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, 2022

CENTESSA PHARMACEUTICALS PLC

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

England and Wales	**001-04321**	**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 (0) 203 9206789, ext. 9999**

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, 2022, Centessa Pharmaceuticals plc (the "Company") presented 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 presentation materials are 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 Additional 18-Months of Continued Treatment Data from Open-Label Extension (OLE) of Phase 2a Study of SerpinPC for 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 Company from time to time presents and/or distributes to the investment community at various industry and other conferences slide presentations to provide updates and summaries of its business. The Company undertakes no obligation to update, supplement or amend the materials attached hereto as Exhibit 99.1.

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 8.01 Other Events.
On December 10, 2022, the Company announced new data from an additional 18-months of continued treatment with SerpinPC, an investigational, subcutaneously administered novel inhibitor of activated protein C (APC), from the open-label extension (OLE) of the Phase 2a study of SerpinPC for hemophilia. The OLE data were shared in an oral presentation at the American Society of Hematology (ASH) Annual Meeting.

The OLE data show a continued favorable safety and tolerability profile for SerpinPC, including at a higher dosing regimen, as well as sustained long-term efficacy results, as measured by a reduction in the all-bleeds annualized bleed rates (ABRs). Consistent with data from the six-month repeat dose portion of the Phase 2a study, there were no thromboembolic events and no treatment-related sustained elevations of D-dimer observed throughout the 18-month OLE period reported on today. D-dimer is a sensitive measure of excess thrombin generation. In addition, there were no SerpinPC-related adverse events during the OLE period.

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.

Initial Study Period (Part 1 and Part 2): Part 1a was a Single Ascending Dose (SAD) study completed in 15 healthy male subjects and Part 1b was a SAD study completed in 12 male subjects with hemophilia A or B (Part 1b: 0.1 to 1.2 mg/kg, 4 cohorts). All 12 subjects in Part 1b chose to participate in Part 2. Part 2 enrolled a total of 23 male subjects with hemophilia who were not on replacement factor prophylaxis to receive SerpinPC at 0.3, 0.6 or 1.2 mg/kg, administered as a subcutaneous injection once every 4 weeks over a 24-week period (6 total doses). As previously disclosed, one subject with a history of a skin disorder discontinued treatment due to an injection site reaction during Part 2. No other SerpinPC-related adverse events were observed during the study. The Company announced the results for Part 2 (six month repeat dose) on September 9, 2021. After Part 2, participants were offered to continue into an open-label extension (OLE) of the Phase 2a study.

OLE Period (Part 3 and Part 4): In Part 3, 22 subjects who completed Part 2 (six month repeat dose) received a flat dose of 60 mg of SerpinPC administered as a subcutaneous injection once every 4 weeks for 48 weeks. One subject emigrated out of the site country and discontinued treatment during Part 3. In Part 4, 21 subjects who completed Part 3 received 1.2 mg/kg of SerpinPC administered as a subcutaneous injection once every 2 weeks for 24 weeks. One subject discontinued treatment during Part 4 following a cancer diagnosis which the Safety Review Group determined was not related to treatment with SerpinPC.

Phase 2a OLE Data from Additional 18-Months of Continued Treatment:

- SerpinPC was well-tolerated throughout the OLE's 18-month treatment period. There were no SerpinPC-related adverse events and no thromboembolic events or treatment-related sustained elevations of D-dimer observed throughout the OLE period. There were no treatment-related discontinuations from the OLE.
- At the highest dose tested (Part 4: 1.2 mg/kg of SerpinPC administered as a subcutaneous injection once every 2 weeks for 24 weeks (n=21)), the median all-bleeds ABR was reduced by 93% as compared to the median all-bleeds ABR prospectively measured during the pre-exposure observation period. A median ABR of 2.2 was achieved for all

subjects in Part 4. Seven subjects had zero bleeds during the 24-week period. The median spontaneous joint bleeds ABR was reduced by 93% as compared to the median spontaneous joint bleeds ABR prospectively measured during the pre-exposure observation period. A median spontaneous joint bleed ABR of 2.2 was achieved for all subjects in Part 4. Nine subjects had zero spontaneous joint bleeds during the 24-week period.

- All breakthrough bleed events during the OLE period were successfully managed with the subject's usual replacement factor without dose adjustment and did not require adjustments to SerpinPC dosing.

