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): December 10, 2023

CENTESSA PHARMACEUTICALS PLC

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

England and Wales	**001-40445**	**98-1612294**
(State or other jurisdiction of incorporation)	(Commission File Number)	(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:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
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 December 10, 2023, Centessa Pharmaceuticals plc (the "Company") shared data from the Open Label Extension of the Company's ongoing Phase 2a study of SerpinPC during an oral presentation at the ASH Annual Meeting. The poster is attached to this Current Report on Form 8-K as Exhibit 99.1. In addition, the Company issued a press release titled "Centessa Pharmaceuticals Announces New Data from an Additional 52-Weeks of Continuous Treatment from Third Year (Part 5) of Ongoing Phase 2a Study of SerpinPC for the Treatment of Hemophilia". A copy of the press release is furnished as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

The information in this Item 7.01 and Exhibits 99.1 and 99.2 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	SerpinPC presentation from ASH annual meeting on December 10, 2023
99.2	Press Release dated December 10, 2023
104	Cover Page Interactive Data (embedded within the Inline XBRL document)

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: December 11, 2023

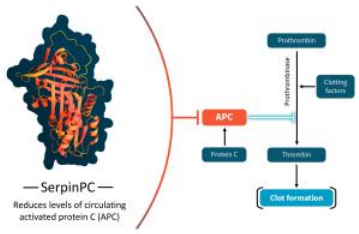
By:	/s/ Saurabh Saha
Name:	Saurabh Saha, M.D., Ph.D.
Title:	Chief Executive Officer

SERPINPC IN PERSONS WITH SEVERE HEMOPHILIA (PWH): UPDATED RESULTS FROM A MULTI-CENTER MULTI-PART FIRST-IN-HUMAN STUDY

T. BAGLIN[1], I. MOCANU[2] , L. MAKHALDIANI[3] , A.KOCH[4] , J. HUNTINGTON[1]
1. Centessa Pharmaceuticals plc, Altrincham, WA14 2DT, United Kingdom
2. Institute of Oncology, ARENSIA Exploratory Medicine, Testemitanu Str. 30, Chisinau, Republic of Moldova
3. Arensia Exploratory Medicine, 13a Tevdore Mgvdeli Str. 0112, Tbilisi, Georgia
4. Simbec-Orion Clinical Pharmacology, Merthyr Tydfil, CF48 4DR, United Kingdom

BACKGROUND

SerpinPC is an investigational serine protease inhibitor (SERPIN) engineered to specifically inhibit Activated Protein C (APC) and facilitate thrombin generation.



APC is an endogenous protein with anticoagulant properties that breaks down prothrombinase and serves as a "brake" on the thrombin generation "engine".

In hemophilia, deficiency of intrinsic Xase leads to a decrease in prothrombinase. This, along with the inhibitory action of APC, leads to a reduction in thrombin generation.

By inhibiting APC, SerpinPC is hypothesized to "release the brake," preserving prothrombinase and restoring thrombin generation.

AP-0101 is a first-in-human Phase 1/2a open-label multicenter study utilizing an adaptive design to investigate the safety, tolerability, pharmacokinetics and efficacy of SerpinPC in subjects with severe hemophilia A and B.

Previously presented data showed that administration of SerpinPC was well tolerated and reduced bleeding in persons with severe hemophilia with no observations of unexplained chronic elevations in D-dimer, an indicator of excessive thrombin generation.

Here we present the results of Part 5, in which 20 subjects who completed Part 4 continued to receive 1.2 mg/kg of SerpinPC once every 2 weeks for 52 weeks.

STUDY DESIGN

Part 1 was a Single Ascending Dose Study of SerpinPC in 15 healthy male volunteers and 12 males with severe hemophilia. Part 2 enrolled 23 males with severe hemophilia (19 hemophilia A and 4 hemophilia B), who were not on replacement factor prophylaxis, to receive SerpinPC at 0.3, 0.6 or 1.2 mg/kg, administered as a subcutaneous (SC) injection once every 4 weeks over a 24-week period (6 total doses). Parts 3, 4 and 5 were sequential extensions in which subjects received either a flat dose of 60 mg once every 4 weeks (Part 3) or 1.2 mg/kg once every 2 weeks (Parts 4 & 5).

