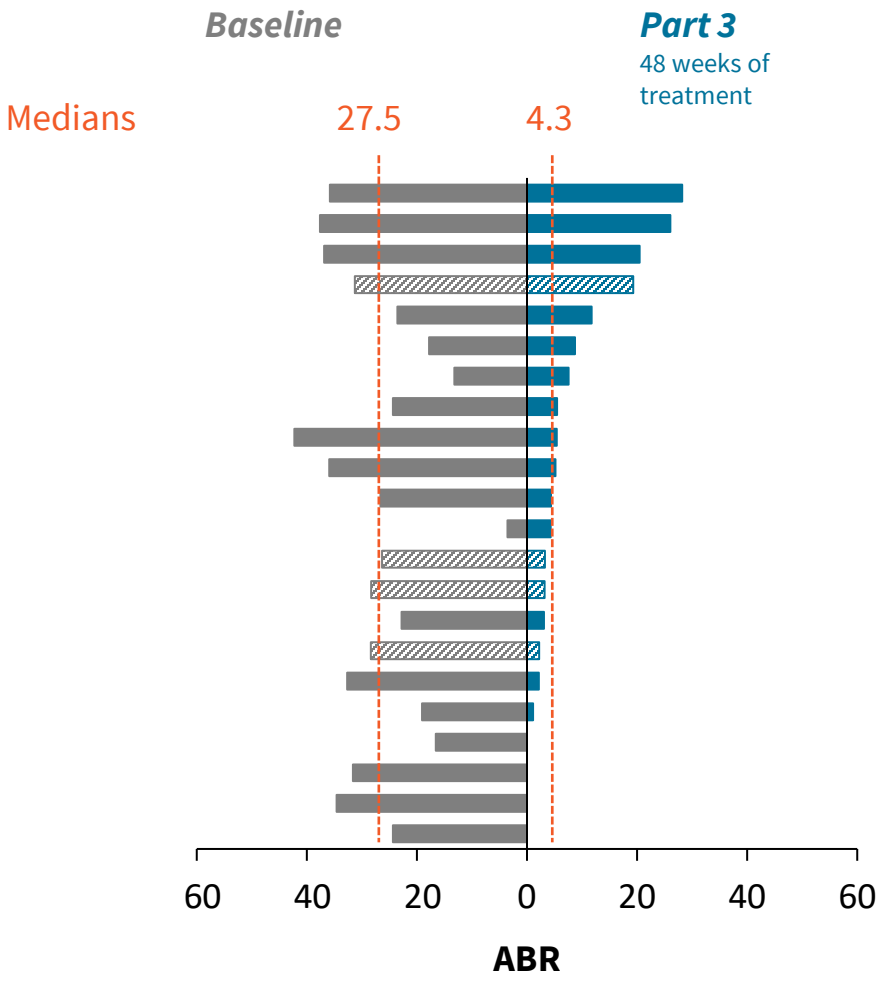
AP-0101 Part 3: ABR at 60mg Q4W flat dose