Detailed ABR data from the OLE are shown below:

All bleed ABR

Part	Dose Tested (administered subcutaneously)	Median ABR from prospective baseline	Median ABR observed in this part	Median % change from baseline
Part 3 (n=22)	60 mg flat dose* once every 4 wks for 48 weeks	34.1	6.2	-83%
Part 4 (n=21)	1.2 mg/kg once every 2 wks for 24 weeks	35.5	2.2	-93%

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 3 (n=22)	60 mg flat dose* once every 4 wks for 48 weeks	27.5	4.3	-86%
Part 4 (n=21)	1.2 mg/kg once every 2 wks for 24 weeks	28.3	2.2	-93%

*60 mg flat dose which was equivalent to ~0.8 mg/kg

The Company's pivotal program for SerpinPC in hemophilia B with and without inhibitors includes a set of studies with multiple components. In the coming weeks, the Company expects to initiate PRESent-5, an observation feeder study to collect prospective observational data for minimum defined periods before switching to dosing subjects in the interventional studies planned for 2023 (https://clinicaltrials.gov/ct2/show/NCT05605678). The interventional studies include PRESent-2 (moderately severe to severe hemophilia B without inhibitors, and severe hemophilia A with and without inhibitors) and PRESent-3 (hemophilia B with inhibitors).

Forward Looking Statements

This Current Report on Form 8-K 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 timing of commencement of new studies or clinical trials of SerpinPC; research and clinical development plans and the timing thereof; and the development and therapeutic potential of SerpinPC.

Any forward-looking statements in this Current Report on Form 8-K 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, risks related to the safety and tolerability profile of our product candidates; 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; 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/or commercialized; the risk that the results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies; geo-political risks such as the Russia-Ukraine war and risks related to the ongoing COVID-19 pandemic including the effects of the Delta, Omicron and any other variants. 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.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	
99.1	SerpinPC Open Label Extension Presentation from ASH Annual Meeting on December 10, 2022
99.2	Press Release dated December 10, 2022
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 12, 2022

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

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

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

*Centessa Pharmaceuticals plc, 1 Ashley Road, Altrincham, Cheshire, United Kingdom, WA14 2DT, [ƒ]Simbec-Orion Clinical Pharmacology, Merthyr Tydfil, CF48 4DR, United Kingdom, [+]Arensia Exploratory Medicine, Testemitanu Str. 30, Chisinau, Republic of Moldova, [$]Arensia Exploratory Medicine, 13a Tevdore Mgvdeli Str. 0112, Tbilisi, Georgia

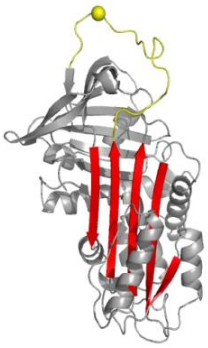
Disclaimer

This presentation has been prepared by Centessa Pharmaceuticals plc (the "Company") for informational purposes only and not for any other purpose. This presentation does not contain all the information that is or may be material to investors or potential investors and should not be considered as advice or a recommendation to investors or potential investors in respect of the holding, purchasing or selling of securities or other financial instruments and does not take into account any investor's particular objectives, financial situation or needs. The communication of this presentation may be restricted by law; it is not intended for distribution to, or use by any person in, any jurisdiction where such distribution or use would be contrary to local law or regulation. This presentation is not directed to or intended for distribution, or transfer, either directly or indirectly to, or use by, any person or entity that is a citizen or resident or located in any locality, state, country or other jurisdiction where such distribution, transfer, publication, availability or use would be contrary to law or regulation or which would require any registration or licensing within such jurisdiction.

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 related to the Company's ability to deliver impactful medicines to patients; the ability of our key executives to drive execution of the Company's 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; the development and therapeutic potential of our product candidates, including SerpinPC; 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 for our product candidates; and our anticipated cash runway. 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 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, 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; risks inherent in developing products 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; 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, Omicron and any other variants, geo-political risks such as the Russia-Ukraine conflict and 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. All projections, valuations and statistical analyses are provided for information purposes only. They may be based on subjective assessments and assumptions and may use one among alternative methodologies that produce different results and to the extent they are based on historical information, they should not be relied upon as an accurate prediction of future performance.

