

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 20549

**FORM 8-K**

**CURRENT REPORT  
PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Date of Report (date of earliest event reported): September 9, 2021

**CENTESSA PHARMACEUTICALS PLC**

(Exact name of Registrant, as specified in its charter)

**England and Wales**  
(State or other jurisdiction of incorporation)

**001-04321**  
(Commission File Number)

**Not applicable**  
(I.R.S. Employer Identification Number)

Mailing address:  
**3rd Floor  
1 Ashley Road  
Altrincham  
Cheshire WA14 2DT  
United Kingdom**

(Address of principal executive offices) (Zip code)

Registrant's telephone number, including area code: **+44 7391 789784**

Former name or address, if changed since last report:

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

<u>Title of each class</u>	<u>Trading Symbol(s)</u>	<u>Name of each exchange on which registered</u>
Ordinary shares, nominal value £0.002 per share	CNTA	Nasdaq Stock Market, LLC*
American Depositary Shares, each representing one ordinary share, nominal value £0.002 per share	CNTA	Nasdaq Stock Market, LLC

\*Not for trading, but only in connection with the listing of the American Depositary Shares on The Nasdaq Stock Market, LLC.

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

**Item 7.01 Regulation FD Disclosure**

On September, 9 2021, Centessa Pharmaceuticals plc (the “Company” or “Centessa”) issued a press release titled “Centessa Pharmaceuticals Announces Positive Topline Data from Proof-of-Concept Study of SerpinPC in Severe Hemophilia A and B Patients not on Prophylaxis.” A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

Following the issuance of the press release, the Company will host a conference call and webcast to discuss the topline data results. A copy of the presentation to be used on the conference call and webcast is furnished as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

The information under this Item 7.01, including Exhibits 99.1 and 99.2 hereto, shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

Exhibit No.

99.1 [Press Release dated September 9, 2021](#)

99.2 [Centessa Pharmaceuticals slide presentation](#)

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: September 9, 2021

**By:** /s/ Saurabh Saha  
**Name:** Saurabh Saha, M.D., Ph.D.  
**Title:** Chief Executive Officer

**Centessa Pharmaceuticals Announces Positive Topline Data from Proof-of-Concept Study of SerpinPC in Severe Hemophilia A and B Patients Not on Prophylaxis**

*~ 88% reduction in median Annualized Bleeding Rate (ABR) for all bleeds and 94% reduction in median ABR for spontaneous joint bleeds in highest dose tested ~*

*~ SerpinPC observed to be well-tolerated ~*

*~ Company has initiated planning for global registrational program ~*

*~ Conference call and webcast scheduled for today at 8:30 a.m. EDT ~*

CAMBRIDGE, Mass. & LONDON, September 9, 2021 – Centessa Pharmaceuticals plc (“Company”) (Nasdaq: CNTA), together with subsidiary ApcinteX Limited (“ApcinteX”), today announced positive topline results from the Phase 2a part of AP-0101, the six-month repeat dose portion of its ongoing first-in-human proof-of-concept study evaluating SerpinPC in severe hemophilia A and B patients.

AP-0101 is a Phase 1/2a proof-of-concept study evaluating SerpinPC, an inhibitor of activated protein C (“APC”), in 23 male subjects with either severe hemophilia A or B who were not on prophylaxis.<sup>1</sup> The Phase 2a part of the study assessed the safety, tolerability and pharmacokinetics across three dose cohorts (0.3 mg/kg, 0.6 mg/kg and 1.2 mg/kg) of SerpinPC administered as a subcutaneous (SC) injection every 4 weeks over a 24-week period (6 total doses). Reduction in the annualized bleeding rates (ABRs) were exploratory outcomes. Although eligible, none of the patients in the study had inhibitors.

SerpinPC was well-tolerated. As previously disclosed, one subject with a history of a skin disorder discontinued treatment on SerpinPC due to an injection site reaction. No other SerpinPC-related adverse events have been recorded. There was no reported sustained elevation in D-dimer, a sensitive measure of excess thrombin generation, throughout the 24-week study. Two subjects had anti-drug antibodies and remained on treatment without apparent impact on ABRs.