HemA
HemB

All bleeds ABR



Spontaneous joint bleeds ABR



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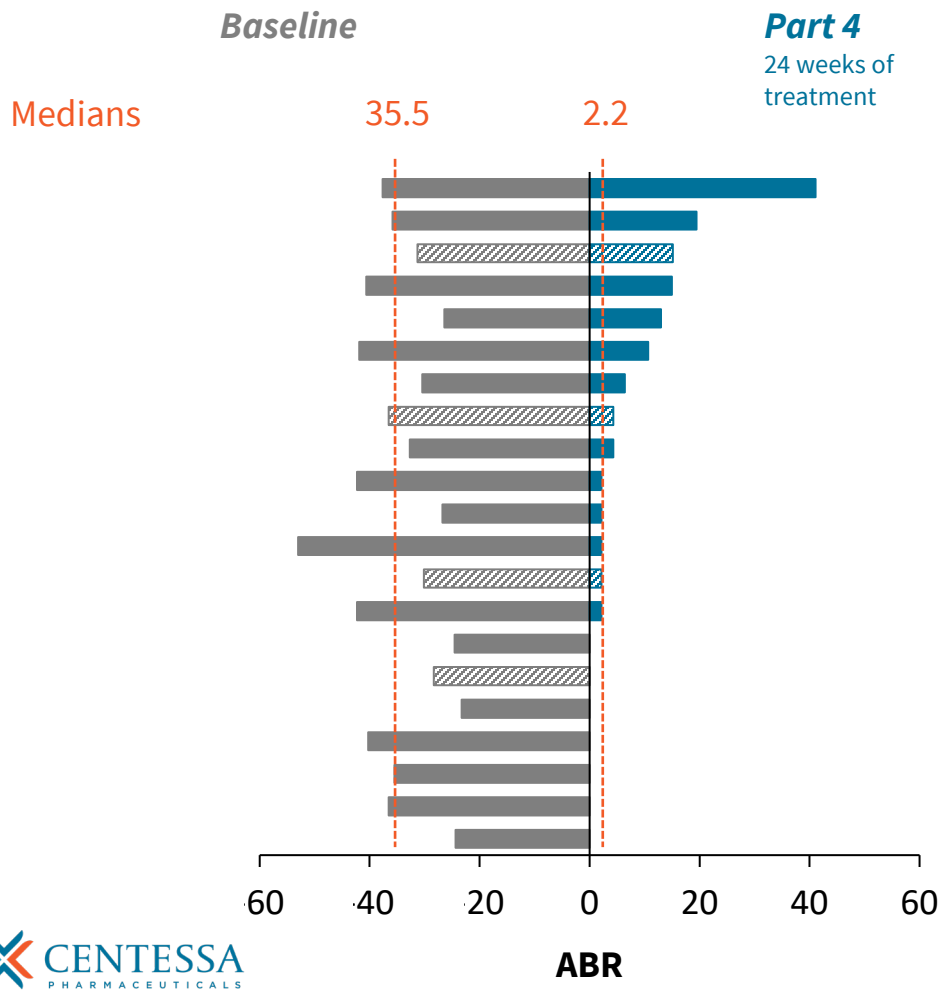
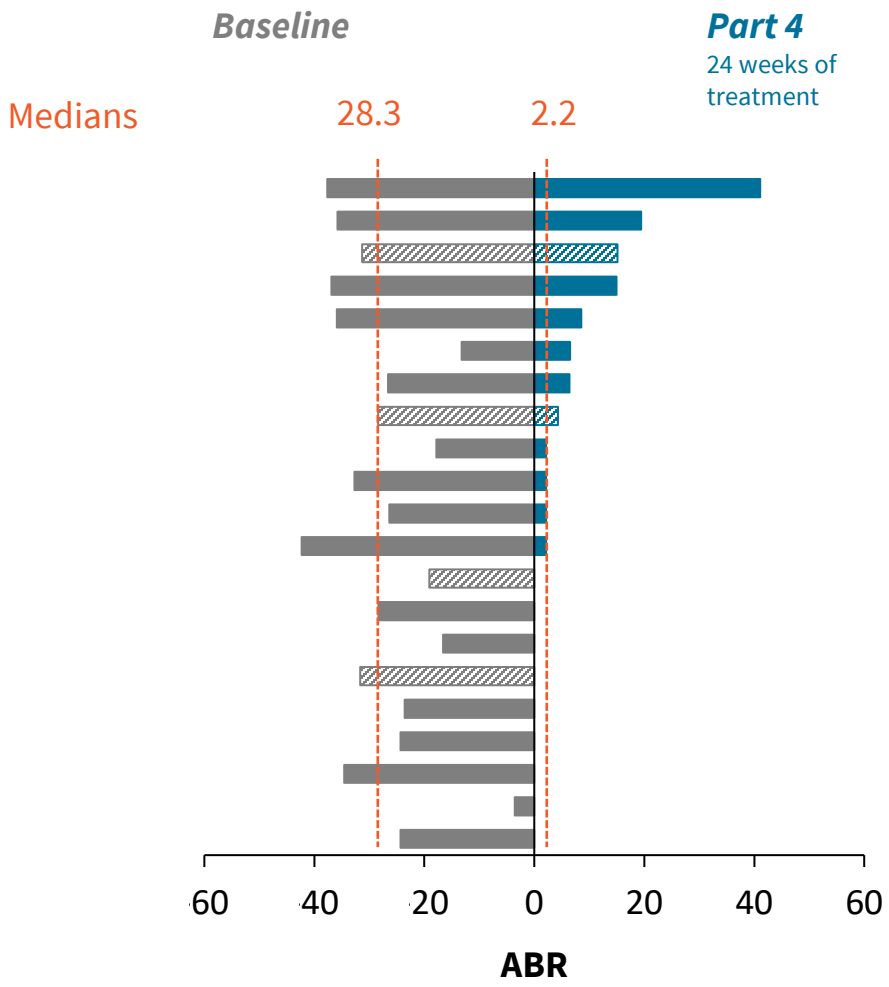
AP-0101 Part 4: ABR at 1.2 mpk Q2W