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 or warranty, express or implied, 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 or warranty, express or implied, 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: a subcutaneously administered biologic inhibitor of APC

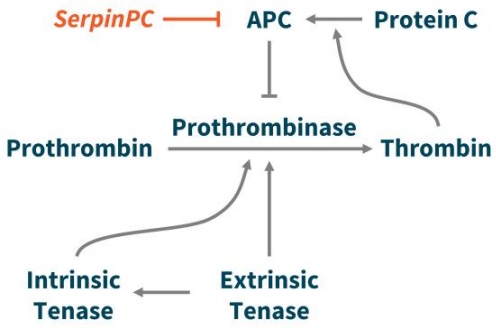


3D-model of SerpinPC*

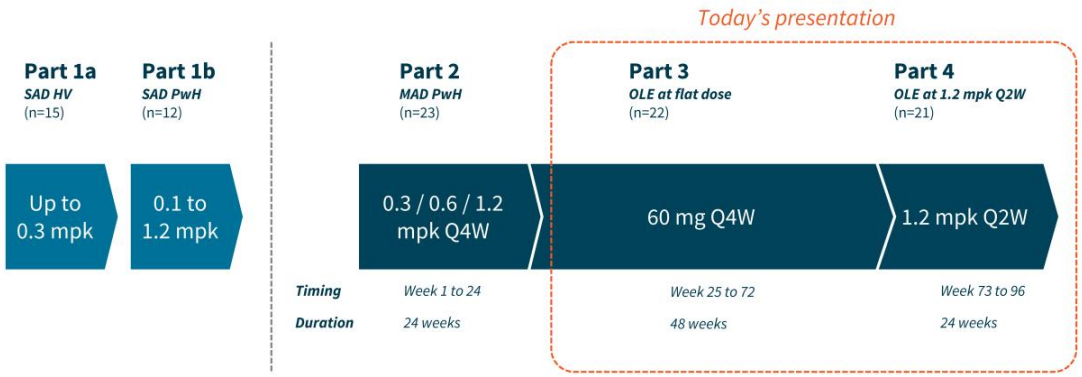
- Unprecedented biology with novel pharmacology
- Intended for subcutaneous prophylaxis across hemophilia subtypes
- Modified α1 anti-trypsin with 3 substitution mutations to confer selective inhibition of activated protein C (APC)
- Prevents bleeds by inhibiting APC to prolong prothrombinase activity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

* 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), median (min to max)	**34.1** (22.8 to 53.0)
% subjects receiving previous prophylaxis	**0%**
% subjects with target joints*	**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**
Part 3	**1 subject** due to emigration to another country
Part 4	**1 subject** due to recto-sigmoid cancer – not related to treatment**

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

** 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

* 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)

* 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

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%

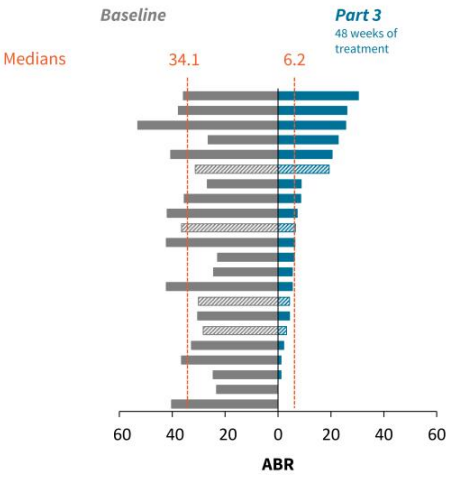
Spontaneous joint bleed ABR

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%

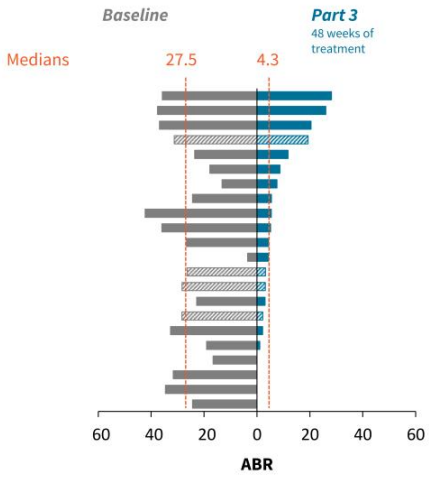
AP-0101 Part 3: ABR at 60mg Q4W flat dose

