CENTESSA PHARMACEUTICALS

SerpinPC Phase 2a Results

SEPTEMBER 9, 2021

Disclaimer

This presentation has been prepared by Centessa Pharmaceuticals plc (the “Company”) for informational purposes only and not for any other purpose. This presentation may contain forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Statements in this presentation that are not statements of historical fact are forward-looking statements, including, without limitation, statements regarding the open label extension study of SerpinPC and its design and conduct; plans for continued development of SerpinPC, including our global development plan and registrational path for this candidate; our expectations with respect to the treatment paradigm for hemophilia A and B, our asset-centric business model and the intended advantages and benefits thereof, research and clinical development plans, the scope, progress, results and costs of developing our product candidates or any other future product candidates, strategy, regulatory matters, including the timing and likelihood of success of obtaining approvals to initiate or continue clinical trials or market any products, market size and opportunity and our ability to complete certain milestones. Words such as "believe," "anticipate," "plan," "expect," "intend," "will," "may," "goal," "project," "estimate," "potential" and similar expressions are intended to identify forward loo king statements, though not all forward-looking statements necessarily contain these identifying words. These forward-looking statements are based on the beliefs of the Company's management as well as assumptions made by and information currently available to the Company. Such statements reflect the current views of the Company with respect to future events and are subject to known and unknown risks, including, without limitation, business, regulatory, economic and competitive risks, uncertainties, contingencies and assumptions about the Company, risks related to our ability to protect and maintain our intellectual property position; risks inherent in developing products and technologies; future results from our ongoing and planned clinical trials; our ability to obtain adequate financing to fund our planned clinical trials and other expenses; trends in the industry; the legal and regulatory framework for the industry; future expenditures risks related to our asset-centric corporate model; the risk that any one or more of our product candidates will not be successfully developed and commercialized; the risk that the results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies; and risks related to the COVID-19 pandemic including the effects of the Delta variant and the other risk factors contained in our filings with the U.S. Securities and Exchange Commission. In light of these risks and uncertainties, the events or circumstances referred to in the forward-looking statements may not occur. The actual results may vary from the anticipated results and the variations may be material. These forward-looking statements should not be taken as forecasts or promises nor should they be taken as implying any indication, assurance or guarantee that the assumptions on which such forward looking statements have been made are correct or exhaustive or, in the case of the assumptions, fully stated in this presentation. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date this presentation is given.

This presentation discusses product candidates that are under clinical study, and which have not yet been approved for marketing by the U.S. Food and Drug Administration or any other regulatory agency. No representation is made as to the safety or effectiveness of these product candidates for the use for which such product candidates are being studied. The trademarks included herein are the property of the owners thereof and are used for reference purposes only. Such use should not be construed as an endorsement of such products. Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third party sources and the Company’s own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this presentation, we have not independently verified, and make no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third party sources. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

SerpinPC Phase 2a Results

TODAY'S SPEAKERS

SAURABH SAHA MD PhD
Chief Executive Officer

TREVOR BAGLIN MedScD PhD
Co-founder & Chief Medical Officer of ApcinteX

ADDITIONALLY AVAILABLE FOR Q&A

ANTOINE YVER MD MSc
Chief Medical Officer

GREG WEINHOFF MD MBA
Chief Financial Officer

Mission

Deliver consequential medicines to patients by striving to make the unprecedented possible

Pipeline

Centessa at a glance

10 Wholly-owned Companies

- **300** Active Patents
- **20+** Subject-matter Experts
- **1000+** Published Papers[1]

16 Disclosed Programs

- **14** Rare Disease Assets
- **6** Oncology Assets
- **4** Assets in the Clinic

1. Publications by members of the Centessa team

Pipeline

Our diverse portfolio includes 16 programs across multiple therapeutic areas

Company	Disease	Mechanism
Palladio Biosciences	Autosomal Dominant Polycystic Kidney Disease	Vasopressin V2 Receptor Inhibitor
ApcinteX	Hemophilia A and B	Activated Protein C Inhibitor
Pega-One	Cutaneous Squamous Cell Carcinoma	Anti-EGFR mAb
Z Factor	Alpha-1 Antitrypsin Deficiency	A1AT Folding Corrector
Morphogen-IX	Pulmonary Arterial Hypertension	BMP9 Engineered Variant
Capella BioScience	Idiopathic Pulmonary Fibrosis	Anti-LIGHT mAb
	Systemic Sclerosis and Lupus Erythematosus	Anti-BDCA-2 mAb
LockBody Therapeutics	Solid Tumors	CD47 LockBody
		CD3 LockBody
Orexia Therapeutics	Narcolepsy Type 1	OX2R Agonist (Oral)
		OX2R Agonist (Intranasal)
Janpix	Acute Myeloid Leukemia	Dual-STAT3/5 Degrader
PearlRiver Bio	Non-Small Cell Lung Cancer	EGFR-C797S Inhibitor
		EGFR-Ex20 Inhibitor
		EGFR-Next Gen

