Centessa Pharmaceuticals Reports Business Highlights and Financial Results for the Fourth Quarter and Full-Year 2023

March 28, 2024

- *Hemophilia Program: Ongoing registrational PRESent-2 and PRESent-3 studies of SerpinPC for the treatment of hemophilia B; PRESent-2 advancing toward interim analysis planned in 2024*
- *Orexin Agonist Program: Clinical proof-of-concept data for ORX750 in sleep-deprived healthy volunteers planned in 2024*
- *LockBody® Technology Platform: Ongoing Phase 1/2a study of LB101 (PD-L1xCD47) for the treatment of solid tumors*

BOSTON and LONDON, March 28, 2024 (GLOBE NEWSWIRE) -- Centessa Pharmaceuticals plc (Nasdaq: CNTA), a clinical-stage pharmaceutical company, today reported recent business highlights and financial results for the fourth quarter and full-year ended December 31, 2023.

“This is an exciting and pivotal time for Centessa,” said Saurabh Saha MD PhD, Chief Executive Officer of Centessa. “We are laser focused on executing the PRESent registrational studies for SerpinPC, a potential first-in-class subcutaneously administered therapy with a differentiated safety profile for individuals with hemophilia B, and advancing our orexin receptor 2 (OX2R) agonist development program into the clinic for the treatment of narcolepsy and other sleep-wake disorders.”

Dr. Saha continued, “SerpinPC’s novel mechanism of action is designed to prevent or reduce bleeding in persons with hemophilia without depleting natural anticoagulants that help prevent blood clots. The most recent clinical data from our ongoing Phase 2a study showed that an additional 52-weeks of continuous treatment with SerpinPC reduced the median all-bleed ABR by 96% relative to baseline, and no thrombosis has been observed across the study to date. Within the PRESent registrational studies for SerpinPC, we are looking to replicate this safety profile and meaningfully reduce bleeding rates for subjects with hemophilia B, with or without inhibitors. We look forward to confirming a dose and advancing to Part 2 of the PRESent-2 study this year.”

“We are very excited with progress within our OX2R agonist development program, and more specifically, ORX750, an orally administered, highly potent and selective OX2R agonist,” said Dr. Saha. “In late 2023, we shared preclinical data that we believe support ORX750’s potential to be a best-in-class oral OX2R agonist for the treatment of narcolepsy and other sleep-wake disorders. We remain on track with our goal to share clinical proof-of-concept data for ORX750 in sleep-deprived healthy volunteers this year.”

“In parallel, we continue to evaluate our proprietary LockBody technology platform in a first-in-human clinical study of LB101, a conditionally tetravalent PD-L1xCD47 bispecific monoclonal antibody designed to selectively drive CD47 into the tumor microenvironment while avoiding systemic toxicity, in solid tumors. We look to this study to provide valuable insights regarding the safety and tolerability of LB101, as well as the performance of our LockBody platform in a clinical setting.”

Recent Highlights

- In December 2023 and February 2024, the Company presented data from an additional 52-weeks of continuous treatment from the third year (Part 5) of the ongoing Phase 2a study of SerpinPC, an investigational subcutaneously administered novel inhibitor of activated protein C (APC) for the treatment of hemophilia, during presentations at the American Society of Hematology (ASH) Annual Meeting and the 17th Annual Congress of the European Association for Haemophilia and Allied Disorders (EAHAD). Part 5 data from the Phase 2a study 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 measured during the pre-exposure observation period. To date, there have been no thromboembolic events and no treatment-related sustained elevations of D-dimer observed throughout the Phase 2a study.
- In October 2023, the Company announced the dosing of the first subject in its registrational PRESent-3 clinical study of SerpinPC for the treatment of hemophilia B with inhibitors. The Company initiated dosing in its registrational PRESent-2 clinical study of SerpinPC for the treatment of hemophilia B without inhibitors in July 2023.
- In October 2023, the Company announced preclinical data from *in vivo* and *in vitro* studies of its investigational, novel OX2R agonist, ORX750, that we believe support a potential best-in-class profile for the treatment of narcolepsy and other sleep-wake disorders.