HemA
HemB

All bleeds ABR



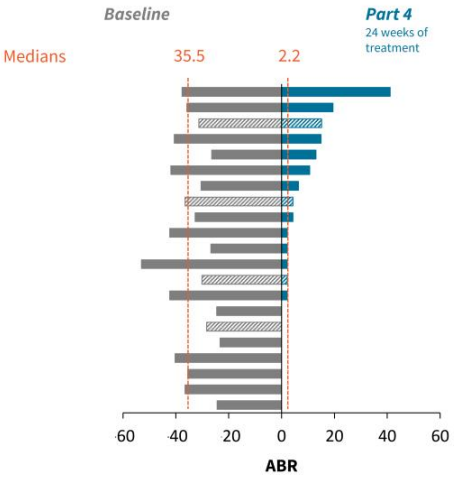
Spontaneous joint bleeds ABR



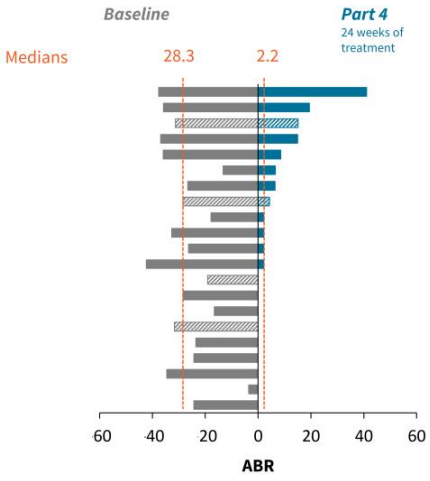
AP-0101 Part 4: ABR at 1.2 mpk Q2W

HemA
HemB

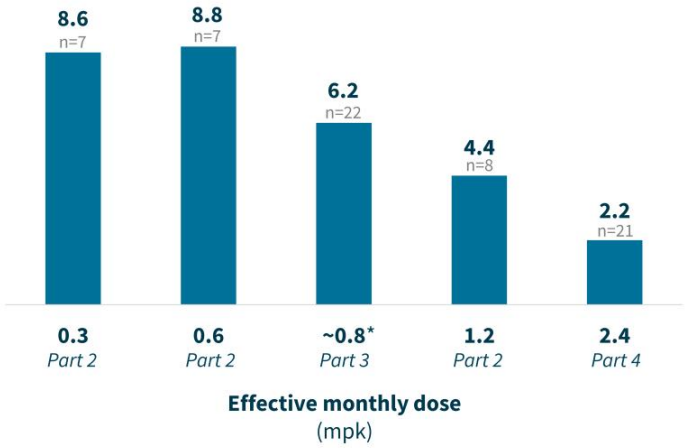
All bleeds ABR



Spontaneous joint bleeds ABR



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

Exhibit 99.2

Centessa Pharmaceuticals Announces Additional 18-Months of Continued Treatment Data from Open-Label Extension (OLE) of Phase 2a Study of SerpinPC for Hemophilia

- *Oral presentation at American Society of Hematology (ASH) Annual Meeting highlights continued favorable safety and tolerability profile and sustained long-term efficacy results for SerpinPC:*
  - *93% reduction in median ABR for both all-bleeds and spontaneous joint bleeds in highest dose tested*
  - *No thromboembolic events or treatment-related sustained elevations of D-dimer observed*
- *Pivotal program for SerpinPC in hemophilia B advancing; PRESent-5 observation study to begin in the coming weeks*

BOSTON and LONDON, December 10, 2022: Centessa Pharmaceuticals plc (Nasdaq: CNTA), today announced new data from an additional 18-months of continued treatment with SerpinPC, an investigational, subcutaneously administered novel inhibitor of activated protein C (APC), from the open-label extension (OLE) of the Phase 2a study of SerpinPC for hemophilia. The OLE data were shared today in an oral presentation at the American Society of Hematology (ASH) Annual Meeting.

The OLE data show a continued favorable safety and tolerability profile for SerpinPC, including at a higher dosing regimen, as well as sustained long-term efficacy results, as measured by a reduction in the all-bleeds annualized bleed rates (ABRs). Consistent with data from the six-month repeat dose portion of the Phase 2a study, there were no thromboembolic events and no treatment-related sustained elevations of D-dimer observed throughout the 18-month OLE period reported on today. D-dimer is a sensitive measure of excess thrombin generation. In addition, there were no SerpinPC-related adverse events during the OLE period.

“SerpinPC’s continued favorable efficacy, safety and tolerability profile with subcutaneous dosing throughout the OLE period, including a dose 2x higher than that previously administered during the

initial six-month Phase 2a study, are very encouraging and have the potential to meaningfully differentiate SerpinPC from other treatment options and product candidates in development," said Saurabh Saha MD PhD, Chief Executive Officer of Centessa. "We're now advancing the *PRESent* pivotal program for SerpinPC which includes elegantly designed studies focused on bringing this potential therapy to individuals with hemophilia B (with and without inhibitors) as quickly as possible, subject to regulatory approval."

Antoine Yver MD MSc, Chairman of Development of Centessa added, "With a total exposure of over 40 patient-years across multiple dosing regimens with SerpinPC, these encouraging new long-term data add further weight to the durability of effect and sustained safety and tolerability observed to date in severe hemophilia. We are excited that these data support the potential of SerpinPC's new mechanism of action to provide a clinically meaningful subcutaneous therapy to people with hemophilia B who have high unmet need and limited options. We would like to extend our sincere thanks to everyone involved in this study including the patients, investigators, and site coordinators."