In the highest dose cohort, SerpinPC reduced the self-reported all bleeds ABR by 88% during the last 12 weeks of treatment (pre-specified primary assessment period) as compared to the all bleeds ABR prospectively measured during the pre-exposure observation period. In the highest dose cohort, five out of eight subjects had zero or one bleed during the 12-week pre-specified primary assessment period. Self-reported spontaneous joint bleeds ABR was reduced by 94% in the highest dose cohort. ABR reductions were similar between patients with either hemophilia A or hemophilia B.

Exploratory Efficacy Endpoints	Dose Tested		
	0.3 mg/kg n=7	0.6 mg/kg n=7	1.2 mg/kg n=8
All Bleeds ABR (median percent change)	-80% p=0.016	-70% p=0.031	-88% p=0.016
Spontaneous Joint Bleeds ABR (median percent change)	-76% p=0.016	-69% p=0.031	-94% p=0.023

Above analyses compared last 12 weeks of treatment (pre-specified primary assessment period) to pre-exposure baseline measures. Bleeding events were self-reported.  
p-values presented are based on small numbers and are exploratory in nature.

The median number of target joints (joint with >3 bleeds in any 6-month period) was reduced to zero at the end of the study from a pre-exposure baseline of 2.5. All subjects had target joints at the start of the study and 15 subjects had zero target joints at the end of the study.

All 22 patients who completed the Phase 2a portion of the study have elected to enroll into the 48-week open label extension ("OLE") portion of the study in which a single flat 60 mg subcutaneous dose of SerpinPC will be administered every 4 weeks over a period of 48 weeks (13 doses total). Centessa expects to report results from the OLE portion of this study in the second half of 2022.

"The compelling reduction in bleeds and continued tolerability that we observed in both hemophilia A and hemophilia B patients in this proof-of-concept study are very encouraging, and we are eager to move SerpinPC into a global development plan aimed at pursuing one or more registrations. We see broad utility of SerpinPC across the hemophilia landscape and will seek the most rapid path to bring this potential subcutaneous therapy to hemophilia patients," said Antoine Yver, M.D., M.Sc., Chief Medical Officer of Centessa Pharmaceuticals.

"The results of this Phase 2a study of SerpinPC continue to show an excellent tolerability profile for this molecule, and the exploratory efficacy results seen in this study of severe hemophilia A and B patients are also very promising. A safe, subcutaneous, prophylaxis option for both hemophilia A and B patients would be an important addition to our treatment choices," said David Lillicrap, M.D., Professor of Pathology and Molecular Medicine at Queen's University, Kingston, Ontario, Canada and previously a World Federation of Hemophilia Advisory Board member.

<sup>1</sup> *Clinicaltrials.gov identifier: NCT04073498 (https://clinicaltrials.gov/ct2/show/NCT04073498)*

**Conference Call and Webcast**

Centessa Pharmaceuticals will host a webcast and conference call today, September 9, 2021, at 8:30 a.m. EDT to discuss top-line data from the proof-of-concept trial. To access the audio webcast with slides, please visit the "Events & Publications" page in the Investors & Media section of the Company's website at <https://investors.centessa.com/events-presentations>. The call can also be accessed by dialing (855) 493-3565 (domestic) or (929) 517-9002 (international) with conference ID 8459296. An archive of today's webcast will be available on the Company's website.

**About Centessa Pharmaceuticals**

Centessa Pharmaceuticals plc aims to bring impactful new medicines to patients by combining the strengths of an asset-centric model with the benefits of scale and diversification typical of larger R&D organizations. The asset-centric model refers to a highly specialized, singular-focused company that is led by a team of well-recognized subject matter experts. Centessa's asset-centric companies' programs range from discovery-stage to late-stage development and include diverse therapeutic areas such as oncology, hematology, immunology/inflammation, neuroscience, hepatology, pulmonology and nephrology. For more information, visit [www.centessa.com](http://www.centessa.com).

**About ApcintEX Limited**

ApcintEX Limited is focused on developing SerpinPC for the treatment of hemophilia A and hemophilia B. Hemophilia is a rare bleeding disorder that is caused by a deficiency of thrombin generation upon vascular damage.

**About SerpinPC**

SerpinPC, a biologic based on the serpin family of proteins, is designed to allow more thrombin to be generated by inhibiting activated protein C (APC) thus rebalancing coagulation in hemophilia patients. SerpinPC has the potential to treat all types of hemophilia regardless of severity or inhibitor status, and may also prevent bleeding associated with other bleeding disorders.