By the end of 2023, all Centessa companies aim to have assets in the clinic

CENTESSA PHARMACEUTICALS

Milestones

Significant momentum with 2021 accomplishments

JANUARY 2021

- Launch
- Acquisition of 10 biotech companies
- $250M Series A

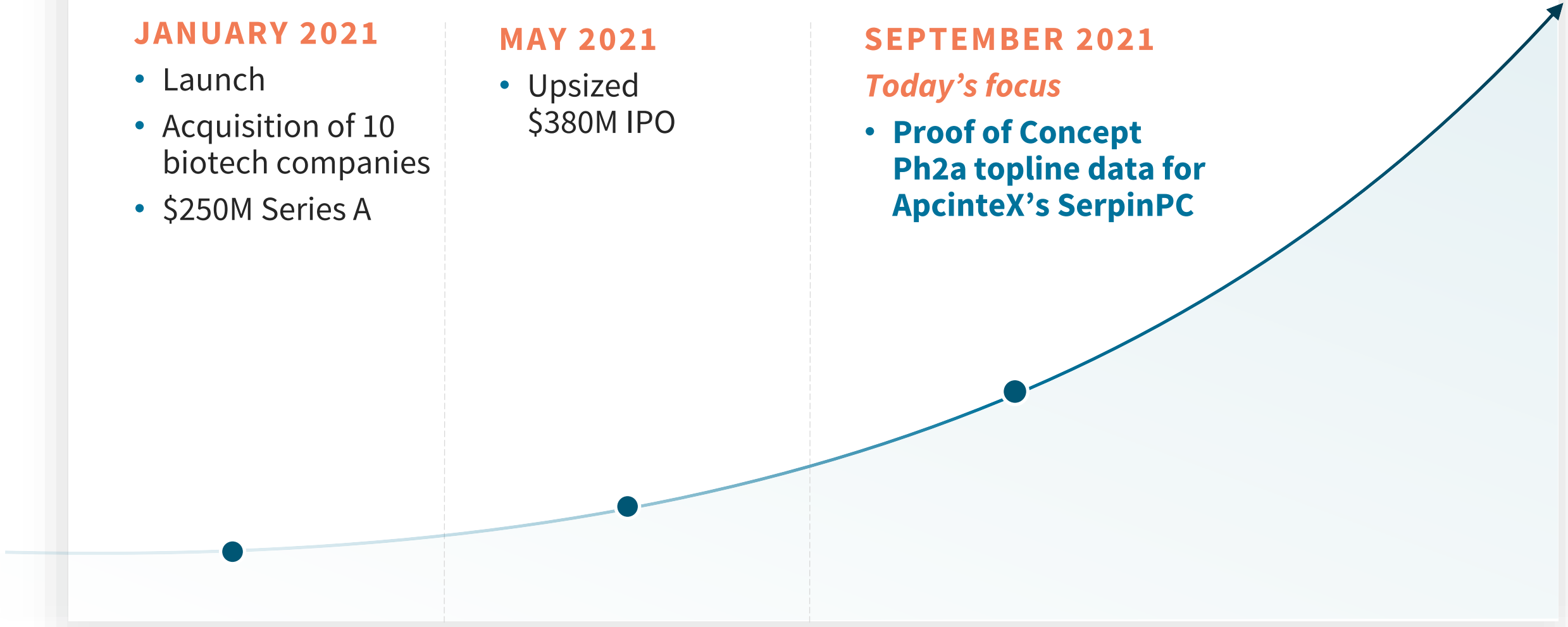
MAY 2021

