CalciMedica Announces Publication of Peer-Reviewed Paper in The Journal of Physiology

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Study Supports Development of CRAC Channel Inhibitors for Acute Pancreatitis

Study indicates that Orai1 inhibition prevents impaired ductal cell function in acute pancreatitis (AP)

Data describes underlying biological mechanisms that may explain key result in a Phase 2a trial of Auxora™ in patients with AP with systemic inflammatory response syndrome and hypoxemia

LA JOLLA, Calif., March 10, 2022 – CalciMedica Inc. (CalciMedica or the Company), the CRAC (calcium release-activated calcium) channel company, today announced the publication of a research paper describing how bile acid- and ethanol-mediated activation of Orai1 damages pancreatic ductal cells in AP. The research paper, entitled "Bile acid- and ethanol-mediated activation of Orai1 damages pancreatic ductal secretion in acute pancreatitis," appears in the peer-reviewed publication *The Journal of Physiology,* and is authored by a group led by Joszef Maleth, M.D., Ph.D., Principal Investigator, University of Szeged, Hungary. The results provide a description of the underlying biological mechanisms that may explain the rapid tolerance of solid food observed in CalciMedica's Phase 2a trial of Auxora, its lead product, in patients with AP with systemic inflammatory response syndrome (SIRS) and hypoxemia.

"The relationship between Orai1 inhibition and bile acid-, and alcohol-induced damage to pancreatic ductal cell secretion was long overdue for attention," said Dr. Maleth. "Our study demonstrates inhibiting Orai1 may improve outcomes for patients with acute pancreatitis by restoring this ductal cell function. We are thrilled to have a journal as respected as *The Journal of Physiology* recognize the significance of our conclusions and are glad that our work is accessible to both the public and the scientific community."

Though sustained intracellular Ca^{2+} overload via over-activation of CRAC channels and Orai1 in pancreatic acinar cells is a known feature of experimental AP, expression and function of Orai1 in ductal cells of the pancreas are not well appreciated and warranted further research. The results of this study indicate that Orai1 inhibition prevents impaired function of both ductal cells, as well as acinar cells in AP caused by both bile acid/gallstones and alcohol, the leading causes of clinical AP, which has implications for improved disease outcomes in AP patients.

"The study led by Dr. Maleth utilizes our proprietary compound CM5480, one of our research tool CRAC channel inhibitors, which has been used in other proof-of-concept studies," said Kenneth Stauderman, Ph.D., Co-founder and Chief Scientific Officer of CalciMedica. "Protection of pancreatic ductal cells by a CRAC channel inhibitor, as demonstrated in Dr. Maleth's study, enables these cells to perform their normal function of transporting digestive enzymes produced in the pancreas to the gut, along with bicarbonate, and we believe helps to explain why, in our Phase 2a AP trial, patients were able to tolerate solid food more rapidly after treatment with Auxora compared to placebo. Together, these findings go a long way to advancing our understanding of the role of CRAC channels in AP and making a difference in the quality of life for these patients."

Auxora is CalciMedica's lead candidate and is currently being evaluated in a Phase 2b trial for acute pancreatitis with accompanying SIRS. The previous Phase 2a trial randomized 21 patients with acute pancreatitis and accompanying SIRS with hypoxemia to receive high- or low-dose Auxora plus standard of care or standard of care alone. From screening to day 5 or discharge, of the patients receiving Auxora, fewer experienced persistent SIRS and more experienced rapid restoration of gut function with better tolerability of solid foods within 72 hours of treatment. This allowed for earlier hospital discharge, resulting in reduced median hospital stay in the Auxora treatment groups compared to those patients receiving only standard of care, especially among patients with moderate or severe acute pancreatitis. Improvements in the severity of AP were observed in three of eight Auxora-treated patients with moderate to severe AP as demonstrated by contrast-enhanced computed tomography (CECT) scans, compared with none of four patients in the standard of care group. Efficacy signals were observed across both high-dose and low-dose cohorts.

To view the online publication, click here.

About Auxora

CalciMedica's lead product candidate is Auxora, a potent and selective intravenous (IV) formulated small molecule CRAC channel inhibitor that in animal models and in 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 acute lymphocytic leukemia (ALL) patients who develop acute pancreatitis as a result of a specific chemotherapy. 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. Results of Part One of the Phase 2 trial, a randomized open label trial in 30 critical and severe COVID-19 pneumonia patients, were published in the peer reviewed journal, *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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