CalciMedica Announces FDA Clearance of IND Application for Phase 2 Trial of Auxora™ for the Treatment of Severe Acute Kidney Injury

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Phase 2 trial, expected to begin in 1H 2024, aims to address the unmet medical need of patients suffering from stage 2 or 3 acute kidney injury with associated acute hypoxemic respiratory failure, a condition associated with a high mortality rate

Development of Auxora in AKI is supported by both clinical and pre-clinical evidence, including results from recently completed studies in a rat model of AKI to be presented at the 29th International Acute Kidney Injury and Continuous Renal Replacement Therapy Conference in March

LA JOLLA, Calif., Feb. 13, 2024 /PRNewswire/ -- CalciMedica, Inc. (CalciMedica or the Company) (Nasdaq: CALC), a clinical-stage biopharmaceutical company focused on developing novel calcium release-activated calcium (CRAC) channel inhibition therapies for acute and chronic inflammatory and immunologic diseases, today announced the clearance of its Investigational New Drug (IND) application by the U.S. Food and Drug Administration (FDA) for the Company's lead product candidate, Auxora™, a potent and selective small molecule inhibitor of Orai1-containing CRAC channels, to be evaluated in a Phase 2 trial in acute kidney injury (AKI) with associated acute hypoxemic respiratory failure (AHRF). CalciMedica expects to initiate the trial, named KOURAGE, in the first half of 2024 and data expected in 2025.

"The IND clearance for the Phase 2 trial of Auxora in severe AKI is a significant milestone for CalciMedica as we work towards addressing the serious unmet medical need faced by patients suffering from this condition," said Rachel Leheny, Ph.D., Chief Executive Officer of CalciMedica. "Through KOURAGE, we aim to determine how Auxora can benefit patients with severe AKI and potentially reduce the high mortality rate associated with this disease."

AKI is classified as stages 1, 2 and 3 depending on the degree of kidney injury. In the presence of AHRF, stage 2 and stage 3 AKI, both classified as severe, put patients at a 50% or greater risk for death while hospitalized and in the 90 days after discharge.[1] Survivors of severe AKI may develop or progress to chronic kidney disease, leading to an eventual need for dialysis. There are approximately 1.1 million patients in the United States suffering from stage 2 and 3 AKI over half of whom have associated AHRF. There are currently no approved therapies for AKI.

KOURAGE is a randomized, double-blind, placebo-controlled study that will evaluate 150 patients with stage 2 and 3 AKI who have AHRF and are receiving oxygen by non-invasive mechanical ventilation, high flow nasal cannula or intermittent mandatory ventilation (IMV). Patients will be stratified by classification of stage of AKI as well as the use of IMV. Patients will receive either a four-hour infusion of Auxora or placebo at 1.25 mL/kg as a first dose, after which they will receive Auxora or placebo at 1.0 mL/kg at hours 24, 48, 72 and 96. The primary endpoint of the trial will be evaluation of patients through day 30 to determine days alive, ventilator-free and dialysis-free. Secondary endpoints will include a composite of all-cause mortality, decrease in estimated glomerular filtration rate (eGFR), and the incidence of dialysis over a period of 90 days, also known as MAKE-90 (Major Adverse Kidney Events at 90 days).

"The rationale for and design of our Phase 2 KOURAGE study is supported by our prior clinical trials and pre-clinical studies that have indicated the potential benefits of Auxora for the treatment of AKI," said Sudarshan Hebbar, M.D., Chief Medical Officer of CalciMedica. "After the learnings from our CARDEA trial revealed that treatment of severe and critical COVID-19 pneumonia patients with Auxora reduced the reported incidence of AKI and improved the survival of patients with kidney disease, we confirmed this potential benefit of Auxora in specific animal models of AKI. Currently, there are no drugs that treat AKI, and through KOURAGE, we hope to demonstrate that treatment with Auxora translates into a treatment option for this critical acute disease."

AKI is a common consequence of severe COVID-19 pneumonia and in CalciMedica's CARDEA trial, which studied Auxora in patients with severe and critical COVID-19 pneumonia, results showed a nearly 40% reduction in reported AKI in Auxora-treated patients as compared to placebo-treated patients. In a post-hoc analysis of CARDEA patients with compromised kidney function (eGFR$\leq$ 60 mL/min/1.73 m^2) at enrollment, the drug was well tolerated and there was a survival benefit for patients treated with Auxora compared to those on placebo. Biomarker analysis from blood samples taken from over 190 CARDEA patients showed that Auxora increased Angiopoietin-1 while decreasing Angiopoietin-2, suggesting stabilization of the endothelium and the potential to treat AKI. Finally, published work from others showed that elevated serum IL–17 levels, a CRAC channel-mediated cytokine, were differentially elevated in critically ill patients with stage 2 and 3 AKI when compared to those without AKI, and the elevation was independently associated with both hospital mortality and long-term adverse outcomes.[2]

CalciMedica's initial pre-clinical studies in an ischemia/reperfusion injury (IRI) model of AKI were encouraging. A single dose of Auxora after IRI increased GFR by 61% and decreased mononuclear (inflammatory) cell infiltration by 30%. Further details from this study and results from CalciMedica's more recent pre-clinical study of multiple doses of Auxora given over several days and initiated after a greater time interval following IRI were also strong and will be presented at the 29th International AKI & Continuous Renal Replacement Therapy Conference taking place March 12-15, 2024 in San Diego, CA.