- Upsized $380M IPO

SEPTEMBER 2021

Today's focus

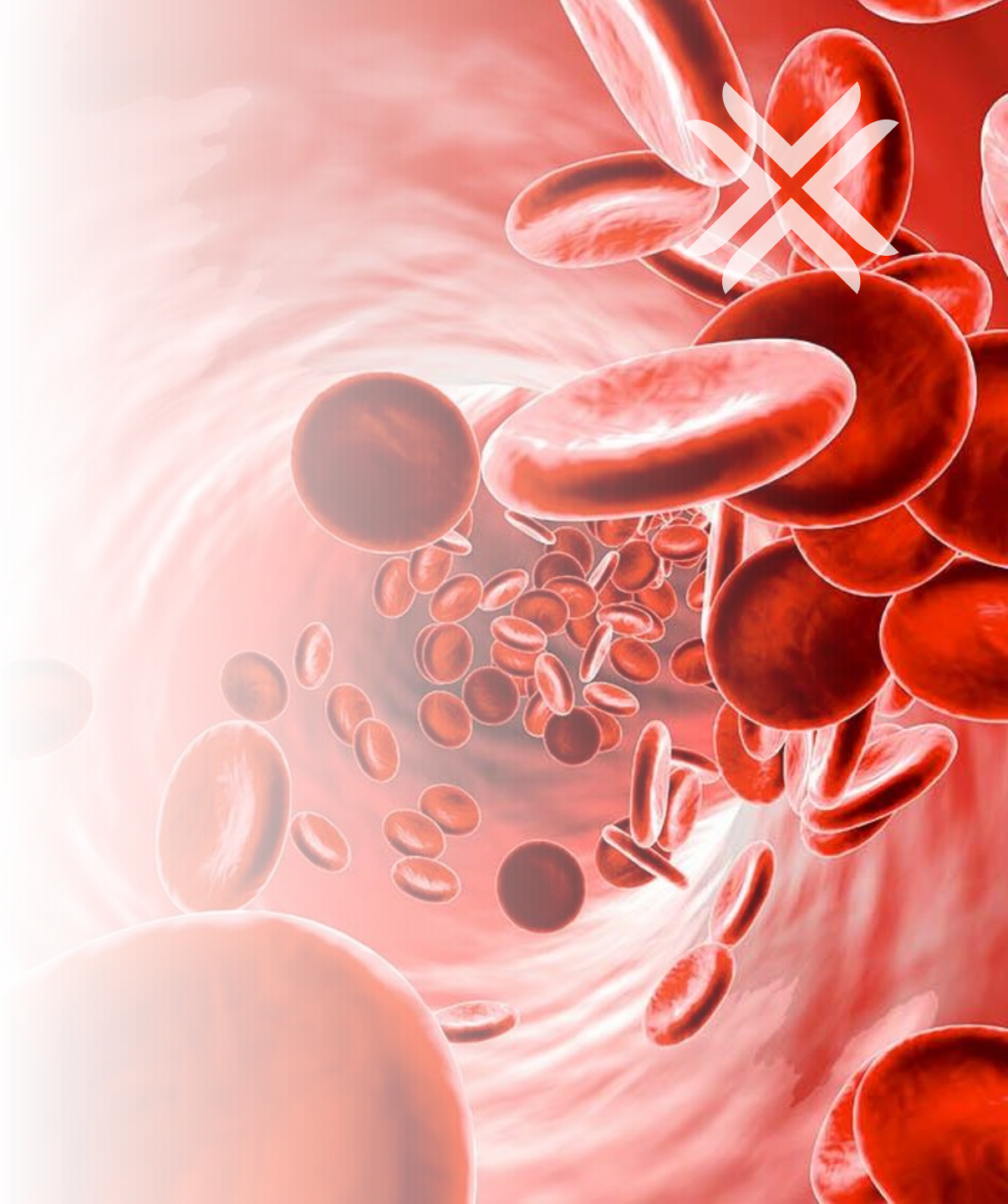
- **Proof of Concept Ph2a topline data for ApcinteX's SerpinPC**



CENTESSA PHARMACEUTICALS

SerpinPC

Designed to be a first-in-class coagulation rebalancing agent for the treatment of **hemophilia A and B**



