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

September 9, 2021

~ 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. and LONDON, Sept. 09, 2021 (GLOBE NEWSWIRE) -- 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.[1] 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.

	Dose Tested		
Exploratory Efficacy Endpoints	**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.

[1] 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 topline 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.

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. 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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