Anticipated Upcoming Program Milestones

- **Hemophilia Program -** The registrational PRESent-2 (hemophilia B without inhibitors) and PRESent-3 (hemophilia B with inhibitors) studies of SerpinPC are ongoing. For PRESent-2, the Company plans to confirm a dose and advance to Part 2 of the study based on a review of Part 1 (dose justification) data in 2024 (interim analysis). The primary endpoint of the PRESent-2 study is the rate of treated bleeds (expressed as ABR) during the first 24 weeks of treatment with SerpinPC (Part 2) compared to the observation period. The Company plans to share Part 1 data at a medical conference in late

2024 or early 2025.

- **Orexin Agonist Program -** Upon Investigational New Drug ("IND") clearance, the Company plans to rapidly advance ORX750 into clinical development with the goal of sharing clinical proof-of-concept data in sleep-deprived healthy volunteers in 2024.
- **LockBody Technology Platform -** The Phase 1/2a first-in-human clinical study of LB101 (PD-L1xCD47 LockBody) is ongoing.

Where applicable, the Company plans to provide updates on preclinical programs including follow-up orexin agonists and LB206, a PD-L1xCD3 LockBody, when they advance toward clinical studies.

Fourth Quarter and Full-Year 2023 Financial Results

- **Cash, Cash Equivalents and Short-term Investments:** $256.5 million as of December 31, 2023, which includes approximately $6.2 million in net proceeds through ATM sales in the fourth quarter ended December 31, 2023. In addition, the Company received approximately $9.7 million in net proceeds through ATM sales in January 2024. The Company expects its cash, cash equivalents and short-term investments will fund operations into 2026, without drawing on the remaining available tranches under the Oberland credit facility.
- **Research & Development Expenses:** $29.7 million for the fourth quarter ended December 31, 2023, compared to $27.8 million for the fourth quarter ended December 31, 2022, and $124.4 million for the full-year 2023 compared to $155.1 million for the full-year 2022.
- **General & Administrative Expenses**: $12.3 million for the fourth quarter ended December 31, 2023, compared to $13.8 million the fourth quarter ended December 31, 2022, and $53.7 million for the full-year 2023 compared to $55.2 million for the full-year 2022.
- **Net Loss Attributable to Ordinary Shareholders:** $36.8 million for the fourth quarter ended December 31, 2023, compared to $43.2 million for the fourth quarter ended December 31, 2022, and $151.1 million for the full-year 2023 compared to $216.2 million for the full-year 2022.

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 most advanced programs include a hemophilia program, an orexin agonist program for the treatment of narcolepsy and other sleep-wake disorders and an immuno-oncology program focused on our LockBody® technology platform. We operate with the conviction that each 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.

About SerpinPC
SerpinPC is an investigational 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 has not been approved by the FDA or any other regulatory authority for any use.

About ORX750
ORX750 is an investigational, orally administered, highly potent and selective orexin receptor 2 (OX2R) agonist designed to directly target the underlying pathophysiology of orexin neuron loss in narcolepsy type 1 (NT1). ORX750 has been shown in preclinical studies to potently activate the OX2R with an in vitro EC50 of 0.11 nM and 9,800-fold selectivity over the human orexin receptor (hOX1R). ORX750 is Centessa's first orexin product candidate being developed for the treatment of narcolepsy with potential expansion into other sleep-wake disorders. ORX750 has not been approved by the FDA or any other regulatory authority.