Summary

Successful proof-of-concept results

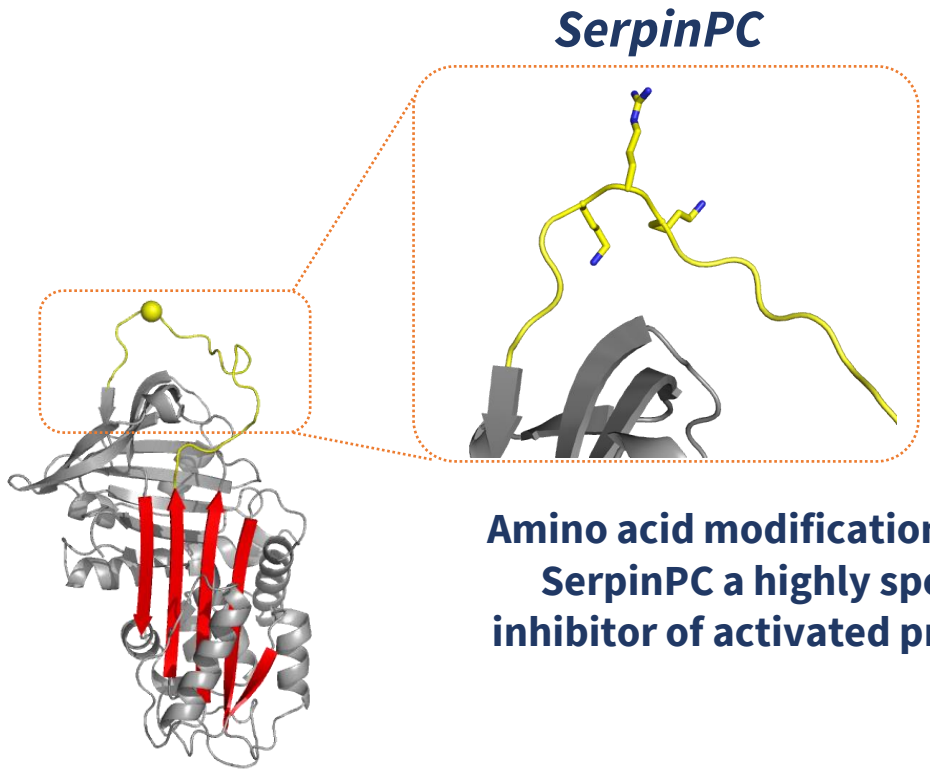
The goals of this Phase 2a clinical proof-of-concept study were to evaluate the safety and efficacy of once monthly, subcutaneous SerpinPC in a population of hemophilia A and B patients not on prophylaxis and with a history of substantial bleeding

We observed compelling reductions in all bleeding measures tested in both hemophilia A and B patients, and SerpinPC was observed to be well-tolerated

We are excited to follow-up these promising results with a global full development plan aimed at one or more registrations

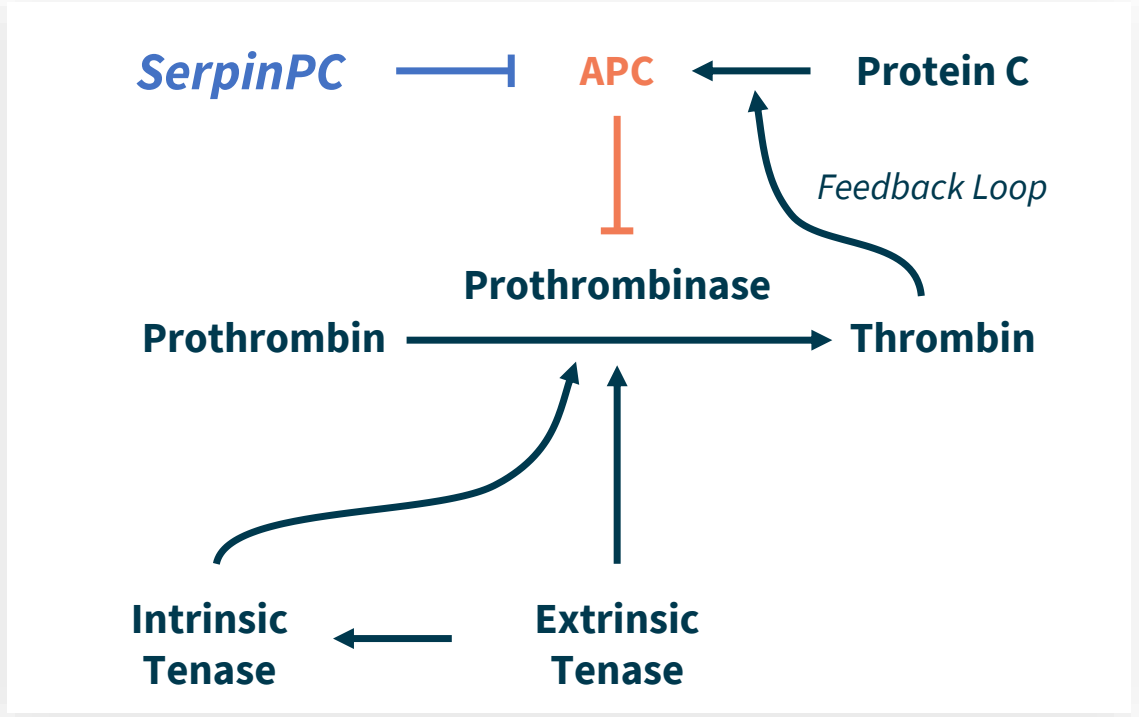
Mechanism of action

Unique MoA, supported by human genetics



Serpin:
alpha-1-antitrypsin

Amino acid modifications make SerpinPC a highly specific inhibitor of activated protein C



