ZyVersa Therapeutics Announces Peer-Reviewed Publication Demonstrating That Inflammasome ASC Inhibitor IC 100 Protects Against Stroke-Related Cardiovascular Injury and Dysfunction in Preclinical Trial

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- Strokes affect 795,000 people annually in the US. Obesity, a top risk factor for strokes, is associated with around one out of five strokes.
- Cardiac complications following a stroke are a leading cause of mortality and morbidity, second only to acute neurological injury.
- The pathomechanism underlying cardiac dysfunction following a stroke includes a surge of catecholamines, such as epinephrine, which induces inflammasome activation triggering a systemic inflammatory response.
- The published data showed that following a stroke, Inflammasome ASC Inhibitor IC 100 blocked AIM2 inflammasome activation and cell death (pyroptosis) in the heart and improved cardiac function.
- Data from this article support ZyVersa's development of Inflammasome ASC Inhibitor IC 100 for obesity and its associated cardiovascular comorbidities.

WESTON, Fla., Nov. 20, 2024 (GLOBE NEWSWIRE) -- ZyVersa Therapeutics, Inc. (Nasdaq: ZVSA, or "ZyVersa"), a clinical stage specialty biopharmaceutical company developing first-in-class drugs for treatment of inflammatory and renal diseases, announces newly published data demonstrating that stroke-related cardiovascular injury and dysfunction is induced by AIM2 inflammasome activation and pyroptosis in the heart, which can be blocked by Inflammasome ASC Inhibitor IC 100.

"These data demonstrate the potential for IC 100 to attenuate stroke-related cardiovascular disease which is common in patients living with obesity. According to the American Heart Association, obesity-related cardiovascular disease deaths tripled between 1999 and 2020, and this is expected to continue to increase without effective therapeutic options," said Stephen C. Glover, ZyVersa's Co-founder, Chairman, CEO and President. "We are excited about the potential of IC 100 to effectively control the inflammation that drives stroke-related cardiovascular injury and dysfunction. Unlike the NLRP3 inhibitors in development, IC 100 targets ASC to inhibit activation of multiple inflammasomes, including AIM2, which triggered the systemic inflammatory response affecting the heart after stroke in this study. More importantly, IC 100 uniquely disrupts the function of ASC specks to attenuate chronic, systemic inflammation leading to comorbidities. We look forward to progressing IC 100's development program into phase 1 around mid-2025.

This study was published in the peer-reviewed journal, *Translational Stroke Research*, by acclaimed inflammasome researchers from the University of Miami Miller School of Medicine and inventors of IC 100. In the publication titled, Catecholamine-Induced Inflammasome Activation in the Heart Following Photothrombotic Stroke, the researchers report data from studies conducted in a mouse model of photothrombotic stroke (PTS) and in excised zebrafish hearts.

Key Findings

- PTS in mice results in activation of the AIM2 inflammasome in the heart resulting in significant increases in IL-1β and ASC oligomerization into ASC specks contributing to a systemic inflammatory response affecting the heart after stroke.
- Treatment with IC 100 (30 mg/kg) at 30 minutes post-PTS significantly reduced the levels of inflammasome proteins and IL-1β in the heart thus reducing cardiac inflammation.
- Epinephrine-treated zebrafish hearts demonstrated a shortened action potential duration (SAPD) which was attenuated by IC 100. SAPD can cause irregular heart rhythm and reduced cardiac efficiency commonly seen in strokes and heart failure.

"These findings indicate that stroke initiates a catecholamine surge that induces inflammasome activation and pyroptosis in the heart that is blocked by IC 100, thus providing a framework for the development of therapeutics for stroke-related cardiovascular injury," stated author Dr. Robert W. Keane, Professor, Physiology and Biophysics, Neurological Surgery and Microbiology, and Immunology, University of Miami Miller School of Medicine.

About Inflammasome ASC Inhibitor IC 100

IC 100 is a novel humanized IgG4 monoclonal antibody that inhibits the inflammasome adaptor protein ASC. IC 100 was designed to attenuate both initiation and perpetuation of the inflammatory response. It does so by binding to a specific region of the ASC component of multiple types of inflammasomes, including NLRP1, NLRP2, NLRP3, NLRC4, AIM2, and Pyrin. Intracellularly, IC 100 binds to ASC monomers, inhibiting inflammasome formation, thereby blocking activation of IL-1β early in the inflammatory cascade. IC 100 also binds to ASC in ASC Specks, both intracellularly and extracellularly, further blocking activation of IL-1β and the perpetuation of the inflammatory response that is pathogenic in inflammatory diseases.

Because active cytokines amplify adaptive immunity through various mechanisms, IC 100, by attenuating cytokine activation, also attenuates the adaptive immune response. The lead indication for IC 100 is obesity and its associated metabolic complications. To review a white paper summarizing the mechanism of action and preclinical data for IC 100, Click Here.

About ZyVersa Therapeutics, Inc.

ZyVersa (Nasdaq: ZVSA) is a clinical stage specialty biopharmaceutical company leveraging advanced proprietary technologies to develop first-in-class drugs for patients with inflammatory or kidney diseases with high unmet medical needs. We are well positioned in the rapidly emerging inflammasome space with a highly differentiated monoclonal antibody, Inflammasome ASC Inhibitor IC 100, and in kidney disease with phase 2 Cholesterol Efflux Mediator™ VAR 200. The lead indication for IC 100 is obesity and its associated metabolic complications, and for VAR 200, focal segmental glomerulosclerosis (FSGS). Each therapeutic area offers a "pipeline within a product," with potential for numerous indications. The total accessible market is over $100 billion. For more information, please visit www.zyversa.com.

Cautionary Statement Regarding Forward-Looking Statements

Certain statements contained in this press release regarding matters that are not historical facts, are forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and the Private Securities Litigation Reform Act of 1995. These include statements regarding management's intentions, plans, beliefs, expectations, or forecasts for the future, and, therefore, you are cautioned not to place undue reliance on them. No forward-looking statement can be guaranteed, and actual results may differ materially from those projected. ZyVersa Therapeutics, Inc ("ZyVersa") uses words such as "anticipates," "believes," "plans," "expects," "projects," "future," "intends," "may," "will," "should," "could," "estimates," "predicts," "potential," "continue," "guidance," and similar expressions to identify these forward-looking statements that are intended to be covered by the safe-harbor provisions. Such forward-looking statements are based on ZyVersa's expectations and involve risks and uncertainties; consequently, actual results may differ materially from those expressed or implied in the statements due to a number of factors, including ZyVersa's plans to develop and commercialize its product candidates, the timing of initiation of ZyVersa's planned preclinical and clinical trials; the timing of the availability of data from ZyVersa's preclinical and clinical trials; the timing of any planned investigational new drug application or new drug application; ZyVersa's plans to research, develop, and commercialize its current and future product candidates; the clinical utility, potential benefits and market acceptance of ZyVersa's product candidates; ZyVersa's commercialization, marketing and manufacturing capabilities and strategy; ZyVersa's ability to protect its intellectual property position; and ZyVersa's estimates regarding future revenue, expenses, capital requirements and need for additional financing.

New factors emerge from time-to-time, and it is not possible for ZyVersa to predict all such factors, nor can ZyVersa assess the impact of each such factor on the business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements. Forward-looking statements included in this press release are based on information available to ZyVersa as of the date of this press release. ZyVersa disclaims any obligation to update such forward-looking statements to reflect events or circumstances after the date of this press release, except as required by applicable law.

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