# Centessa Pharmaceuticals Announces Poster Presentation of New Preclinical Data Supporting Expansion of Orexin Receptor 2 (OX2R) Agonist Pipeline into Neuropsychiatric Indications at the 64th ACNP Annual Meeting

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**Antidepressive effects and enhanced wakefulness were observed with OX2R activation in established animal model of major depressive disorder**

BOSTON and LONDON, Jan. 14, 2026 (GLOBE NEWSWIRE) -- Centessa Pharmaceuticals plc (Nasdaq: CNTA), a clinical-stage pharmaceutical company focused on developing transformational medicines, today announced the presentation of new preclinical data showing that OX2R activation with a highly potent and selective OX2R agonist reduced behavioral despair and enhanced wakefulness in an established animal model of major depressive disorder at the 64th Annual Meeting of the American College of Neuropsychopharmacology (ACNP). These results support OX2R activation as a potential mechanism of action for rapid-onset treatment to improve mood symptoms and alleviate hypersomnolence in neuropsychiatric indications.

“As a leader in orexin science, we continue to explore orexin pharmacology within a suite of well validated translational non-clinical studies with the goal of unlocking the full potential of our multi-asset OX2R agonist pipeline for patients,” said Mario Alberto Accardi PhD, Chief Executive Officer of Centessa. “These compelling preclinical findings reinforce our strategy of targeting the orexin pathway for the development of new therapeutic options with the potential to address mood symptoms, excessive daytime sleepiness (EDS), impaired attention, cognitive deficits, fatigue and other symptoms across multiple neuroscience indications. We’re excited by the potential opportunity to expand our OX2R pipeline beyond the rare hypersomnias and into additional high-value indications with high unmet clinical need.”

The preclinical data will be featured today in a poster presentation entitled, **“***CNT-9982, an orexin receptor 2 agonist, enhances wakefulness in marmosets, and in the Wistar Kyoto rat model of major depressive disorder, normalizes the arousal state phenotype and alleviates behavioral despair,”* by Sarah Wurts Black PhD, Head of Biology, Orexin Program, at the 64th Annual Meeting of the ACNP at 5:00 - 7:00 PM ET.

ACNP abstracts are available on the conference website and the Company’s poster will be available on the Centessa website at https://investors.centessa.com/events-presentations after the poster presentation concludes.

**About Centessa’s Orexin Receptor 2 (OX2R) Agonist Program**
Orexin is a neuropeptide that regulates the sleep-wake cycle, leading to arousal and promoting wakefulness. Targeting the orexin pathway with novel OX2R agonists represents a potential promising approach to address excessive daytime sleepiness (EDS), impaired attention, cognitive deficits and fatigue associated with a broad range of neurological, neurodegenerative and neuropsychiatric disorders. Centessa is developing a pipeline of potential best-in-class OX2R agonists, including ORX750 for the treatment of sleep-wake disorders including narcolepsy type 1 (NT1), narcolepsy type 2 (NT2) and idiopathic hypersomnia (IH), and ORX142 and ORX489 for the treatment of select neurological, neurodegenerative and neuropsychiatric disorders. ORX750 is being evaluated in the Phase 2a *CRYSTAL-1* study. Information about the trial can also be found at ClinicalTrials.gov (NCT06752668 and NCT07096674). ORX750, ORX142 and ORX489 are investigational candidates and have not been approved by the FDA or any other regulatory authority.

**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 OX2R agonist program for the treatment of EDS, impaired attention, cognitive deficits and fatigue across neurological, neurodegenerative and neuropsychiatric disorders. 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; 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; 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 from other treatment options, including those being developed by competitors; the development, design and therapeutic potential of ORX750, ORX142, ORX489 and other OX2R agonist molecules, including the potential for ORX750 to be a best-in-class OX2R agonist for the treatment of NT1, NT2 and IH, and potentially the first OX2R agonist to treat NT2 and IH; 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 and ORX142, 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, 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 or trade wars and impact of imposition of tariffs. 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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