CENTESSA PHARMACEUTICALS

Differentiation

Potential benefits of SerpinPC

Novel MoA for **hemophilia A and B**

Compelling efficacy

Excellent safety profile without potential thrombosis

Convenient **subcutaneous administration**

CENTESSA PHARMACEUTICALS

Overview of AP-0101

Phase 1/2a proof of concept study

AP-0101

	PHASE 1, HEALTHY VOLUNTEERS	PHASE 1, PERSONS WITH HEMOPHILIA	PHASE 2a	ONGOING OPEN-LABEL EXTENSION
Objectives	Evaluate safety, tolerability, PK in healthy volunteers (HV)	Evaluate safety, tolerability, PK in persons with hemophilia (PwH)	Evaluate safety, tolerability, PK and effects of 3 dose levels in PwH	Evaluate long-term impact of flat dose in PwH
Patient population and study overview	• 15 HV • Single ascending dose • 8 weeks	• 12 PwH • Single ascending dose • 8 weeks	• 23 PwH, including all 12 from Phase 1, PwH • Repeat dose • 24 weeks	• 22 PwH from Phase 2a • Flat dose • 48 weeks

Clinicaltrials.gov identifier: NCT04073498 (https://clinicaltrials.gov/ct2/show/NCT04073498)

CENTESSA PHARMACEUTICALS

Positive proof of concept data from Phase 2a

SerpinPC was observed to be well-tolerated with no evidence of thrombotic risk

Improvements observed in multiple bleeding measures

At highest dose of **1.2 mg/kg SC once monthly**:

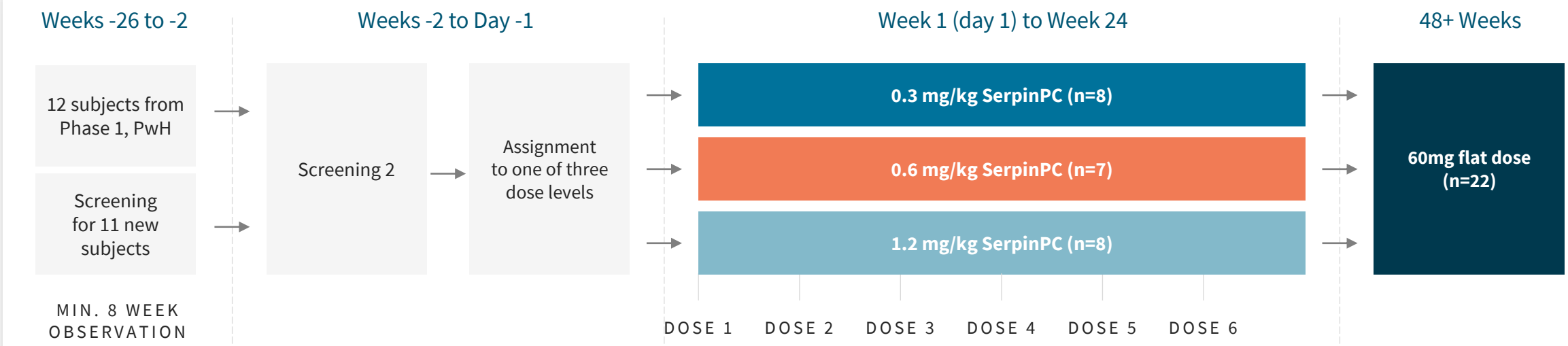
- All bleed ABR: Median **88% reduction**
- Spontaneous joint bleed ABR: Median **94% reduction**
- Zero target joints* at end of treatment period: **6 of 8 subjects**
- Zero or one bleeds during assessment period**: **5 of 8 subjects**
- Zero visible bleeds during the assessment period**: **8 of 8 subjects**

Note: all bleeding events are self reported
* Target joint = joint with >3 bleeds in any 6-month period
** Pre-specified assessment period: second half of treatment (weeks 13-24)

All patients who successfully completed Phase 2a have enrolled in the ongoing open-label extension study

CENTESSA PHARMACEUTICALS

Clinical trial design and exploratory efficacy analyses



Pre-exposure baseline period

All exploratory efficacy analyses compared last 12 weeks of treatment (pre-specified primary assessment period) to pre-exposure baseline measures. Bleeding events were self-reported.

