



Redefining Regenerative Medicine

Histogen and Amerimmune Report Publication on Emricasan in COVID-19

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Study Demonstrated Potential *In Vitro* Benefit in Acute and Long-Haul Phases of COVID-19

SAN DIEGO, May 19, 2021 (GLOBE NEWSWIRE) -- Histogen Inc. (NASDAQ: HSTO), a clinical-stage therapeutics company focused on developing potential first-in-class restorative therapeutics that ignite the body's natural process to repair and maintain healthy biological function and its partner, Amerimmune, LLC, today reported the publication of the potential utility of emricasan in COVID-19 in *Allergy*, the official Journal of the European Academy of Allergy and Clinical Immunology.

Amerimmune, in collaboration with Dr. Raavi Gupta from SUNY Downstate Medical Center and Dr. Lishomva Ndhlovu from Weill Cornell Medicine, demonstrated the impact of caspases in multiple blood cells beyond the acute stage of the disease. Their research concluded that caspases are elevated in patients with co-morbidities and persisted into much later stages of the disease, also referred to as long COVID. Moreover, the results were not just limited to the elevation of caspase-1 in white blood cells. There was also an elevation of caspase-3 in red blood cells (erythrocytes). These findings have potential implications to understand the pathogenesis of complications of SARS-CoV2 infection such as extensive blood clot formation, resulting in significant morbidity and mortality. The collaborative work of SUNY Downstate and Weill Cornell Medical Center with Amerimmune demonstrated how in certain individuals regarded as "high risk", such as asthma, immune deficiencies and chronic sinopulmonary disease, there is already increased baseline caspase-1 expression, potentially setting the stage for complications if they were to be infected with SARS CoV2. All the assays used in this study were developed and validated by Amerimmune. This study now leads to more research opportunities to explore why some individuals develop worse outcomes, whereas some others remain asymptomatic. Most importantly, the team showed that Emricasan, a pan-caspase inhibitor, can effectively reduce the caspase expression in *in vitro*, paving the way to the use of pan-caspase inhibition as a treatment modality in COVID-19.

"Emricasan is a small molecule pan-caspase inhibitor that is administered orally, which has been shown to reduce caspase related inflammation in tissues. This therapeutic modality could address the events at the onset of the COVID-19 process and may have the potential to prevent the down-stream COVID-19 related complications," said Oral Alpan, MD, CEO of Amerimmune.

"The findings from this important research support the potential of emricasan as a treatment option for COVID-19 in the acute and long-haul phases of the disease," said Richard Pascoe, President and CEO of Histogen. "We look forward to the anticipated completion of our ongoing Phase 1 Study in mild- symptomatic COVID-19 patients at SUNY Downstate Medical Center, in the second quarter of 2021."

The research paper entitled "Caspases in Moderate-Severe, Long COVID-19 Disease and the Therapeutic Potential of Caspase Inhibitors" has been published in *Allergy*, the Journal of the European Academy of Allergy and Clinical Immunology, and is currently available electronically at <https://onlinelibrary.wiley.com/doi/10.1111/all.14907>

About Emricasan

Emricasan is a potential first-in-class, orally active, pan-caspase inhibitor designed to reduce the activity of enzymes that mediate inflammation and apoptosis. Histogen acquired certain rights to emricasan and other caspase inhibitor compounds as a part of its merger with Conatus Pharmaceuticals Inc. in 2020. Histogen believes that by reducing the activity of these enzymes, caspase inhibitors have the potential to interrupt the progression of a variety of diseases. To date, emricasan has been studied in over 950 patients in 19 completed clinical trials across a broad range of liver diseases. In NASH cirrhosis patients in multiple clinical Phase II trials conducted by Conatus, emricasan demonstrated rapid and sustained reductions in elevated levels of key biomarkers of inflammation and cell death. Similarly, elevated biomarkers are also believed to play a role in the severity and progression of COVID-19.

About Histogen Inc.

Histogen Inc. is a clinical-stage therapeutics company focused on developing potential first-in-class restorative therapeutics that ignite the body's natural process to repair and maintain healthy biological function. Histogen's innovative technology platform utilizes cell conditioned media and extracellular matrix materials produced by hypoxia-induced multipotent cells. Histogen's proprietary, reproducible manufacturing process provides targeted solutions across a broad range of therapeutic indications including hair growth, dermal rejuvenation, joint cartilage regeneration and spinal disk repair. For more information, please visit www.histogen.com.

About Amerimmune

Amerimmune LLC is a research center and immunology laboratory with a strong focus on identifying underlying mechanisms of immune disorders. Amerimmune's mission is to bring relevant science, data, and diagnostic and therapeutic solutions to diseases that involve the immune system. Amerimmune LLC is a spinoff of Amerimmune Diagnostics LLC, which is focused on establishing a network of physician-owned immunology labs across the United States. Amerimmune Diagnostics' clinical approach led to the development of the innovative therapeutics' technology upon which Amerimmune was founded. When the COVID-19 pandemic emerged early this year, Amerimmune brought its expertise to bear against this devastating disease. Amerimmune is a privately held development-stage company based in Fairfax, VA. For more information and to explore partnering opportunities, please visit www.amerimmune.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995 and other Federal securities laws. For example, we are using forward-looking statements when we discuss Histogen's future operations

and its ability to successfully initiate and complete clinical trials, obtain clinical trial data and achieve regulatory milestones and related timing, including those related to the completion of the Phase 1 study of emricasan for the treatment of COVID-19 and receipt of top-line data; the nature, strategy and focus of Histogen's business; the sufficiency of Histogen's cash resources and Histogen's ability to achieve value for its stockholders; the sufficiency of Amerimmune's cash resources and its ability to complete the Phase 1 study of emricasan and achieve value for Histogen's stockholders; and the development and commercial potential and potential benefits of any of Histogen's product candidates, such as HST-001, and HST-003, and the Collaborative Development and Commercialization Agreement with Amerimmune and any other collaboration agreements. Histogen may not actually achieve the plans, carry out the intentions or meet the expectations or projections disclosed in the forward-looking statements and you should not place undue reliance on these forward-looking statements. Because such statements deal with future events and are based on Histogen's current expectations, they are subject to various risks and uncertainties and actual results, performance or achievements of Histogen that could differ materially from those described in or implied by the statements in this press release, including: the uncertainties associated with the clinical development and regulatory approval of Histogen's product candidates, including potential delays in the commencement, enrollment and completion of clinical trials and Amerimmune's ability to further develop emricasan for the treatment of COVID-19, including the complexity and length of studies required to commercialize emricasan for COVID-19 and potential delays in the completion of clinical trials, such as the emricasan Phase 1 study for the treatment of COVID-19; Histogen's dependence on its collaboration partner, Amerimmune, to carry out the development of emricasan and the potential for delays in the timing of regulatory approval; competition in the COVID-19 market and other markets in which Histogen and its collaboration partner operate; the potential that earlier clinical trials and studies of Histogen's product candidates may not be predictive of future results; risks related to business interruptions, including the outbreak of COVID-19 coronavirus, which could seriously harm Histogen's financial condition and increase its costs and expenses; and the requirement for additional capital to continue to advance these product candidates, which may not be available on favorable terms or at all. The foregoing review of important factors that could cause actual events to differ from expectations should not be construed as exhaustive and should be read in conjunction with statements that are included herein and elsewhere, including those risks discussed in Histogen's filings with the Securities and Exchange Commission. Except as otherwise required by law, Histogen disclaims any intention or obligation to update or revise any forward-looking statements, which speak only as of the date hereof, whether as a result of new information, future events, or circumstances or otherwise.

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