CalciMedica Announces Publication of Preclinical Data in EMBO Molecular Medicine Supporting the Development of CRAC Channel Inhibitors for Inflammatory Bowel Disease (IBD)

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– Study provides further validation of the potentially broad utility for CRAC channel inhibitors in inflammatory diseases

– Data show that inhibiting store-operated Ca^{2+} entry (SOCE) with a selective CRAC channel inhibitor reduced IBD severity in murine models

LA JOLLA, Calif., [August 9, 2022] – CalciMedica Inc. ("CalciMedica" or the "Company), the CRAC (calcium release-activated calcium) channel company, today announced the publication of preclinical data in *EMBO Molecular Medicine* that describes the potential utility for CRAC channel inhibitors in inflammatory bowel disease (IBD). The paper, titled "Store-operated calcium entry controls innate and adaptive immune cell function in inflammatory bowel disease," was conducted by CalciMedica's scientific co-founder, Stefan Feske, M.D., and his team at NYU Grossman School of Medicine in collaboration with senior researchers at the Charité – Universitätsmedizin Berlin, Germany, Britta Siegmund, M.D. and Carl Weidinger, M.D. and co-authored by CalciMedica's co-founder and Chief Scientific Officer, Ken Stauderman, Ph.D.

"The data gathered in this study indicate that inhibiting store-operated calcium entry (SOCE) may represent a potential new treatment approach for IBD," said Dr. Stauderman. "By investigating immune cell composition in the lamina propria of patients with ulcerative colitis and Crohn's disease, this study demonstrates not only that SOCE regulates the function of immune cells that drive IBD pathology, but also that inhibiting SOCE with a CRAC channel inhibitor slows the production of pro-inflammatory cytokines. Similar results were observed in a murine adoptive T cell transfer model of IBD. This work is important as it confirms the potential utility of using CRAC channel inhibitors as a treatment for IBD."

IBD is characterized by dysregulated intestinal immune responses and manifests primarily as ulcerative colitis (UC) and Crohn's disease (CD). The study authors used mass cytometry to analyze the immune cell composition in the lamina propria in patients with UC and CD. They observed an enrichment of CD4+ effector T cells producing IL-17A and TNF, $IFNg^{+}$ $CD8^{+}$ T cells, T regulatory (Treg) cells, and innate lymphoid cells. The function of these immune cells is regulated by store-operated Ca^{2+} entry (SOCE), which results from the opening of Ca^{2+} release-activated Ca^{2+} (CRAC) channels formed primarily by ORAI1 and STIM1 proteins. By inhibiting SOCE in cultured cells with a CRAC channel inhibitor, the authors observed a reduction in the production of pathogenic cytokines while having no effect on the viability, differentiation, and function of intestinal epithelial cells.

Additionally, in a mouse model of IBD, T cell-specific deletion of CRAC channel genes showed that Stim2, Orai1, and Stim1- deficient T cells have quantitatively increasing defects in SOCE, which correlate with gradually more pronounced impairment of cytokine production by Th1 and Th17 cells and decreases in intestinal inflammation. Moreover, inhibiting SOCE with CM4620 (zegocractin, the active agent in Auxora), CalciMedica's selective ORAI1 CRAC channel inhibitor, resulted in reduced intestinal inflammation, colitogenic T cell function and weight loss, suggesting that inhibition of ORAI1 CRAC channels could be a viable treatment for IBD in humans.

Dr. Feske has a financial interest in CalciMedica with the relationship managed according to the policies of NYU Langone Health.

About CM4620 (Zegocractin)

CM4620 (zegocractin) is the active ingredient in CalciMedica's lead product candidate Auxora, an intravenous (IV) formulation that in animal models and clinical trials has prevented acute epithelial and/or endothelial cell injury and inflammation in organs, such as the pancreas, lungs and kidneys. Auxora is currently being evaluated in multiple ongoing clinical trials: a blinded, placebo-controlled Phase 2b trial in patients with acute pancreatitis with accompanying systemic inflammatory response syndrome (SIRS), a Phase 2 dose-escalation trial in patients with COVID-19 pneumonia and acute respiratory distress syndrome (ARDS) requiring invasive mechanical ventilation, and an investigator-initiated Phase 1/2 trial in pediatric asparaginase-associated pancreatitis (AAP), which develops in approximately 10% of lymphocytic leukemia (ALL) patients who receive asparaginase as part of their chemotherapy regimen. Auxora has been evaluated in CARDEA, a 284-patient randomized, placebo-controlled trial in hospitalized COVID-19 pneumonia patients that was Part Two of a Phase 2 trial. The results were published in the peer reviewed journal *Critical Care* in April 2022. The results of Part One of the trial, a randomized open label trial in 30 critical and severe COVID-19 pneumonia patients, were also published *Critical Care* in August 2020. Results of a randomized open label Phase 2a trial in 21 acute pancreatitis patients with SIRS were published in the peer reviewed journal, *Pancreas*, in June 2021.

About CalciMedica, Inc.

CalciMedica is a clinical-stage biopharmaceutical company advancing a new class of medicines designed to act upon calcium release-activated calcium (CRAC) channels, a group of ion channel targets not addressed by any approved drugs. CalciMedica is developing CRAC channel inhibitors for unmet needs in acute critical illness and looks to expand the potential uses of CRAC channel inhibitors to certain chronic diseases that have the common thread of inflammation in their pathogenesis. The Company has a portfolio of potent and selective small molecule CRAC channel inhibitors including Auxora, its lead product candidate, which is formulated as a proprietary IV nanoemulsion specifically designed for acute critical illnesses.

CalciMedica is headquartered in La Jolla, CA. For more information, please visit the company website at www.calcimedica.com.

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