12-week pre-specified primary assessment period

p-values are based on small numbers and are exploratory in nature.

CENTESSA PHARMACEUTICALS

Endpoints, subjects and inclusion criteria

ENDPOINTS

Primary endpoint: Safety and tolerability

Secondary endpoint: PK

Exploratory endpoint: Reduction in ABR

SUBJECTS

23 PwH in Georgia and Moldova

19 Hemophilia A without inhibitors

4 Hemophilia B without inhibitors

KEY INCLUSION CRITERIA

- **Males ages 18-60** with severe hemophilia
- **On-demand therapy** only
- **ABR** of 6 or more during the observational phase

CENTESSA PHARMACEUTICALS

Demographics and baseline characteristics

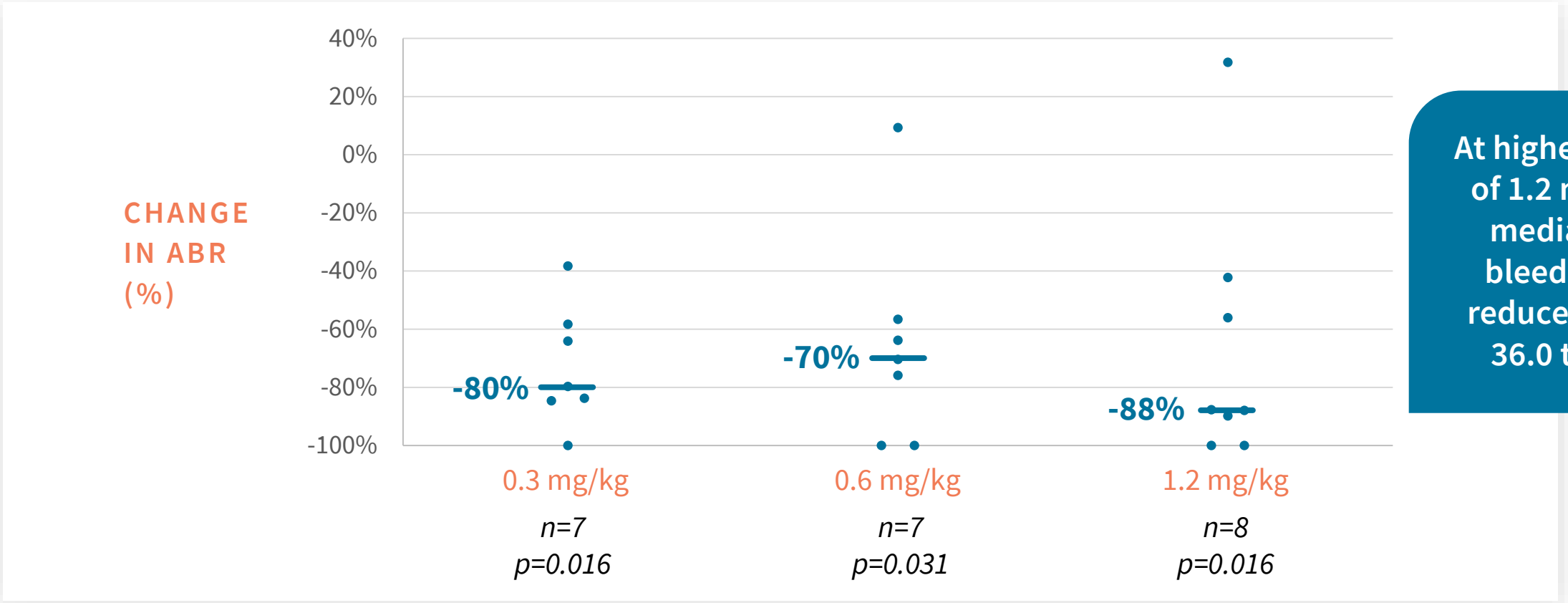
CHARACTERISTIC	PHASE 2a (n=23)
Age, median (min-max)	39 years (21-56 years)
Male, %	100%
Hemophilia A, %	83% (n=19)
Hemophilia B, %	17% (n=4)
Baseline ABR*, median total bleeds	35.5
Target joints**, %	100%
Target joints, median	2.5

