Centessa Pharmaceuticals Reports Business Highlights and Financial Results for the Fourth Quarter and Full-Year 2024

March 24, 2025

- *Advancing a broad, potential best-in-class orexin receptor 2 (OX2R) agonist franchise with key data readouts expected in 2025*
  - *ORX750 Phase 2a CRYSTAL-1 study for the treatment of narcolepsy type 1 (NT1), narcolepsy type 2 (NT2) and idiopathic hypersomnia (IH) well underway and on track with data expected across all three indications in 2025 with first-in-class potential in NT2 and IH*
  - *ORX142 in IND-enabling studies for the treatment of neurological and neurodegenerative disorders; Clinical data in acutely sleep-deprived healthy volunteers planned for 2025*
  - *ORX489 in IND-enabling studies for the treatment of neuropsychiatric disorders*

BOSTON and LONDON, March 24, 2025 (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, 2024.

"Centessa is proud to be at the forefront of developing OX2R agonists, a groundbreaking new drug class with the potential to transform the standard of care for patients across multiple therapeutic areas," said Saurabh Saha MD PhD, Chief Executive Officer of Centessa. "Our team's drug optimization techniques have enabled a growing pipeline of novel, potential best-in-class OX2R agonists aimed at restoring normative wakefulness for individuals living with excessive daytime sleepiness (EDS) in neurological, neurodegenerative and neuropsychiatric disorders, and potentially addressing other key symptoms such as impaired attention, cognitive deficits and fatigue."

Dr. Saha continued, "Our most advanced OX2R agonist, ORX750, is progressing in the Phase 2a *CRYSTAL-1* study for the treatment of NT1, NT2 and IH, and is on track with data expected across all three indications this year. Data from the Phase 1 study of ORX750 showed compelling activity in acutely sleep-deprived healthy volunteers at low doses with a favorable initial safety and tolerability profile. Based on the strength of these data, we believe ORX750 has the potential to be best-in-class and to enable the full range of doses required to meet the needs of patients living with NT1, NT2 and IH. We look forward to sharing data this year and expect the Phase 2a study to enable dose selection for future registrational studies of ORX750."

Dr. Saha concluded, "In addition to the transformational potential of ORX750 for individuals living with sleep-wake disorders, we see tremendous opportunity with our follow-up OX2R agonists that are being advanced for the treatment of EDS, impaired attention, cognitive deficits and fatigue in neurological, neurodegenerative and neuropsychiatric disorders. ORX142 is progressing in IND-enabling studies, and subject to IND clearance, we expect to initiate clinical development and share clinical data in acutely sleep-deprived healthy volunteers this year. We are also pleased to have ORX489, our most potent OX2R agonist to date based on preclinical data, advancing in IND-enabling studies. With this ongoing momentum across our pipeline, we expect 2025 to be an exciting, data-rich year for Centessa."

Recent Highlights

- In January 2025, the Company shared positive data from the Phase 1 clinical study of ORX750, a highly potent and selective OX2R agonist, in healthy volunteers as of December 5, 2024, the most recent data cutoff date. These data showed ORX750 significantly increased wakefulness in acutely sleep-deprived healthy volunteers compared to placebo at all doses tested, with a clear dose response. More specifically, in the 2.5 mg (n=8), 3.5 mg (n=10) and 5.0 mg (n=8) dose cohorts, ORX750 was shown to restore normative wakefulness with mean sleep latencies (MSL) >30 minutes (out of a score of 40 minutes) as measured by the Maintenance of Wakefulness Test (MWT); the 5.0 mg dose cohort achieved an MSL of 38 minutes, compared to 15 minutes for placebo. A favorable safety and tolerability profile was observed with all treatment-emergent adverse events (AEs) being transient with none leading to treatment discontinuation. There were no cases of hepatotoxicity or visual disturbances observed. Additionally, there were no clinically significant treatment-emergent changes in hepatic and renal parameters, vital signs or ECG parameters. These data also showed linear pharmacokinetics (PK) with a profile that supports the use of ORX750 as a once-daily oral dosing regimen with rapid absorption. The Company believes these data continue to support ORX750's profile as a potential best-in-class OX2R agonist for the treatment of NT1, NT2 and IH, with first-in-class potential in NT2 and IH. Data from the Phase 1 study of ORX750 will be presented in a poster session at the American Academy of Neurology (AAN) Annual Meeting on April 5, 2025.
- In November 2024, the Company announced the initiation of the Phase 2a *CRYSTAL-1* study of ORX750 in participants with NT1, NT2 and IH.

