Centessa Pharmaceuticals Makes Strategic Decision to Discontinue Clinical Development of Lixivaptan for Autosomal Dominant Polycystic Kidney Disease (ADPKD)

June 2, 2022

- Decision based on reassessment of commercial potential of lixivaptan following recent observation of ALT/AST elevations in ALERT Study -

- Discontinuation of lixivaptan development expected to significantly reduce cash burn and extend cash runway into 2026 -

- Company continues to focus on the development of its innovative high impact rare disease and immuno-oncology pipeline of investigational medicines for patients -

BOSTON and LONDON, June 02, 2022 (GLOBE NEWSWIRE) -- Centessa Pharmaceuticals plc (Nasdaq: CNTA), today announced that it has made the strategic decision to discontinue development of lixivaptan for Autosomal Dominant Polycystic Kidney Disease (ADPKD) including both the Phase 3 ACTION Study and the open-label ALERT Study. The decision is based on a thorough reassessment of the commercial potential of lixivaptan as a potential best-in-class therapy for patients with ADPKD, and the incremental development challenges and associated costs, following a recent observation of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) elevations in one subject in the ALERT Study.

"The ALERT Study was designed to help provide an early assessment of the safety profile of lixivaptan in ADPKD patients who previously experienced liver chemistry abnormalities while treated with tolvaptan, the only FDA approved therapy for ADPKD. In assessing the recent data from a subject in the ALERT Study, we believe that lixivaptan is unlikely to achieve the differentiated safety and tolerability profile Centessa required for further development of the program. Given the revised commercial potential of lixivaptan and our commitment to being financially disciplined, we made the data-driven decision to voluntarily discontinue development of lixivaptan," said Saurabh Saha, MD, PhD, Chief Executive Officer of Centessa. "As an organization focused on developing best-in-class therapies and innovative medicines for patients, we had hoped lixivaptan would provide patients with ADPKD a safer alternative treatment option to the current approved therapy. We are incredibly grateful to all the patients, their families and the investigators who participated in the lixivaptan trials and contributed to this research."

Dr. Saha continued, "Going forward, we remain focused on continuing to advance our innovative rare disease and immuno-oncology programs with the potential for multiple clinical proof of concept readouts over the next 12 to 24 months. With our decision to discontinue development of lixivaptan, we believe we are well positioned with the capital and resources to execute these programs. We expect a significant reduction in annual cash burn and that our cash runway will now extend into 2026."

About the ACTION Study

The ACTION Study was a Phase 3 trial consisting of a two-arm, double-blind, placebo-controlled, randomized phase ("Part 1") followed by a single-arm, open-label phase ("Part 2"). The ACTION Study was designed to evaluate the efficacy and safety of lixivaptan in subjects with ADPKD. Further information on the ACTION Study can be found at clinicaltrials.gov at https://clinicaltrials.gov/ct2/show/NCT04064346

About the ALERT Study

The ALERT Study was an open-label, non-registrational repeat-dose study designed to assess liver and non-liver safety in subjects who previously experienced liver chemistry test abnormalities while treated with tolvaptan and were permanently discontinued from the drug for that reason. Further information on the ALERT Study can be found at clinicaltrials.gov at https://clinicaltrials.gov/ct2/show/NCT04152837

About Centessa Pharmaceuticals

Centessa Pharmaceuticals plc ("Centessa") 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 key executives 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; 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 SerpinPC and ZF874; strategy; regulatory matters, including the timing and likelihood of success of obtaining approvals to initiate or continue clinical trials or market any products; market size and opportunity for our product candidates; and our anticipated cash runway. 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 products 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 preclinical 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 Quarterly Report on Form 10-Q for the quarter ended March 31, 2022 and our other reports, which are on file with the U.S. Securities and Exchange Commission. We explicitly disclaim any obligation to update any forward-looking statements except to the extent required by law.

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