* Annualized rate of self-reported bleeds
** Target joint = joint with >3 bleeds in any 6-month period

SerpinPC was well tolerated, with no evidence of thrombotic risk

- No thrombosis
- No instances of sustained elevations in D-dimer
- 1 moderate skin reaction that led to withdrawal of a patient with a history of a skin disorder
- 2 patients with ADAs, with no apparent impact on ABRs
- No other SerpinPC-related AEs

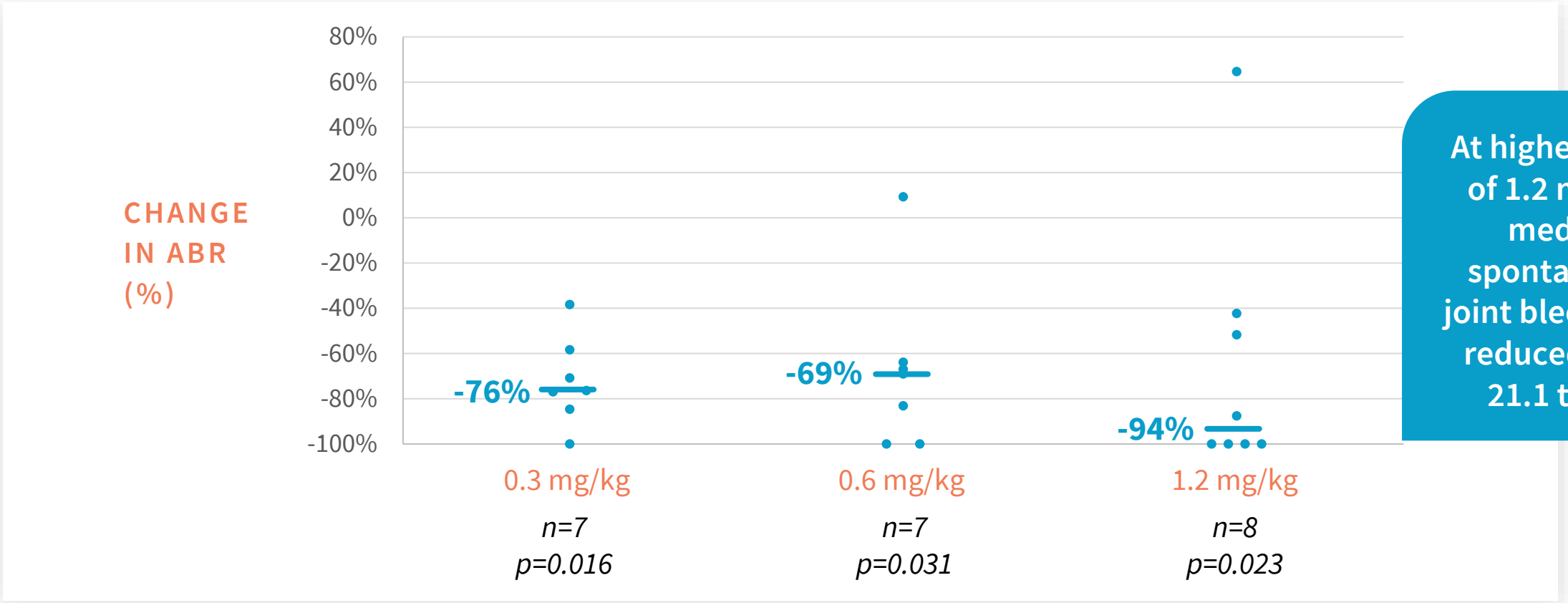
Median 88% reduction in ABR for all bleeds at 1.2 mg/kg