**About AP-0101**

AP-0101 is an ongoing Phase 1/2a open-label clinical trial to investigate the safety, tolerability and pharmacokinetics of intravenous and subcutaneous doses of SerpinPC in healthy male volunteers and male persons with severe hemophilia (<https://clinicaltrials.gov/ct2/show/NCT04073498>).

**About Hemophilia A (HA) and Hemophilia B (HB)**

HA and HB are X-linked genetic disorders affecting one in 5,000 and one in 20,000 live male births, respectively, resulting in spontaneous internal bleeding that can be life-threatening. More than 70% of bleeds occur into joints (hemarthrosis) causing chronic joint damage (arthropathy) with musculoskeletal destruction. The bleeding associated with these disorders is the result of a defect or deficiency in factor VIII (in the case of HA) or factor IX (in the case of HB), the two components of the intrinsic tenase complex.

Normal blood coagulation (hemostasis) is a crucial part of the physiological response to tissue damage. When blood components come into contact with extravascular cells and proteins, platelets accumulate and ultimately lead to the formation of thrombin, the effector enzyme of blood coagulation. Prothrombinase activity is required for the rapid, localized production of thrombin needed for adequate blood clotting. Prothrombinase is continuously degraded by APC, which is present in the circulation at

low concentrations. In the setting of deficient intrinsic tenase activity (hemophilia), the natural anticoagulant activity of the circulating APC results in insufficient prothrombinase activity for normal blood clotting.

#### **Forward Looking Statements**

This press release contains forward-looking statements. These statements may be identified by words such as "believe," "anticipate," "plan," "expect," "intend," "will," "may," "goal," "project," "estimate," "potential," and variations of these words or similar expressions that are intended to identify forward-looking statements. Any such statements in this press release that are not statements of historical fact may be deemed to be forward-looking statements. These statements include discussions of 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 ability to deliver impactful medicines to patients; the ability of our key executives to drive execution of our portfolio of programs; 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.

Any forward-looking statements in this press release are based on our current expectations, estimates and projections only as of the date of this release and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to, the safety, tolerability and efficacy profile of SerpinPC observed to date may change adversely in future clinical trials, ongoing analyses of trial data or subsequent to commercialization; foreign regulatory agencies may not agree with our regulatory approval strategies, components of our filings, such as clinical trial designs, conduct and methodologies, or the sufficiency of data submitted; risks inherent in developing products and technologies; risks related to our ability to protect and maintain our intellectual property position; business, regulatory, economic and competitive risks, uncertainties, contingencies and assumptions about the Company; 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. These and other risks concerning our programs and operations are described in additional detail in our most recent Form 10-Q, which is on file with the SEC and available on the SEC's website at [www.sec.gov](http://www.sec.gov). We operate in a very competitive environment in which new risks emerge from time to time. These forward-looking statements are based on our current expectations, and speak only as of the date hereof. We explicitly disclaim any obligation to update any forward-looking statements except to the extent required by law.

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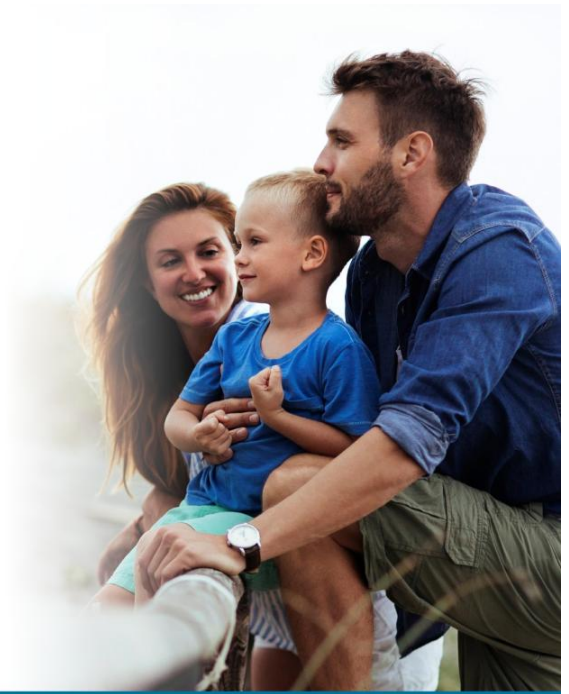
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# SerpinPC Phase 2a Results