Phase 2a Study and OLE

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.

Initial Study Period (Part 1 and Part 2): Part 1a was a Single Ascending Dose (SAD) study completed in 15 healthy male subjects and Part 1b was a SAD study completed in 12 male subjects with hemophilia A or B (Part 1b: 0.1 to 1.2 mg/kg, 4 cohorts). All 12 subjects in Part 1b chose to participate in Part 2. Part 2 enrolled a total of 23 male subjects with hemophilia who were not on replacement factor prophylaxis to receive SerpinPC at 0.3, 0.6 or 1.2 mg/kg, administered as a subcutaneous injection once every 4 weeks over a 24-week period (6 total doses). As previously disclosed, one subject with a history of a skin disorder discontinued treatment due to an injection site reaction during Part 2. No other SerpinPC-related adverse events were observed during the study. The Company announced the results for Part 2 (six month repeat dose) on September 9, 2021. After Part 2, participants were offered to continue into an open-label extension (OLE) of the Phase 2a study.

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Phase 2a OLE Data from Additional 18-Months of Continued Treatment:

- SerpinPC was well-tolerated throughout the OLE's 18-month treatment period. There were no SerpinPC-related adverse events and no thromboembolic events or treatment-related sustained elevations of D-dimer observed throughout the OLE period. There were no treatment-related discontinuations from the OLE.
- At the highest dose tested (Part 4: 1.2 mg/kg of SerpinPC administered as a subcutaneous injection once every 2 weeks for 24 weeks (n=21)), the median all-bleeds ABR was reduced by 93% as compared to the median all-bleeds ABR prospectively measured during the pre-exposure observation period. A median ABR of 2.2 was achieved for all subjects in Part 4. Seven subjects had zero bleeds during the 24-week period. The median spontaneous joint bleeds ABR was reduced by 93% as compared to the median spontaneous joint bleeds ABR prospectively measured during the pre-exposure observation period. A median spontaneous joint bleed ABR of 2.2 was achieved for all subjects in Part 4. Nine subjects had zero spontaneous joint bleeds during the 24-week period.
- All breakthrough bleed events during the OLE period were successfully managed with the subject's usual replacement factor without dose adjustment and did not require adjustments to SerpinPC dosing.

Detailed ABR data from the OLE are shown below:

All bleed ABR

Part	Dose Tested (administered subcutaneously)	Median ABR from prospective baseline	Median ABR observed in this part	Median % change from baseline
Part 3 (n=22)	60 mg flat dose* once every 4 wks for 48 weeks	34.1	6.2	-83%
Part 4 (n=21)	1.2 mg/kg once every 2 wks for 24 weeks	35.5	2.2	-93%

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 3 (n=22)	60 mg flat dose* once every 4 wks for 48 weeks	27.5	4.3	-86%
Part 4 (n=21)	1.2 mg/kg once every 2 wks for 24 weeks	28.3	2.2	-93%

*60 mg flat dose which was equivalent to ~0.8 mg/kg

The Company's pivotal program for SerpinPC in hemophilia B with and without inhibitors includes a set of studies with multiple components. In the coming weeks, the Company expects to initiate *PRESent-5*, an observation feeder study to collect prospective observational data for minimum defined periods before switching to dosing subjects in the interventional studies planned for 2023 (https://clinicaltrials.gov/ct2/show/NCT05605678). The interventional studies include *PRESent-2* (moderately severe to severe hemophilia B without inhibitors, and severe hemophilia A with and without inhibitors) and *PRESent-3* (hemophilia B with inhibitors).

Data from the OLE were presented today at the ASH Annual Meeting by Trevor Baglin MedScD PhD, Vice President and Global Head of Hemophilia for Centessa, during the session titled: *SerpinPC in persons with severe hemophilia (PwH): Updated results from a multi-center, multi-part, first-in-human study*. Drs. Yver and Baglin share the OLE data slides presented at ASH and discuss the SerpinPC registrational program within a recorded webcast now available on the Company's website at https://investors.centessa.com/events-presentations.

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 is being developed as a potential treatment for all types of hemophilia regardless of severity or

inhibitor status, and may also prevent bleeding associated with other bleeding disorders. 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 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 and Hemophilia B

Hemophilia A and hemophilia B 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 hemophilia A) or factor IX (in the case of hemophilia B), 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.

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 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; the timing of commencement of new studies or clinical trials of SerpinPC; 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 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 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; 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/or commercialized; the risk that the results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies; geo-political risks such as the Russia-Ukraine war and risks related to the ongoing COVID-19 pandemic including the effects of the Delta, Omicron and any other variants. 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.

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