All self-reported treated bleeds were recorded in patient diaries. The baseline ABR was determined from a prospective observation period of 2 to 6 months before exposure to SerpinPC, during which time patients received usual on-demand clotting factor concentrate to treat breakthrough bleeds.

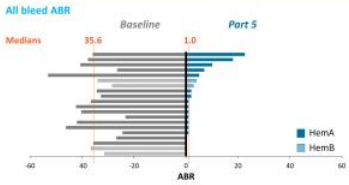
During treatment with SerpinPC all breakthrough bleeds were treated on-demand with usual clotting factor concentrate, without dose reduction and without limitation of number of infusions.

SUBJECTS

Patient Characteristics	Value
Number of subjects (Hemophilia A / B)	20 (16 / 4)
Age in years, median (min to max)	40 (21 to 56)
Weight kg (min to max)	74 (54 to 91)
Prospective ABR, median (min to max)	35.6 (30 to 40)
% subjects receiving previous prophylaxis	0%
% subjects with target joints	100%
No. of target joints, median (min to max) (>3 bleeds in 6 months prior to SerpinPC exposure)	3 (2 to 3.5)
Total number of target joints	53
Early terminations	3*

* All early terminations unrelated to study drug; two subjects emigrated (week 10 and week 22) and one subject exited after a femur fracture

EFFICACY



Individual baseline and Part 5 ABRs are shown above. Baseline ABRs in grey and ABRs during treatment with SerpinPC in blue. Subjects with hemophilia B shown by hatched bars.

Annualized Bleed Rate (ABR)			
	Baseline	Part 5	Change (%)
All bleeds (median)	35.63	1.00	-31.01 (-96%)
95% CI	31.85; 38.89	1.17; 7.00	-35.58; -26.99
Spont. joint bleeds (median)	30.28	1.00	-26.13 (-95%)
95% CI	23.59; 32.75	0.60; 6.17	-29.26; -20.30

All 20 patients had target joints before exposure to SerpinPC. At the end of Part 5 only 2 subjects still had a target joint. One subject still had 2 target joints and one subject who started with 3 had only 1. Total number of target joints was reduced by 94% from 53 to 3.

Target Joints			
	Baseline	Part 5	Change (%)
median	3.00	0.00	-2.50 (-100%)
95% CI	2.16; 3.14	-0.08; 0.38	-3.06; -1.94

SAFETY

Treatment Emergent Adverse Events (TEAEs)	Numb
All TEAEs (total 41 events)	
Related to SerpinPC	
Leading to discontinuation	
Leading to death	
AEs of special interest	
Serious adverse events	
Thromboembolic events	
Injection site reactions	
Anti-drug antibodies	
Transient	
Persistent	

D-Dimer	
% results < 500 ng/ml	
No. of patients with sustained elevated D-dimer	
No. of patients with unexplained sustained elevated D-dimer	

*Two SAEs occurred and were considered unrelated to stu
fracture of femur (led to discontinuation) (2) traumatic epid
Preliminary finding
† One subject with periodontitis with jaw swelling. D-dimer
commencement of antibiotics.

