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

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- *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, Dec. 10, 2022 (GLOBE NEWSWIRE) -- 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.

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).

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 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; 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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