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 looking 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

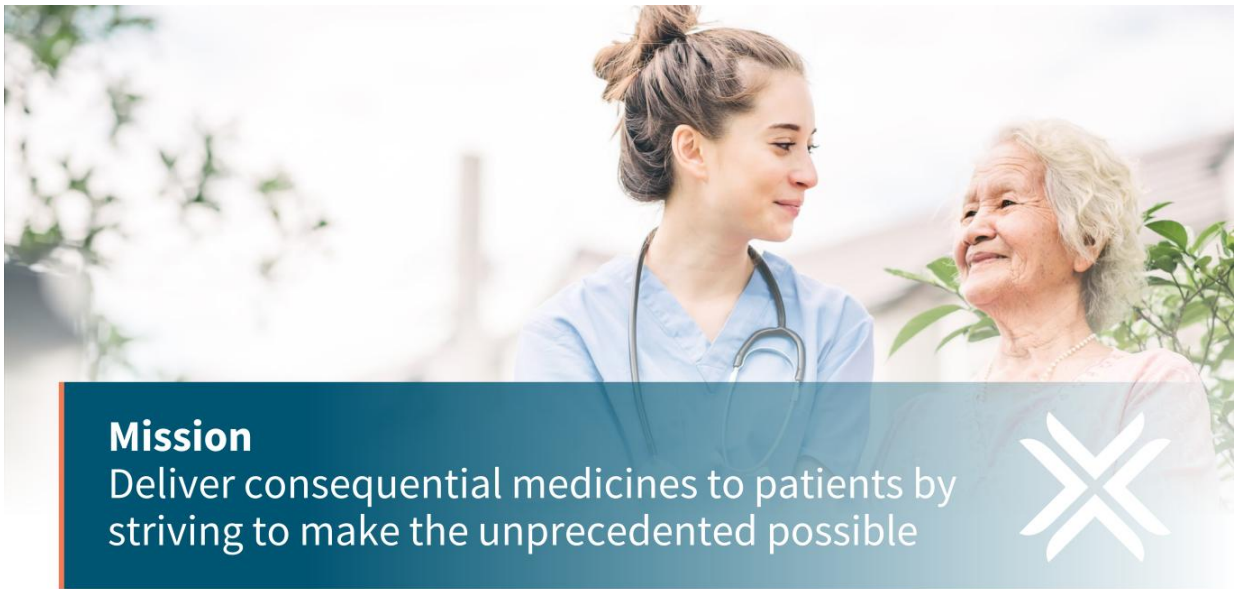
## ADDITIONALLY AVAILABLE FOR Q&A



**ANTOINE YVER MD MSc**  
Chief Medical Officer



**GREG WEINHOFF MD MBA**  
Chief Financial Officer



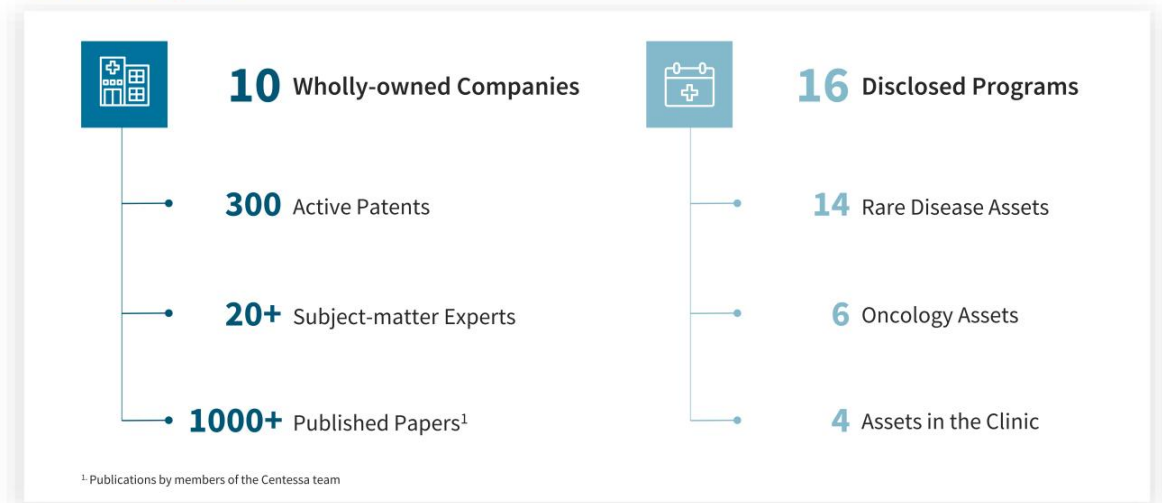
**Mission**

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