HemA
HemB

All bleeds ABR



Spontaneous joint bleeds ABR



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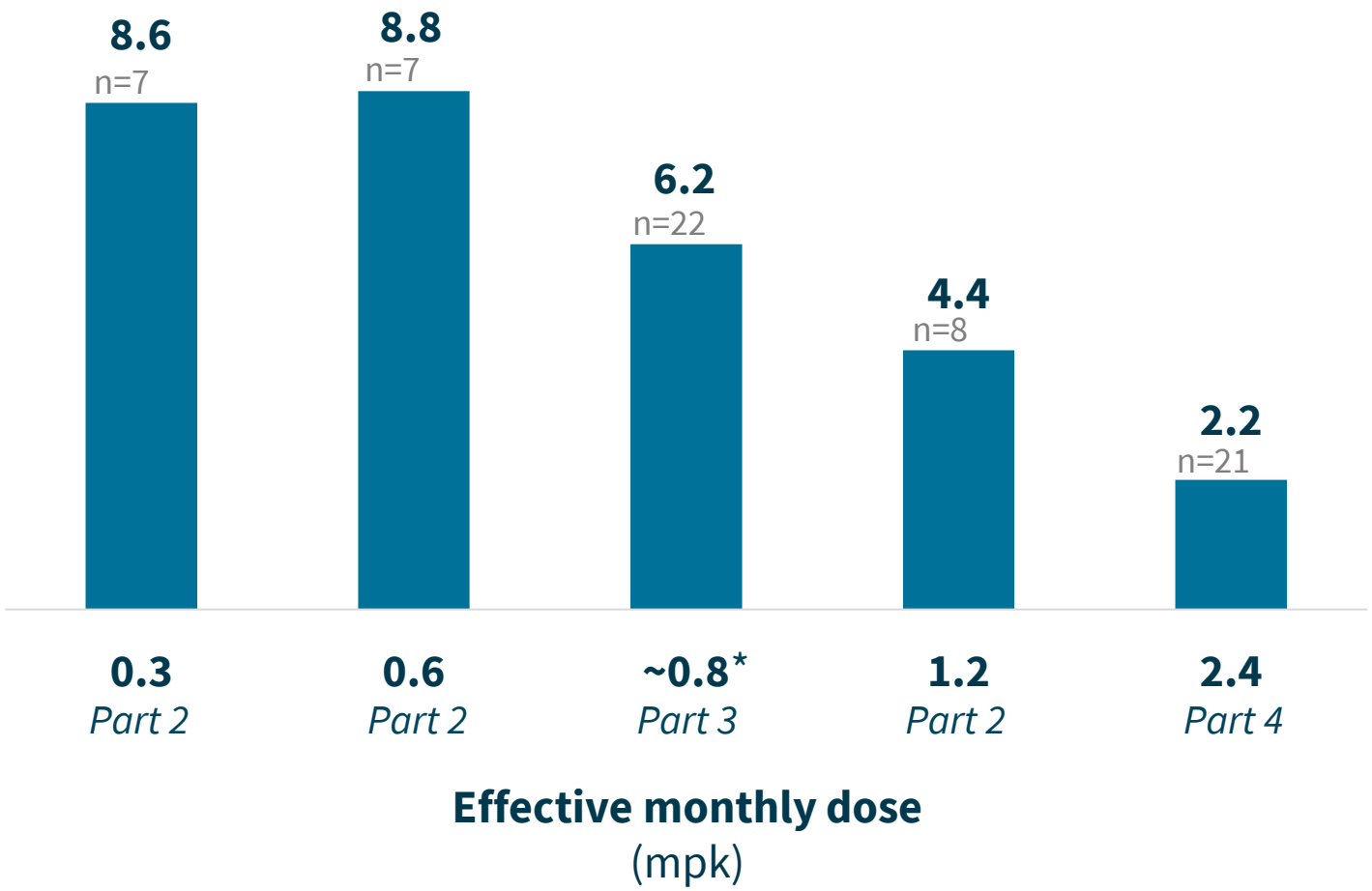
AP-0101: All bleed median ABR by dose level



* 60 mg Flat dose which was equivalent to ~0.8 mpk

Summary

- **SerpinPC**
  - Novel MoA: inhibition of APC to rebalance coagulation
  - Broad potential to treat all subtypes of hemophilia
  - Subcutaneous route of administration

- **Results of Phase 2, Parts 3 and 4**
  - No observations of treatment-related adverse events
  - No observations of treatment-related sustained elevations of D-dimer
  - All bleed median ABR of 2.2 (median percentage reduction from baseline of 93%) in Part 4

