ZyVersa Therapeutics Highlights Data Demonstrating NLRP3 Inflammasome Inhibition Reduces Inflammation, Improves Heart Function, and Restores Glucose Homeostasis and Insulin Sensitivity in Obese Animal Model of Heart Failure (HFpEF) and Type 2 Diabetes

Mar 5, 2025

- Heart failure with preserved ejection fraction (HFpEF), a chronic inflammatory condition, is a leading cause of morbidity and mortality globally. Obesity, diabetes, and hypertension are highly prevalent in this population and usually precede HFpEF development.
- Authors of the published data report that the cardioprotective effects and improvements in metabolic parameters with inflammasome inhibition were correlated with reduced inflammation and macrophage activation in both cardiac and visceral adipose tissue.
- These data support the potential of ZyVersa's Inflammasome ASC Inhibitor IC 100 as an effective treatment option for patients with obesity and its associated cardiovascular and metabolic comorbidities.
- By targeting ASC, IC 100 inhibits activation of multiple inflammasome pathways activated in obesity (NLRP3, AIM2), heart failure (AIM2, NLRP3, NLRC4), and insulin resistance (AIM2, NLRP1, NLRP3, NLRC4, NLRP6). Likewise, IC 100 disrupts the function of extracellular ASC specks that perpetuate and spread inflammation to surrounding tissues leading to comorbidities.

WESTON, Fla. , March 05, 2025 (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, highlights newly published data demonstrating cardioprotective effects and improvements in metabolic parameters with inhibition of NLRP3 inflammasome pathways in an obese animal model of heart failure (HFpEF) and type 2 diabetes.

"We are excited about this data which provides further support for our selection of obesity with certain metabolic complications as the lead indication for our Inflammasome ASC Inhibitor IC 100," said Stephen C. Glover, ZyVersa's Co-founder, Chairman, CEO and President. "This comprehensive study is among the first to correlate comorbidity-driven systemic inflammation to heart disease pathogenesis. Consistent with the reported data, IC 100 protected against cardiovascular injury and dysfunction resulting from stroke-induced systemic inflammation that led to cardiac inflammation and dysfunction in a mouse model. Additionally, IC 100 has demonstrated improved insulin sensitivity and reduced fasting blood glucose in an obese mouse model of type 2 diabetic kidney disease. The premise behind development of IC 100 was to uniquely disrupt the function of extracellular ASC specks released from inflamed, injured cells that spread inflammation to surrounding tissues, perpetuating the inflammation leading to comorbidities. Likewise, by targeting ASC, IC 100 inhibits activation of multiple types of inflammasomes that are associated with pathogenesis and progression of most diseases, which we believe will lead to better control of inflammation than targeting just one inflammasome (e.g., NLRP3). We look forward to initiating two IC 100 preclinical studies in diet-induced obesity mouse models in the first half of this year. The first study will compare the effects of IC 100 to semaglutide, and the second will assess the effects of IC 100 administered concurrently with semaglutide."

The new study data were published in the peer-reviewed journal, *Biomedicine & Pharmacotherapy.* In the publication titled The NLRP3-inflammasome inhibitor MCC950 improves cardiac function in a HFpEF mouse model, the researchers report data from studies conducted in a mouse model that develops HFpEF and comorbidities including obesity, type 2 diabetes, and hypertension.

Key Findings

Inhibition of Inflammasome NLRP3 pathways:

- Attenuated circulating levels of pro-inflammatory cytokine, IL-18, and lowered macrophage infiltration into the heart leading to a substantial reduction in cardiac inflammation.
- Reduced cardiac hypertrophy and fibrosis, and improved cardiac diastolic function.
- Reduced fat mass, adipocyte size, and macrophage infiltration into visceral adipose tissue associated with obesity and metabolic disease.
- Improved glucose homeostasis and insulin sensitivity.

The authors concluded, "Overall, this suggests that NLRP3 inhibition could be a promising treatment for HFpEF patients with a pro-inflammatory profile, potentially improving heart function, systemic inflammation, and metabolic parameters."

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 with certain 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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