# Pipeline

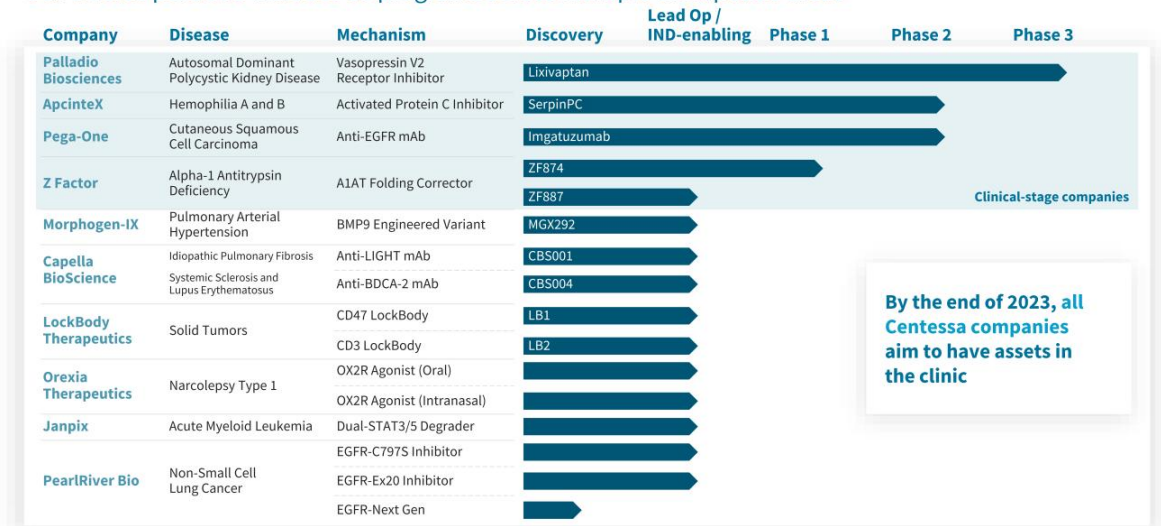
Centessa at a glance



<sup>1</sup> Publications by members of the Centessa team

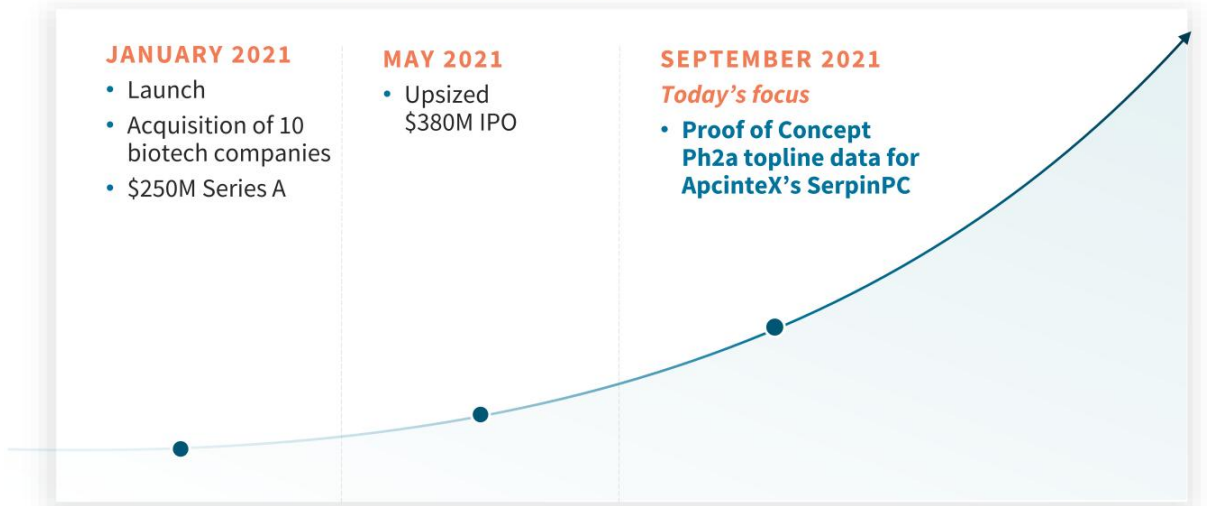
# Pipeline

Our diverse portfolio includes 16 programs across multiple therapeutic areas



## Milestones

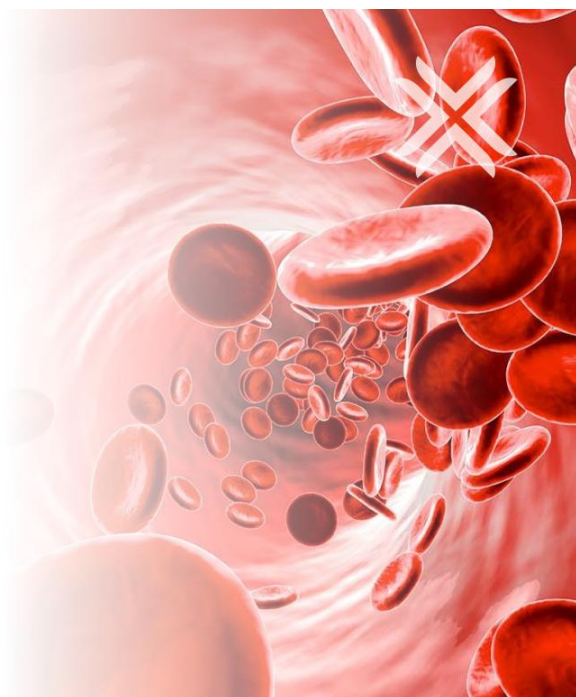
Significant momentum with 2021 accomplishments



SerpinPC

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

