Centessa Pharmaceuticals Announces Poster Presentation Featuring Novel Orexin Receptor 2 (OX2R) Agonist Discovery Pipeline at the 26th Conference of the European Sleep Research Society (Sleep Europe 2022)

September 20, 2022

– Data demonstrate potent efficacy of small-molecule OX2R agonists in a non-clinical model of narcolepsy type 1 (NT1) –
– Company recognizes World Narcolepsy Day on September 22nd –

BOSTON and LONDON, Sept. 20, 2022 (GLOBE NEWSWIRE) -- Centessa Pharmaceuticals plc (Nasdaq: CNTA), today announced that non-clinical data from its oral orexin receptor 2 (OX2R) agonist discovery pipeline have been accepted for poster presentation at the 26th Conference of the European Sleep Research Society meeting (*Sleep Europe 2022*) being held on September 27-30, 2022, in Athens, Greece. Centessa's OX2R agonists are designed to directly target the underlying pathophysiology of orexin neuron loss in narcolepsy type 1 (NT1), with potential expansion into narcolepsy type 2 (NT2), and other sleep disorders.

The poster presentation will feature the non-clinical activity profiles of small-molecule OX2R agonists from multiple lead chemical series developed using structure-based drug design with an OX2R protein stabilized in the agonist conformation (Sosei Heptares' Stabilized Receptor Technology (StaR®)), together with CryoEM (cryogenic electron microscopy) and high-resolution protein crystallography. These novel OX2R agonist compounds showed high potency in activating recombinant human and endogenous mouse OX2Rs, with more than a thousand-fold selectivity for OX2R compared to OX1R. The OX2R agonists also showed efficacy in promoting wakefulness and in reducing cataplexy events in NT1 model mice, and increased wakefulness in healthy mice.

"Over the past year, we have made significant advances building a deep pipeline of novel, potent and selective OX2R agonists," said Saurabh Saha, MD, PhD, Chief Executive Officer of Centessa. "Centessa's orexin program is led by some of the most experienced and insightful scientists in this field. Our innovative pipeline is both a testament to their expertise and strong validation of our approach to structure-based drug design. We are encouraged by the non-clinical data and are rapidly progressing several potentially best-in-class oral small-molecule OX2R agonists through our discovery pipeline."

"We are excited to showcase some of our small-molecule OX2R agonist discovery pipeline and share these data at *Sleep Europe 2022*," said Mario Alberto Accardi, PhD, Head, Centessa Orexin Program. "Additionally, as part of our ongoing commitment to patients, we look forward to joining the entire narcolepsy community in recognizing World Narcolepsy Day on September 22nd to reinforce the critical need for broader disease awareness and additional treatment options for narcolepsy and other sleep disorders."

Details of the poster are as follows:
Title: Novel Orexin Receptor-2 Agonists Developed Using Structure-based Drug Design: Prototype Compounds Promote Wakefulness and Reduce Cataplexy in Orexin/Ataxin-3 and WT Mice
Abstract number: 401 **Poster code:** P001
Presenters: Sarah Wurts Black, Karl Gibson, Deborah S. Hartman
Session name: Late Breaking Abstracts
Session details: September 29, 2022, at 12:15 PM (local time)

The abstract and additional meeting information can be found on the *Sleep Europe 2022* website at https://esrs.eu/sleep-congress/. The poster will also be available on the Centessa website at https://investors.centessa.com/events-publications/events-presentations after the conference concludes.

About Centessa Pharmaceuticals
Centessa Pharmaceuticals plc is a clinical-stage pharmaceutical company with a Research & Development ("R&D") innovation engine that aims to discover, develop and ultimately deliver impactful medicines to patients. Our programs span discovery-stage to late-stage development and cover a range of high-value indications in rare diseases and immuno-oncology. We are led by a management team with extensive R&D experience, providing direct guidance to our program teams to rapidly advance our candidates from research through all stages of development. 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 deliver impactful medicines to patients; the ability of our management team and board to drive execution of the Company's portfolio of programs; our asset-centric business model and the intended advantages and benefits thereof; research and clinical development plans and the timing thereof; the scope, progress, results and costs of developing our product candidates or any other future product candidates; the development and therapeutic potential of our product candidates, including OX2R agonists; strategy; regulatory matters, including the timing and likelihood of initiating clinical trials, reporting clinical trial results, submitting an IND and the success of obtaining authorizations to initiate or continue clinical trials or market any products; and the market size and opportunity for our product candidates. 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, risks related to the safety and tolerability profile of our product candidates; 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; 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/or commercialized; the risk that the results of non-clinical studies or clinical studies will not be predictive of future results in connection with future studies; geo-political risks such as the Russia-Ukraine war and risks related to the ongoing COVID-19 pandemic including the effects of the Delta, Omicron and any other variants. 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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