NEWS RELEASE

Centessa Pharmaceuticals Presents Preclinical Data for ORX142, a Novel Orexin Receptor 2 (OX2R) Agonist, at the 27th Congress of the European Sleep Research Society (Sleep Europe 2024)

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Late-breaking poster presentation of non-human primate (NHP) data support ORX142 as novel drug candidate for the treatment of excessive daytime sleepiness (EDS) in select neurological, neurodegenerative, and psychiatric disorders

BOSTON and LONDON, Sept. 26, 2024 (GLOBE NEWSWIRE) -- **Centessa Pharmaceuticals plc** (Nasdaq: CNTA), a clinical-stage pharmaceutical company that aims to discover and develop medicines that are transformational for patients, today shared new preclinical data from non-human primate (NHP) studies of ORX142, an investigational, novel, orexin receptor 2 (OX2R) agonist being advanced for the treatment of excessive daytime sleepiness (EDS) in select neurological, neurodegenerative and psychiatric disorders. ORX142 is the second drug candidate from the Company's growing pipeline of OX2R agonists and is in IND-enabling studies.

The preclinical data were featured today in a late-breaking poster presentation entitled, "ORX142, an Oral, Highly Potent and Selective Orexin Receptor 2 Agonist, Promotes Wakefulness in Non-Human Primates," by Sarah Wurts Black PhD, Head of Biology for Centessa's Orexin Agonist Program, at the 27th Congress of the European Sleep Research Society (Sleep Europe 2024) in Seville, Spain.

"ORX142 has shown significant activity in promoting wakefulness at very low doses in highly predictive and translational preclinical models," said Saurabh Saha MD PhD, Chief Executive Officer of Centessa. "More specifically, the preclinical data showed ORX142 achieved significant increases in wake times at 0.03 mg/kg, the lowest oral

dose tested in the NHP model. We're excited to share these data at ESRS highlighting the breadth of ORX142's potential as a novel treatment for individuals living with EDS in select neurodegenerative, neurological and psychiatric disorders. Based on the totality of data from our OX2R agonist program and the significant potential market opportunity for ORX142, we are focused on rapidly moving ORX142 through IND-enabling studies."

Overview of ORX142 Preclinical Poster Presentation at Sleep Europe 2024:

- ORX142 is a full OX2R agonist designed by Centessa with the aid of high-resolution crystallography and cryo-EM structural chemistry capabilities.
- ORX142 potently activated the human OX2R with an EC50 of 0.069 nM and > 13,000-fold selective over the human orexin receptor (hOX1R).1
- In highly predictive, translational NHP models, oral administration of ORX142 showed significant activity at the lowest dose tested, which was 0.03 mg/kg.
- ORX142 induced sustained increases in wakefulness that suppressed NREM and REM sleep at the lowest dose tested, 0.03 mg/kg.
- Wakefulness induced by ORX142 was associated with normal physiological arousal and EEG power spectra signatures of enhanced alertness and attention.
- No significant pharmacological activity was observed in GPCR selectivity and in vitro safety panels.

References: 1. Fluorescent imaging plate reader (FLIPR) assay with Chinese hamster ovary (CHO) cells stably expressing recombinant human OX1R or OX2R; OXA EC50 at hOX2R = 0.035 nM; ORX142 EC50 at hOX1R = 930 nM.

Additional meeting information can be found on the Sleep Europe 2024 website at **https://esrs.eu/sleep-congress/**. The poster will also be available on the Centessa website at **https://investors.centessa.com/events-presentations** after the conference concludes.

About Centessa's Orexin Agonist Program

Orexin is a neuropeptide that regulates the sleep-wake cycle, leading to arousal and promoting wakefulness. Low levels of orexin result in excessive daytime sleepiness (EDS) and poor regulation of rapid eye movement (REM) sleep and, in narcolepsy type 1 (NT1), cataplexy and other symptoms. Centessa is developing a pipeline of potential best-in-class orexin receptor 2 (OX2R) agonists, including ORX750 for the treatment of sleep-wake disorders, including NT1, narcolepsy type 2 (NT2) and idiopathic hypersomnia (IH), and ORX142 for the treatment of EDS in select neurological, neurodegenerative, and psychiatric disorders. ORX750 is in a Phase 1 clinical study. ORX750 and ORX142 have not been approved by the FDA or any other regulatory authority.

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.

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; the timing of commencement of new studies or clinical trials or clinical and preclinical data related to ORX750 and ORX142; 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 in respect of ORX750 and ORX142; its expectations on executing its research and clinical development plans and the timing thereof, including its ability to rapidly move ORX142 through IND-enabling studies; its expectations as to the potential results and impact of each of its clinical programs and trials; the Company's ability to differentiate ORX750 and ORX142 from other treatment options; the development, design and therapeutic potential of ORX750 and ORX142; 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, including ORX750 and ORX142; whether ORX750 and ORX142 could be shown to be ineffective; 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 ORX750 and ORX142 or within anticipated timelines; our expectations relating to the further clinical development of ORX750 and ORX142 including initiation of phase 1 and/or phase 2 studies, including the predicted timing of enrollment, the predicted efficacious doses of ORX750 and ORX142 and our ability to successfully conduct our clinical development of ORX750 and ORX142; whether preclinical and initial clinical results for ORX750 and ORX142 will be predictive of results of further clinical trials; 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 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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