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## Summary

Successful proof-of-concept results

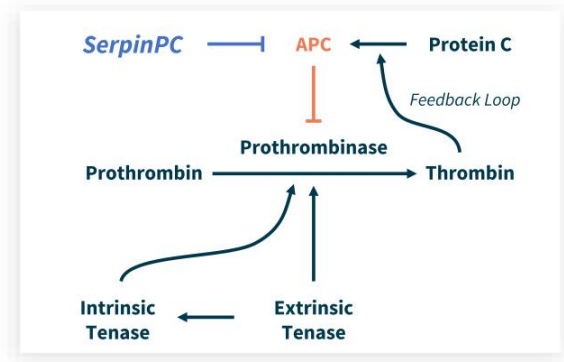
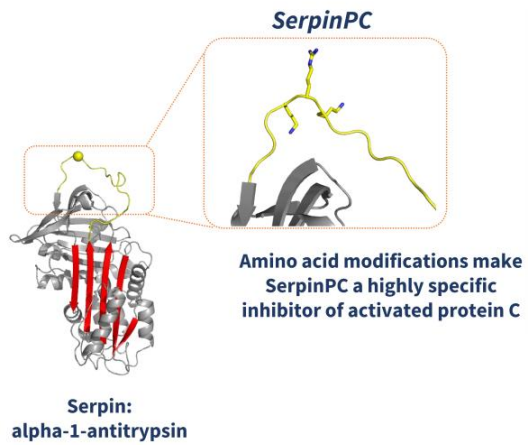
The goals of this Phase 2a clinical proof-of-concept study were to evaluate the safety and efficacy of once monthly, subcutaneous SerpinPC in a population of hemophilia A and B patients not on prophylaxis and with a history of substantial bleeding