Pipeline and Anticipated Upcoming Milestones

- **ORX750**: Phase 2a *CRYSTAL-1* study ongoing in participants with NT1, NT2 and IH. The Company expects to share Phase 2a data across all three indications in 2025. In addition, data from the Phase 1 study will be presented in a poster session at the AAN Annual Meeting on April 5, 2025.
- **ORX142**: Advancing through IND-enabling studies. The Company is focused on obtaining IND clearance and initiating clinical development with the goal of sharing clinical data in acutely sleep-deprived healthy volunteers in 2025.
- **ORX489**: Advancing in IND-enabling studies.

Fourth Quarter and Full-Year 2024 Financial Results

- **Cash, Cash Equivalents and Short-term Investments**: Cash, cash equivalents and short-term investments totaled $482.2 million as of December 31, 2024. The Company expects its cash, cash equivalents and short-term investments as of December 31, 2024 will fund operations into mid-2027.
- **Research & Development (R&D) Expenses**: R&D expenses were $60.9 million for the fourth quarter ended December 31, 2024, compared to $29.7 million for the fourth quarter ended December 31, 2023, and $150.2 million for the full-year 2024 compared to $124.4 million for the full-year 2023. R&D expenses for the quarter and full-year 2024 included a one-time charge of $31.5 million related to the discontinuation of the global clinical development program for SerpinPC that was being progressed for the treatment of hemophilia B.
- **General & Administrative Expenses**: General and administrative expenses were $13.7 million for the fourth quarter ended December 31, 2024, compared to $12.3 million the fourth quarter ended December 31, 2023, and $50.8 million for the full-year 2024 compared to $53.7 million for the full-year 2023.
- **Net Loss Attributable to Ordinary Shareholders (Net loss)**: Net loss was $111.3 million for the fourth quarter ended December 31, 2024, compared to $36.8 million for the fourth quarter ended December 31, 2023, and $235.8 million for the full-year 2024 compared to $151.1 million for the full-year 2023. Net loss for the quarter and full-year 2024 reflects non-recurring items including a $34.1 million loss on debt extinguishment and a charge of $31.5 million related to the discontinuation of the global clinical development program for SerpinPC which was included in R&D expenses. In addition, net loss for full-year 2023 included a non-recurring non-cash tax benefit of $24.2 million.

About the Phase 2a *CRYSTAL-1* Clinical Study of ORX750
The Phase 2a *CRYSTAL-1* study is a randomized, double-blind, placebo-controlled, cross-over basket study to evaluate the safety, tolerability, and PK of ORX750 in participants with NT1, NT2 and IH. There are separate cohorts for each indication. Initial dosing is 1.0 mg for NT1 and 2.0 mg for NT2 and IH with sequential dose escalation/de-escalation between cohorts. Each dosing cohort consists of a 6-week treatment duration with crossover study design. During the 6 weeks of treatment, each participant will be randomized to one of two blinded treatment sequences and receive a total of 4 weeks of treatment with ORX750 and 2 weeks of treatment with placebo. Efficacy assessments will evaluate the effect of ORX750 on excessive daytime sleepiness (using the MWT and Epworth Sleepiness Scale (ESS)), cataplexy (NT1 only) and overall symptom improvement (measured by Narcolepsy Severity Scale (NSS) and Idiopathic Hypersomnia Severity Scale (IHSS)). Other exploratory assessments include measures of sleep, cognition, attention, memory and general health.