About AKI
Acute kidney injury (AKI) denotes a sudden reduction in kidney function, or the organ's ability to clean and filter the blood, as measured by increased serum creatinine (a cellular waste product) or decreased urine volume. AKI can result as a complication of other serious illnesses such as sepsis,

respiratory infections and failure, acute pancreatitis, trauma, surgery and burns. There are approximately 3.7 million hospitalized with AKI in the United States each year. The majority have Stage 1 AKI and recover with supportive care alone. However, approximately 1.1 million of these patients advance to stage 2 and stage 3 AKI, over half of whom have associated AHRF. The risk of serious morbidities and mortality is significant for advanced stage 2 and stage 3 AKI patients. There are currently no approved therapies for AKI.

About Auxora™
CalciMedica's lead clinical compound, Auxora™, is a potent and selective small molecule inhibitor of Orai1-containing CRAC channels that is being developed for use in patients with acute inflammatory and immunologic illnesses. CRAC channels are found on many cell types, including pancreatic acinar cells, lung endothelium cells and immune system cells, where aberrant activation of these channels may play a key role in the pathobiology of acute and chronic inflammatory syndromes. Auxora is currently being evaluated in: (i) a Phase 2b trial for acute pancreatitis (AP) with accompanying systemic inflammatory response syndrome (SIRS), called CARPO, (ii) an investigator-sponsored Phase 1/2 trial called CRSPA being conducted in pediatric patients with asparaginase-induced pancreatic toxicity (AIPT) as a side effect of pediatric acute lymphoblastic leukemia treatment with asparaginase, and (iii) a Phase 2 dose-ranging pharmacodynamic study in critical COVID-19 patients, with a Phase 2 trial in AKI, called KOURAGE expected to initiate in the first half of 2024. There are currently no approved therapies to treat either AP, AIPT or AKI. In previous trials, patients responded well to Auxora regardless of severity or cause of disease. CalciMedica is also exploring the potential of Auxora treatment for other acute indications including acute respiratory distress syndrome**.**

About CalciMedica
CalciMedica is a clinical-stage biopharmaceutical company focused on developing novel CRAC channel inhibition therapies for inflammatory and immunologic diseases. CalciMedica's proprietary technology targets the inhibition of CRAC channels to modulate the immune response and protect against tissue cell injury, with the potential to provide therapeutic benefits in life-threatening inflammatory and immunologic diseases for which there are currently no approved therapies. CalciMedica's lead product candidate Auxora™, a proprietary, intravenous-formulated CRAC channel inhibitor, has demonstrated positive and consistent clinical results in multiple completed efficacy clinical trials. CalciMedica is currently conducting a Phase 2b trial for a planned 216 patients (called CARPO – NCT04681066) for AP with SIRS, with topline data expected in the first half of 2024, as well as supporting the ongoing Phase 1/2 CRSPA *AIPT* study (called CRSPA – NCT04195347), with additional data expected by 2H 2024. CalciMedica plans to initiate a Phase 2 study in AKI in 1H 2024. CalciMedica was founded by scientists from Torrey Pines Therapeutics and the Harvard CBR Institute for Biomedical Research, and is headquartered in La Jolla, CA. For more information, please visit www.calcimedica.com.

Sources
[1] Faubel, Sarah, and Charles L. Edelstein. "Mechanisms and mediators of lung injury after acute kidney injury." *Nature Reviews Nephrology* 12.1 (2016): 48-60.

[2] Collett, Jason A., et al. "Serum IL-17 levels are higher in critically ill patients with AKI and associated with worse outcomes." *Critical Care* 26.1 (2022): 107.

Forward-Looking Statements

This communication contains forward-looking statements which include, but are not limited to, statements regarding CalciMedica's planned and ongoing clinical trials and the timing, design and expected patient enrollment thereof, including its planned Phase 2 clinical trial of Auxora in AKI with associated AHRF, its ongoing Phase 2b trial of Auxora for AP with accompanying SIRS, its ongoing Phase 1/2 trial of Auxora in pediatric patients with AIPT; the potential benefits of Auxora for the treatment of AKI, AP and AIPT; the estimated patient population in the United States for AKI; pre-clinical and clinical studies of Auxora in animal models and critical COVID-19 pneumonia patients, respectively, supporting the rationale for and the design of CalciMedica's planned Phase 2 KOURAGE trial and the potential benefits of Auxora in AKI; plans to present results from CalciMedica's pre-clinical studies in an IRI model of AKI at the 29th International AKI & Continuous Renal Replacement Therapy Conference; CalciMedica's development plans for Auxora; the expected timing for release of data in CalciMedica's ongoing clinical trials. These forward-looking statements are subject to the safe harbor provisions under the Private Securities Litigation Reform Act of 1995. CalciMedica's expectations and beliefs regarding these matters may not materialize. Actual outcomes and results may differ materially from those contemplated by these forward-looking statements as a result of uncertainties, risks, and changes in circumstances, including but not limited to risks and uncertainties related to: the impact of fluctuations in global financial markets on CalciMedica's business and the actions it may take in response thereto; CalciMedica's ability to execute its plans and strategies; the ability to obtain and maintain regulatory approval for Auxora; results from clinical trials or preclinical studies may not be indicative of results that may be observed in the future; potential safety and other complications from Auxora; the scope progress and expansion of developing and commercializing Auxora; the size and growth of the market therefor and the rate and degree of market acceptance thereof; economic, business, competitive, and/or regulatory factors affecting the business of CalciMedica generally; CalciMedica's ability to protect its intellectual property position; and the impact of government laws and regulations. Additional risks and uncertainties that could cause actual outcomes and results to differ materially from those contemplated by the forward-looking statements are included under the caption "Risk Factors" in CalciMedica's Quarterly Report on Form 10-Q for the quarter ended September 30, 2023 and elsewhere in CalciMedica's subsequent reports on Form 10-K, Form 10-Q or Form 8-K filed with the SEC from time to time and available at www.sec.gov. These documents can be accessed on CalciMedica's web page at ir.calcimedica.com/financials-filings/sec-filings.

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