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



## Differentiation

Potential benefits of SerpinPC



Novel MoA for  
**hemophilia A and B**



Compelling efficacy



Excellent  
**safety profile**  
without potential  
thrombosis

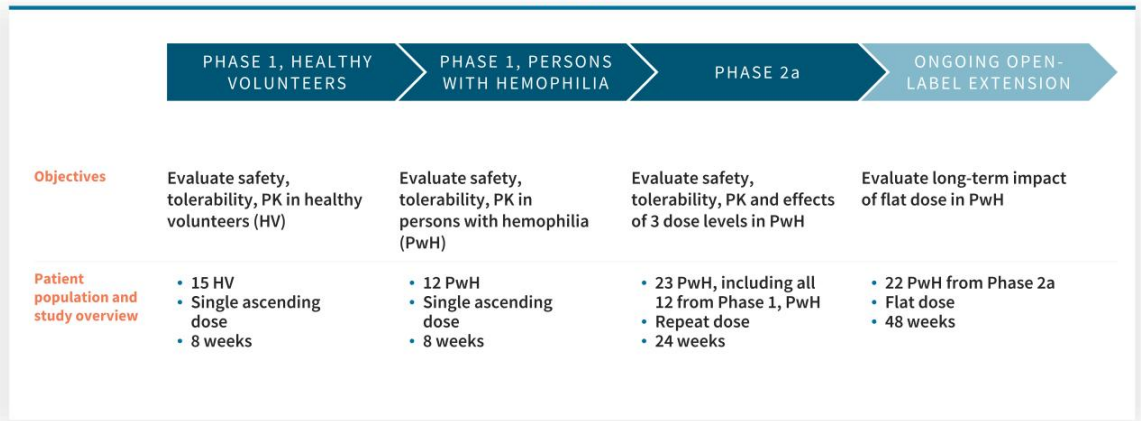


Convenient  
**subcutaneous  
administration**

# Overview of AP-0101

Phase 1/2a proof of concept study

## AP-0101



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

## 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**

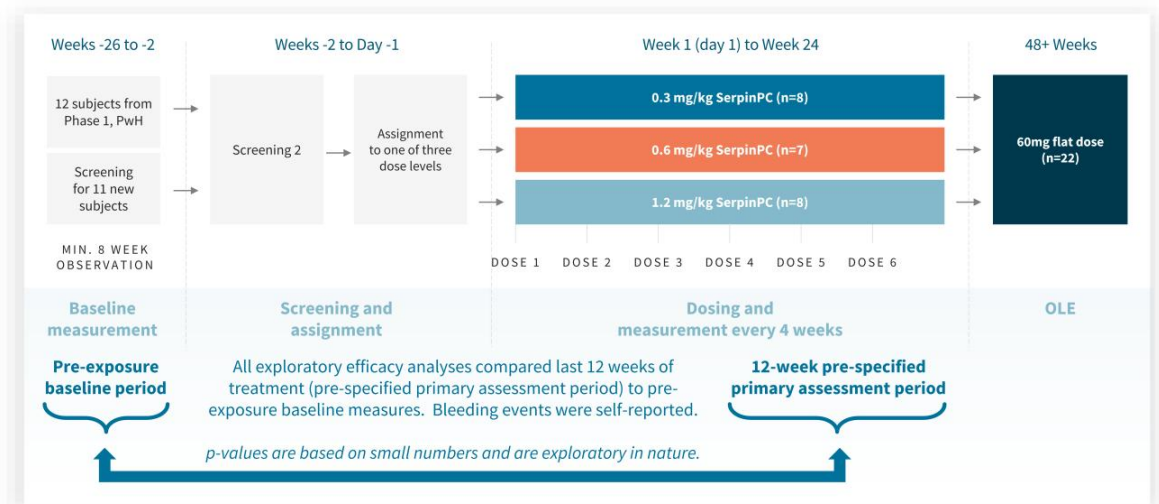
Note: all bleeding events are self reported

\* 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**

## Clinical trial design and exploratory efficacy analyses



## 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

## 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

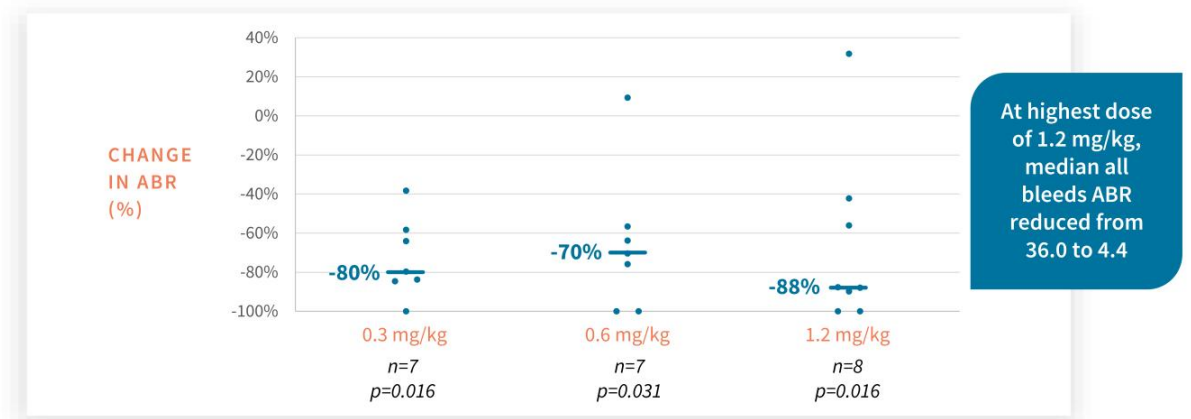
\* Annualized rate of self-reported bleeds  
\*\* Target joint = joint with >3 bleeds in any 6-month period



