Centessa Pharmaceuticals Doses First Subject in Global Phase 3 ACTION Study of Lixivaptan in Autosomal Dominant Polycystic Kidney Disease

February 24, 2022

BOSTON and LONDON, Feb. 24, 2022 (GLOBE NEWSWIRE) -- Centessa Pharmaceuticals plc (Nasdaq: CNTA) (the "Company"), together with its subsidiary Palladio Biosciences, Inc. ("Palladio"), today announced it has started dosing of the first subject in its pivotal Phase 3 clinical trial ("ACTION Study") evaluating lixivaptan as a potential treatment for Autosomal Dominant Polycystic Kidney Disease ("ADPKD"). The trial is expected to enroll approximately 1,350 subjects across more than 200 sites in over 20 countries. The Company anticipates completing enrollment in the second half of 2023 and, if results are supportive, plans to submit a New Drug Application ("NDA") after completion of the one-year double-blind portion of the study.

"The start of dosing in the ACTION Study marks a major clinical milestone for Centessa, as we work towards providing ADPKD patients a new treatment option with a differentiated tolerability profile," said Saurabh Saha, MD, PhD, Chief Executive Officer of Centessa. "With its unique structure and metabolite profile, lixivaptan has the potential to avoid the liver toxicity associated with the only FDA-approved ADPKD therapy. The ACTION Study has been designed to serve as a single registration trial and will evaluate the efficacy and safety of lixivaptan in a broad group of ADPKD patients."

Dosing of the first subject in the ACTION Study is the trigger for payment of the contingent value rights ("CVR") originally issued to former shareholders and option holders of Palladio in January 2021 in connection with Centessa's acquisition of Palladio. The CVR will be settled in newly issued ADSs of Centessa.

About the ACTION Study

The ACTION Study is 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 will evaluate the efficacy and safety of lixivaptan that has been titrated to a maximum tolerated dose between 100-200 mg BID in subjects with ADPKD and a Mayo Clinic MRI imaging classification of 1C, 1D or 1E and an estimated glomerular filtration rate ("eGFR") ≥25 and ≤90 mL/min/1.73 m^2. The primary analysis of the ACTION Study will be performed at the end of Part 1 of the trial, which will have a 2:1 randomization (lixivaptan:placebo) and is designed to assess lixivaptan in slowing the decline in renal function as measured at 52 weeks by the difference in eGFR between the lixivaptan-treated and placebo-treated subjects. Final efficacy measurements at the end of the double-blind period will be conducted while subjects are off study drug during three clinic visits over a 28 day period. The trial is expected to enroll approximately 1,350 subjects across more than 200 sites in over 20 countries. All subjects successfully completing Part 1 are expected to continue into Part 2 of the study and will be treated with lixivaptan for an additional year to further assess the sustainability of the potential benefit on eGFR change over a two-year period. Consistent with Part 1, final efficacy measurements will be conducted off study drug. Both parts of the study will contribute to further evaluating the safety profile of lixivaptan. An independent data monitoring committee will periodically review all safety data, including the liver chemistry data for all subjects, throughout the study. The Company anticipates completing enrollment in the second half of 2023 and, if results are supportive, plans to submit an NDA after completion of the one-year double-blind portion of the study ("Part 1").

Further information on the ACTION Study can be found at www.clinicaltrials.gov at the following link: https://clinicaltrials.gov/ct2/show/NCT04064346

About Centessa Pharmaceuticals
Centessa Pharmaceuticals plc ("Centessa") aims to bring impactful new medicines to patients by combining the strengths of an asset-centric model with the benefits of scale and diversification typical of larger R&D organizations. Centessa's programs range from discovery-stage to late-stage development and include diverse therapeutic areas such as oncology, hematology, immunology/inflammation, neuroscience, hepatology, pulmonology and nephrology. For more information, visit www.centessa.com.

About Palladio Biosciences
Palladio Biosciences, Inc. ("Palladio") aims to develop transformative medicines for rare diseases of the kidney. Palladio is actively investigating the potential of its lead product candidate, lixivaptan, in subjects with Autosomal Dominant Polycystic Kidney Disease ("ADPKD").

About Lixivaptan
Lixivaptan is an investigational, oral, nonpeptide selective vasopressin V2 receptor antagonist in development for the potential treatment of ADPKD. The development program is designed to show that lixivaptan can slow the decline in renal function that is typically observed in ADPKD patients while avoiding the liver safety issues associated with JYNARQUE®, a form of branded tolvaptan indicated for ADPKD, which is the only drug currently approved for ADPKD. Lixivaptan has been granted Orphan Drug Designation from the FDA.

About ADPKD
ADPKD is a rare hereditary disorder characterized by the formation and enlargement of cysts in the kidney, liver, and other organs. It is the fourth leading cause of kidney failure in the U.S. and one of the most common inherited genetic diseases in humans, occurring equally in women and men, in all races, globally. There are an estimated 140,000 diagnosed ADPKD patients in the U.S.

Forward Looking Statements
This press release contains forward-looking statements. These statements may be identified by words such as "aims," "anticipates," "believes," "could," "estimates," "expects," "forecasts," "goal," "intends," "may," "plans," "possible," "potential," "seeks," "will," 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 enrollment, timing and conduct of the Company's ACTION study; timing of a New Drug Application for lixivaptan as a as a potential treatment for Autosomal Dominant Polycystic Kidney Disease; the Company's ability to deliver impactful medicines to patients; the ability of our key executives and subject-matter experts 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 design, scope and purpose of our ongoing ACTION Study; the development and therapeutic potential of our product candidates, including lixivaptan; strategy; regulatory matters, including the timing and likelihood of success of obtaining approvals to initiate or continue clinical trials or market any products; and 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 our ability to protect and maintain our intellectual property position; business, 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 to fund our planned clinical trials and other expenses; our ability to recruit and retain subjects in our trials; 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 or the acceptance and approval of a New Drug Application; 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 commercialized; the risk that the results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies; and risks related to the 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 most recent Form 10-Q, which is on file with the SEC. We explicitly disclaim any obligation to update any forward-looking statements except to the extent required by law.

Contacts:
Investors:
investors@centessa.com

John Fraunces, LifeSci Advisors
jfraunces@lifesciadvisors.com

Media:
media@centessa.com