CONCLUSIONS

- **SerpinPC was shown to be well tole exposures up to 3.8 years.**
- **No unexplained sustained D-dimer e were observed in Part 5, consistent**
- **No SerpinPC-related AEs were obse**
- **Part 5 median all bleed ABR was 1.0 reduction from the pre-exposure bas**
- **Data showed that 94% of target joint resolved by the completion of Part 5**

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

Exhibit 99.2

Centessa Pharmaceuticals Announces New Data from an Additional 52-Weeks of Continuous Treatment from Third Year (Part 5) of Ongoing Phase 2a Study of SerpinPC for the Treatment of Hemophilia

- *Part 5 data reinforces favorable safety and tolerability profile and long-term efficacy results for SerpinPC:*
  - *Median all-bleed ABR of 1.0, a 96% reduction from prospective baseline*
  - *No thromboembolic events or treatment-related sustained elevations of D-dimer observed*
- *Poster presentation at American Society of Hematology (ASH) Annual meeting*
- *Registrational PRESent-2 and PRESent-3 studies of SerpinPC in hemophilia B are ongoing*

BOSTON and LONDON, December 10, 2023: Centessa Pharmaceuticals plc (Nasdaq: CNTA), today announced new data from an additional 52-weeks of continuous treatment from the third year (Part 5) of the ongoing Phase 2a study of SerpinPC for the treatment of hemophilia. The data were shared in a poster presentation at the American Society of Hematology (ASH) Annual Meeting on Sunday, December 10, 2023. SerpinPC is an investigational subcutaneously administered novel inhibitor of activated protein C (APC) in registrational studies for the treatment for hemophilia B, with or without inhibitors.

Part 5 data from the Phase 2a study (AP-0101) showed a continued favorable safety and tolerability profile for SerpinPC, as well as sustained long-term efficacy results, as measured by a 96% reduction in the median all-bleed annualized bleeding rate (ABR) from the prospective baseline. Consistent with data from earlier portions of the Phase 2a study, there were no thromboembolic events and no treatment-related sustained elevations of D-dimer observed throughout Part 5. D-dimer is a sensitive measure of excess thrombin generation. In addition, there were no SerpinPC-related adverse events observed during Part 5.

“We are excited to share additional data that further demonstrate the potential for SerpinPC to be a convenient subcutaneous treatment with a differentiated safety profile for people living with hemophilia,” said Saurabh Saha MD PhD, Chief Executive Officer of Centessa. “Specifically, these data show that an additional 52-weeks of continuous treatment with SerpinPC further reduced the median all-bleed ABR to 1.0, representing a 96% reduction from the prospective baseline. These data highlight the strong

foundation on which we are advancing SerpinPC in registrational studies for the treatment of hemophilia B. We would like to extend our sincere thanks to everyone involved in this study including the patients, investigators, and site coordinators."

Detailed ABR data from Part 5:

All bleed ABR

Part	Dose Tested (administered subcutaneously)	Median ABR from prospective baseline	Median ABR observed in this part	Median % change from baseline
Part 5 (n=20)	1.2 mg/kg once every 2 weeks for 52 weeks	35.63	1.0	-96%

Spontaneous joint bleed ABR

Part	Dose Tested (administered subcutaneously)	Median ABR from prospective baseline	Median ABR observed in this part	Median % change from baseline
Part 5 (n=20)	1.2 mg/kg once every 2 weeks for 52 weeks	30.28	1.0	-95%

All self-reported treated bleeds were recorded in subject diaries. The baseline ABR was determined from a prospective observation period of 2 to 6 months before exposure to SerpinPC, during which time subjects received usual on-demand clotting factor concentrate to treat breakthrough bleeds. During treatment with SerpinPC all breakthrough bleeds were treated on-demand with usual clotting factor concentrate, without dose reduction and without limitation of number of infusions.

Data from Part 5 were presented today at the ASH Annual Meeting in a poster titled: *SerpinPC in persons with severe hemophilia (PwH): Updated results from a multi-center, multi-part, first-in-human study*. A copy of the poster is available on the Company's website at https://investors.centessa.com/events-presentations.