At highest dose of 1.2 mg/kg, median all bleeds ABR reduced from 36.0 to 4.4

CENTESSA PHARMACEUTICALS

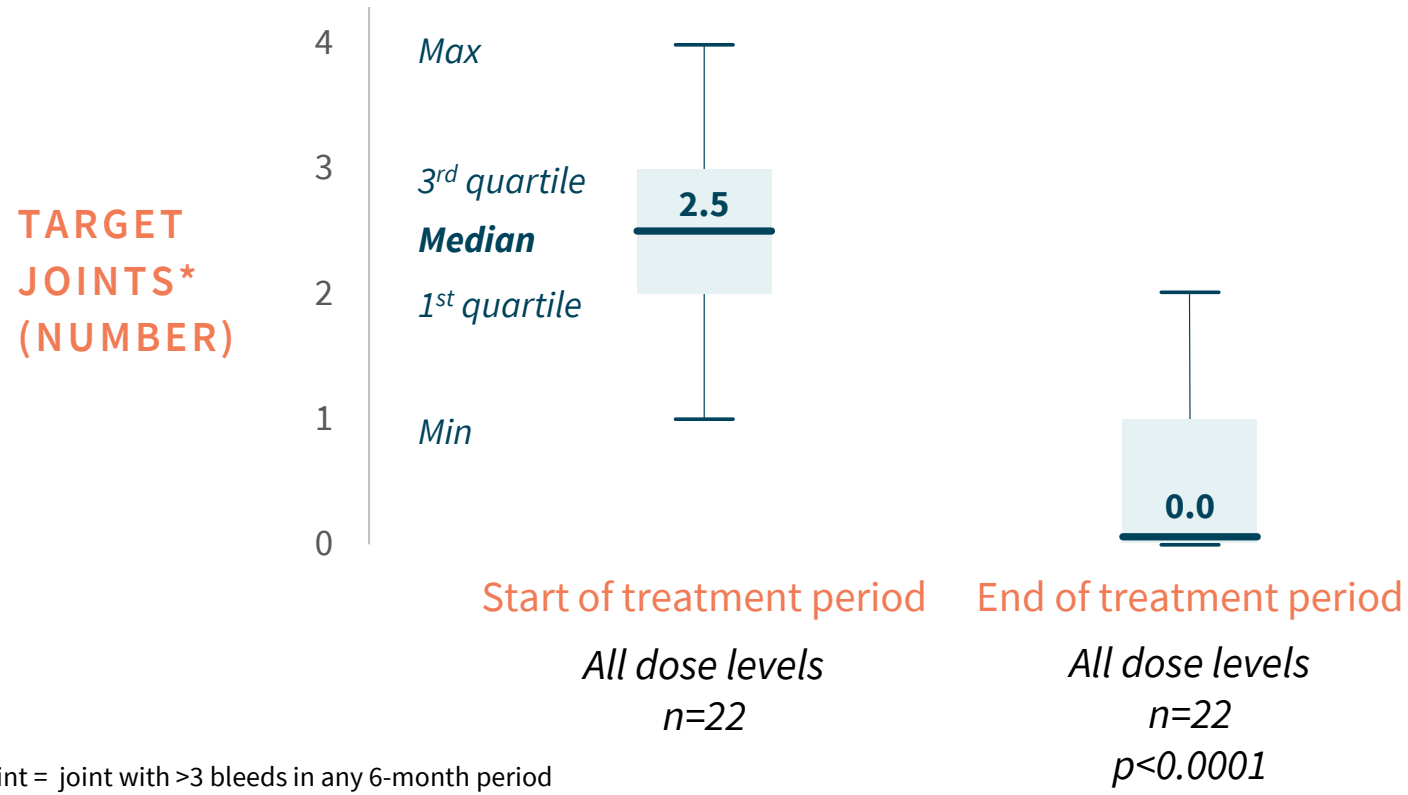
Median 94% reduction in ABR for spontaneous joint bleeds at 1.2 mg/kg



At highest dose of 1.2 mg/kg, median spontaneous joint bleeds ABR reduced from 21.1 to 2.2

CENTESSA PHARMACEUTICALS

Observed reduction in median target joints from 2.5 to 0 at all dose levels



Target joints reduced to zero in 6 of 8 subjects at 1.2 mg/kg and in 15 of 22 subjects for all dose levels

* Target joint = joint with >3 bleeds in any 6-month period

CENTESSA PHARMACEUTICALS

Similar reduction in ABR for all bleeds observed in hemophilia A and hemophilia B

Median change in all bleeds ABR	0.3 mg/kg	0.6 mg/kg	1.2 mg/kg
Hemophilia A	**-80%** (n=5)	**-64%** (n=5)	**-88%** (n=8)
Hemophilia B	**-72%** (n=2)	**-73%** (n=2)	No subjects

* Post hoc analysis, no p-values calculated

Potential benefits of SerpinPC

Novel MoA for
hemophilia A and B

Compelling efficacy

Excellent safety profile without potential thrombosis

Convenient **subcutaneous administration**

CENTESSA PHARMACEUTICALS

PATH FORWARD

Following our positive readout in hemophilia A and B, we will pursue a global full development plan aimed at one or more registrations

Thank you

Thank you to all patients who participated in this trial and to the clinical study team