About the LockBody Technology Platform and LB101
Centessa's proprietary LockBody technology platform aims to redefine immuno-oncology treatment for patients with cancer. LockBody drug candidates are designed to selectively drive potent effector function activity, such as CD47 or CD3, to the tumor micro-environment (TME) while avoiding systemic toxicity. The first LockBody candidate is LB101, a conditionally tetravalent PD-L1xCD47 bispecific monoclonal antibody which has two anti-CD47 domains blocked by two anti-PD-L1 domains, with proprietary human IgG-derived hinges linking the anti-CD47 and anti-PD-L1 domains. The cell-killing mechanism of action, CD47, is designed to be blocked by the PD-L1 tumor targeting domain until the IgG-derived hinges are naturally degraded in the TME, thus unlocking and activating the CD47 effector function activity in the tumor. LB101 is in a Phase 1/2a clinical trial. Additional information on the trial can be accessed at www.clinicaltrials.gov (NCT05821777). LB101 is an investigational agent that has not been approved by the FDA or any other regulatory authority.

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; its expectations on its anticipated cash runway; the timing of commencement of new studies or clinical trials or clinical and preclinical data related to SerpinPC, LB101, LB206, other LockBody candidates, the LockBody technology platform, ORX750 and other orexin agonist molecules; 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 studies or trials of LB101, LB206, and any other LockBody candidates, ORX750 and other orexin agonist molecules and its expectations on executing its research and clinical development plans and the timing thereof; the Company's ability to differentiate SerpinPC, LB101, LB206, other LockBody candidates, ORX750 and other orexin agonist molecules from other treatment options; the development, design and therapeutic potential of SerpinPC, LB101, LB206, other LockBody candidates, the LockBody technology platform, ORX750 and other orexin agonist molecules; and regulatory matters, including the timing and likelihood of success of obtaining regulatory clearance, 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, and studies or trials of LB101 or within anticipated timelines; our ability to execute IND-enabling activities in a timely manner or at all, including with respect to ORX750 and LB206; 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

Centessa Pharmaceuticals plc
Consolidated Statements of Operations and Comprehensive Loss
(unaudited)
(amounts in thousands except share and per share data)

	Quarter Ended December 31, 2023	Quarter Ended December 31, 2022	Year Ended December 31, 2023	Year Ended December 31, 2022
License and other revenue	$ 6,853	$ —	$ 6,853	$ —
Operating expenses:				
Research and development	29,716	27,835	124,405	155,083
General and administrative	12,315	13,768	53,731	55,200
Change in fair value of contingent value rights	—	—	—	1,980
Loss from operations	(35,178)	(41,603)	(171,283)	(212,263)
Interest income	2,933	39	10,476	244
Interest expense	(2,570)	(2,203)	(9,906)	(7,277)
Other (expense) income, net	(878)	(70)	(5,428)	2,342
Loss before income taxes	(35,693)	(43,837)	(176,141)	(216,954)
Income tax (benefit) expense	1,144	(664)	(25,056)	(747)
Net loss	(36,837)	(43,173)	(151,085)	(216,207)
Other comprehensive income (loss):				
Foreign currency translation adjustment	459	198	1,700	(2,185)
Unrealized gain on available for sale securities, net of tax	255	—	1,290	—
Total comprehensive loss	$ (36,123)	$ (42,975)	$ (148,095)	$ (218,392)
Net loss per ordinary share - basic and diluted	$ (0.38)	$ (0.45)	$ (1.57)	$ (2.31)
Weighted average ordinary shares outstanding - basic and diluted	97,923,585	94,603,860	96,177,578	93,400,513

Centessa Pharmaceuticals plc
Condensed Consolidated Balance Sheets
(unaudited)
(amounts in thousands)

	December 31, 2023	December 31, 2022
Total assets:		
Cash and cash equivalents	$ 128,030	$ 393,644
Short-term investments	128,519	—
Other assets	103,697	50,663
Total assets	$ 360,246	$ 444,307
Total liabilities		
Other liabilities	$ 48,302	$ 38,338
Long term debt	75,700	69,800
Total liabilities	124,002	108,138
Total shareholders’ equity	236,244	336,169
Total liabilities and shareholders' equity	$ 360,246	$ 444,307