Thank you to all the persons who have and continue to participate in this study

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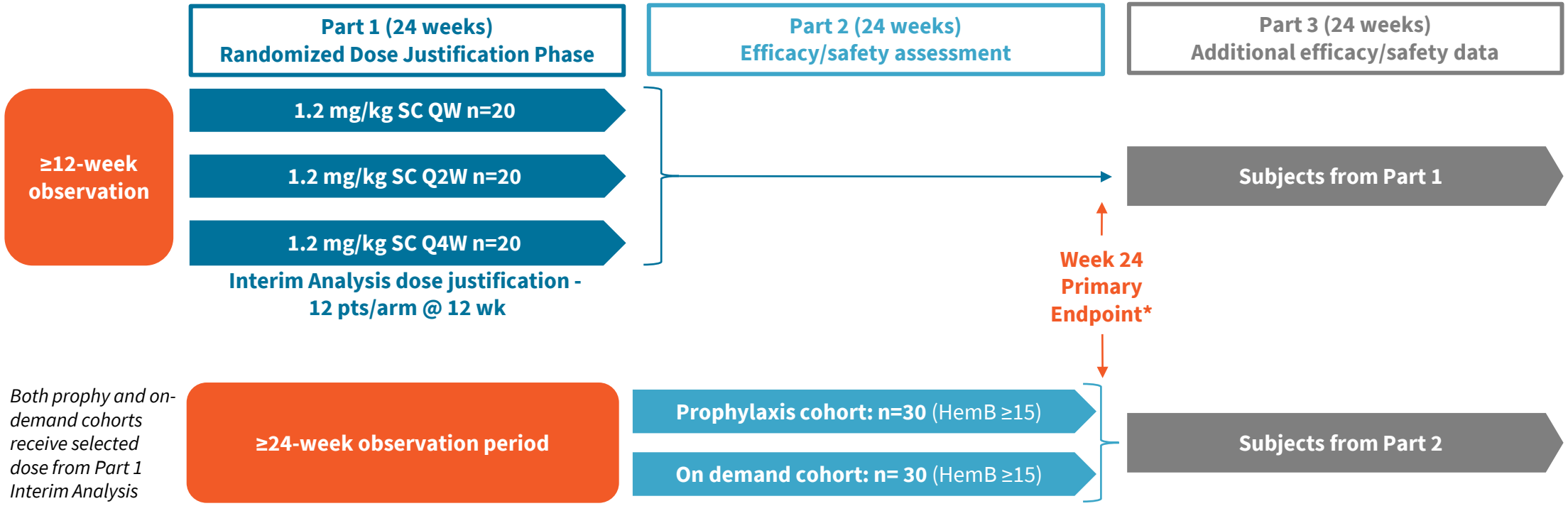
SerpinPC registrational development plan (Hemophilia B without inhibitors)

1 **≥12 Week Observation Study (PRESent-5):** *Designed to enroll patients and prospectively establish baseline ABR before initiation of interventional studies*

2 **Hemophilia B without inhibitors (PRESent-2)** (n=120) *Study to also include hemophilia A subjects to support safety database*



***Primary Endpoint:** Rate of treated bleeds (expressed as annualized bleeding rate [ABR]) in the observation period and during the first 24 weeks with SerpinPC*

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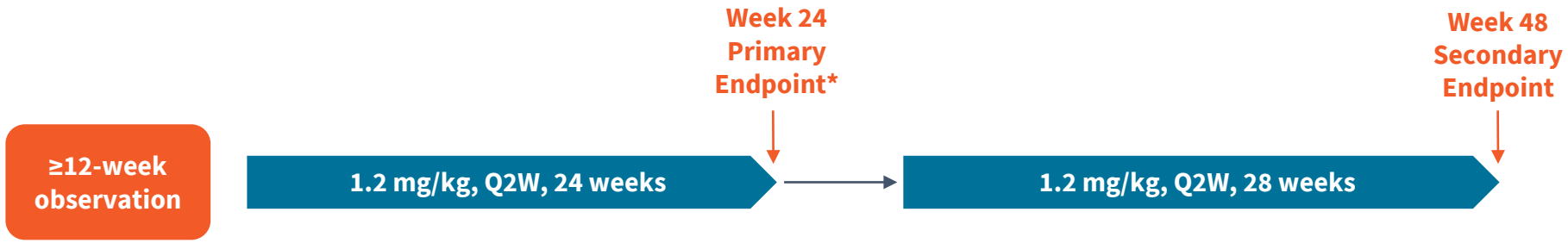
SerpinPC registrational development plan (Hemophilia B with inhibitors)

1 **≥12 Week Observation Study (PRESent-5):** *Designed to enroll patients and prospectively establish baseline ABR before initiation of interventional studies*

3 **Hemophilia B with inhibitors (PRESent-3)** (n<20)



***Primary Endpoint:** Rate of treated bleeds (expressed as annualized bleeding rate [ABR]) in the observation period and during the first 24 weeks with SerpinPC*

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