About SerpinPC

SerpinPC is a subcutaneously administered novel inhibitor of APC being developed as a potential treatment for hemophilia, regardless of severity or inhibitor status, and which may also be developed to prevent bleeding associated with other bleeding disorders. The registrational program for SerpinPC in hemophilia B includes a set of clinical studies with multiple components. PRESent-5 is an observational feeder study to collect prospective observational data for minimum defined periods before switching to dosing subjects in the interventional

studies. The interventional studies include PRESent-2 (moderately severe to severe hemophilia B without inhibitors, and severe hemophilia A with or without inhibitors) and PRESent-3 (hemophilia B with inhibitors). Additional information on the trials can be accessed at www.clinicaltrials.gov (NCT05605678, NCT05789524, NCT05789537). The U.S. Food and Drug Administration (FDA) has granted Fast Track designation to SerpinPC for the treatment of hemophilia B, with or without inhibitors. SerpinPC is an investigational agent that has not been approved by the FDA or any other regulatory authority.

About AP-0101

AP-0101 is an ongoing first-in-human open-label multi-center study to investigate the safety, tolerability, pharmacokinetics, and efficacy of subcutaneous doses of SerpinPC in male participants with severe hemophilia. (https://clinicaltrials.gov/ct2/show/NCT04073498).

About Centessa Pharmaceuticals

Centessa Pharmaceuticals plc is a clinical-stage pharmaceutical company that aims to discover and develop medicines that are transformational for patients. Our programs span discovery-stage to late-stage development and cover a range of high-value indications. We operate with the conviction that each one of our programs has the potential to change the current treatment paradigm and establish a new standard of care. For more information, visit http://www.centessa.com/, which does not form part of this release.

Forward Looking Statements

This press release contains forward-looking statements. These statements may be identified by words such as “may,” “might,” “will,” “could,” “would,” “should,” “expect,” “intend,” “plan,” “objective,” “anticipate,” “believe,” “estimate,” “predict,” “potential,” “continue,” “ongoing,” “aim,” “seek,” 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, including statements related to the Company’s ability to discover and develop transformational medicines for patients; its expectations for executing on the Company's pipeline; the timing of commencement of new studies or clinical trials or clinical and preclinical data related to SerpinPC; its ability to identify, screen, recruit and maintain a sufficient number of or any subjects in its

existing and anticipated studies or clinical trials including PRESent-5, the observational feeder study, PRESent-2 and PRESent-3 and its expectations on executing its research and clinical development plans and the timing thereof; the Company's ability to differentiate SerpinPC from other treatment options; the development and therapeutic potential of SerpinPC; and regulatory matters, including the timing and likelihood of success of obtaining authorizations to initiate or continue clinical trials. Any forward-looking statements in this press release are based on our current expectations, estimates, assumptions 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, risks related to the safety and tolerability profile of our product candidates; our ability to identify, screen and recruit a sufficient number of or any subjects in our existing and anticipated new studies or clinical trials including PRESent-2, PRESent-3, PRESent-5, or within anticipated timelines; our ability to protect and maintain our intellectual property position; business (including commercial viability), regulatory, economic and competitive risks, uncertainties, contingencies and assumptions about the Company; risks inherent in developing product candidates and technologies; future results from our ongoing and planned clinical trials; our ability to obtain adequate financing, including through our financing facility with Oberland, to fund our planned clinical trials and other expenses; trends in the industry; the legal and regulatory framework for the industry, including the receipt and maintenance of clearances to conduct or continue clinical testing; our operating costs and use of cash, including cash runway, cost of development activities and conducting clinical trials, future expenditures risks; the risk that any one or more of our product candidates will not be successfully developed and/or commercialized; the risk that the historical results of preclinical studies or clinical studies will not be predictive of future results in ongoing or future studies; economic risks to the United States and United Kingdom banking systems; and geo-political risks such as the Russia-Ukraine war or the Israeli-Palestinian conflict. These and other risks concerning our programs and operations are described in additional detail in our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and our other reports, which are on file with the U.S. Securities and Exchange Commission (SEC). We explicitly disclaim any obligation to update any forward-looking statements except to the extent required by law.

Contact:
Kristen K. Sheppard, Esq.
SVP of Investor Relations
investors@centessa.com