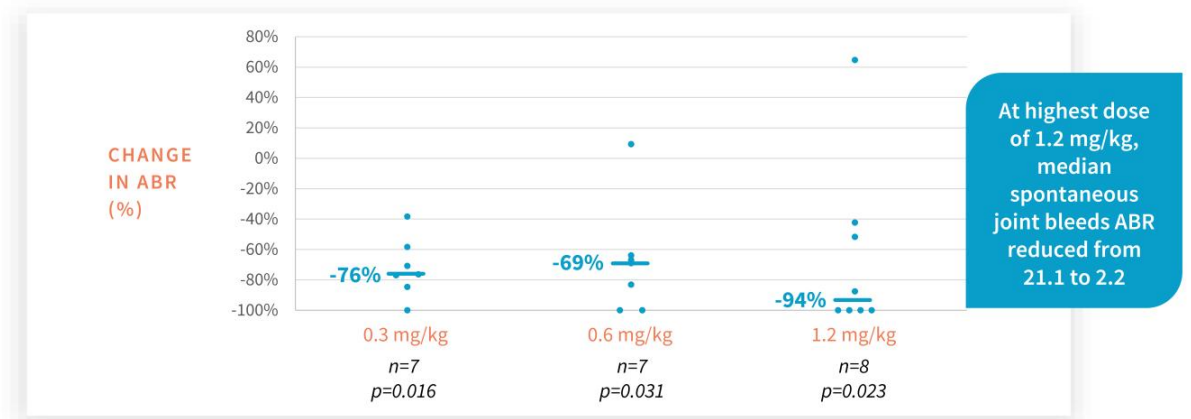
## **SerpinPC was well tolerated, with no evidence of thrombotic risk**

- 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

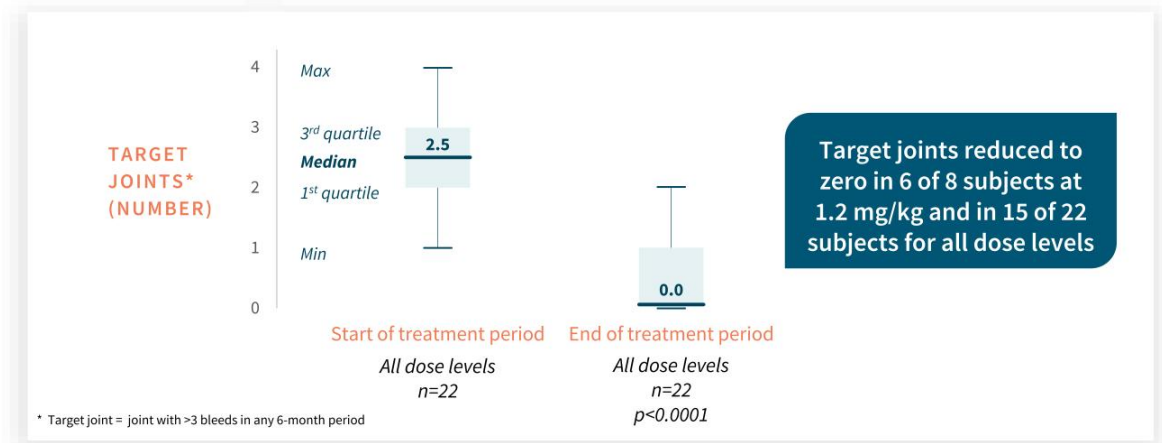
## Median 88% reduction in ABR for all bleeds at 1.2 mg/kg



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



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



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

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

\* Post hoc analysis, no p-values calculated

## Potential benefits of SerpinPC



**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