About Centessa Pharmaceuticals
Centessa Pharmaceuticals, plc is a clinical-stage pharmaceutical company with a mission to discover, develop and ultimately deliver medicines that are transformational for patients. We are pioneering a new class of potential therapies within our orexin receptor 2 (OX2R) agonist program for the treatment of excessive daytime sleepiness (EDS), impaired attention, cognitive deficits and fatigue across neurological, neurodegenerative and neuropsychiatric disorders. We also have an early-stage immuno-oncology program focused on our novel LockBody® technology platform. 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; 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 ORX750, ORX142, ORX489 and other OX2R agonist molecules, and the LockBody technology platform; its ability to identify, screen, recruit and maintain a sufficient number of or any subjects in its existing and anticipated studies or clinical trials of ORX750, ORX142, ORX489 and other OX2R agonist molecules, and any LockBody candidates; its expectations on executing its research and clinical development plans and the timing thereof; its expectations as to the potential results and impact of each of its clinical programs and trials; the Company’s ability to differentiate ORX750, ORX142, ORX489 and other OX2R agonist molecules, any LockBody candidates from other treatment options; the development, design and therapeutic potential of ORX750, ORX142, ORX489 and other OX2R agonist molecules, and the LockBody technology platform; the anticipated net savings associated with the discontinuation of the SerpinPC program; 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 of ORX750, ORX142, ORX489 or within anticipated timelines; our expectations relating to the clinical trials of ORX750, including the predicted timing of enrollment, the predicted efficacious doses of ORX750 and our ability to successfully conduct our clinical development of ORX750, 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 Oxford Finance, 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 Middle East conflicts. 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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Centessa Pharmaceuticals plc
Consolidated Statements of Operations and Comprehensive Loss
(unaudited)
(amounts in thousands except share and per share data)

	Quarter Ended December 31, 2024	Quarter Ended December 31, 2023	Year Ended December 31, 2024	Year Ended December 31, 2023
License and other revenue	$ —	$ 6,853	$ —	$ 6,853
Operating expenses:				
Research and development	60,874	29,716	150,244	124,405
General and administrative	13,706	12,315	50,811	53,731
Loss from operations	(74,580)	(35,178)	(201,055)	(171,283)
Interest income	4,845	2,933	14,016	10,476
Interest expense	(2,479)	(2,570)	(10,090)	(9,906)
Loss on extinguishment of debt	(34,097)	—	(34,097)	—
Other non-operating expenses, net	(3,968)	(878)	(1,687)	(5,428)
Loss before income taxes	(110,279)	(35,693)	(232,913)	(176,141)
Income tax expense (benefit)	1,050	1,144	2,844	(25,056)
Net loss	(111,329)	(36,837)	(235,757)	(151,085)
Other comprehensive income:				
Foreign currency translation adjustment	1,721	459	1,223	1,700
Unrealized gain on available for sale securities, net of tax	397	255	1,497	1,290
Other comprehensive income	2,118	714	2,720	2,990
Total comprehensive loss	$ (109,211)	$ (36,123)	$ (233,037)	$ (148,095)
Net loss per ordinary share - basic and diluted	$ (0.84)	$ (0.38)	$ (2.06)	$ (1.57)
Weighted average ordinary shares outstanding - basic and diluted	132,050,271	97,923,585	114,473,449	96,177,578

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

	December 31, 2024	December 31, 2023
Total assets:		
Cash and cash equivalents	$ 383,221	$ 128,030
Short-term investments	98,956	128,519
Other assets	94,621	103,697
Total assets	$ 576,798	$ 360,246
Total liabilities		
Other liabilities	$ 66,313	$ 48,302
Long term debt	108,940	75,700
Total liabilities	175,253	124,002
Total shareholders' equity	401,545	236,244
Total liabilities and shareholders' equity	$ 576,798	$ 360,246