ZyVersa Therapeutics Highlights Data Published in the Journal of the American Heart Association Demonstrating Inflammasome Inhibition Attenuates Obesity-Associated Cardiomyopathy in Animal Model Study

Mar 18, 2025

- In obesity-associated cardiomyopathy (OAC), heart muscle is structurally and functionally abnormal, impairing the ability to effectively pump blood. Five-year survival rate is less than 50%, with congestive heart failure and sudden cardiac death predominant causes of death.
- Data showed that NLRP3 inflammasome inhibition attenuated inflammation, heart muscle enlargement and fibrosis, and improved heart function.
- 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 comorbidities.

WESTON, Fla., March 18, 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 animal model data demonstrating that inflammasome inhibition attenuates obesity-associated cardiomyopathy, which has a 5-year survival rate <50%.

"These data contribute to a growing body of scientific evidence that obesity-related heart disease can be attenuated with inflammasome inhibition, providing support for ZyVersa's Inflammasome ASC Inhibitor IC 100 as a potential therapeutic option for this obesity-related metabolic comorbidity," said Stephen C. Glover, ZyVersa's Co-founder, Chairman, CEO and President. "Various cardiovascular diseases are associated with activation of multiple inflammasomes (NLRP1, NLRP3, NLRC4, and AIM2). IC 100, which targets the ASC component of inflammasomes, inhibits all four of these inflammasomes, which we believe will lead to better control of inflammation than targeting just the NLRP3 inflammasome. Likewise, IC 100 inhibits the function of ASC Specks released from inflamed, injured cells that spread inflammation to surrounding tissues leading to development and progression of comorbidities, such as heart disease."

The article published in the peer-reviewed *Journal of the American Heart Association* was titled Impeding Nucleotide-Binding Oligomerization Domain-Like Receptor 3 Inflammasome Ameliorates Cardiac Remodeling and Dysfunction in Obesity-Associated Cardiomyopathy. The researchers report data from studies conducted in a diet-induced obesity cardiomyopathy mouse model.

Key Findings

NLRP3 Inflammasome Inhibition:

- Reduced body weight and fasting blood glucose in obese mice after 24 weeks on a high fat diet.
- Reduced cardiac inflammation.
- Prevented myocardial hypertrophy (enlarged heart muscle), fibrosis, and cardiac dysfunction (both systolic and diastolic), restoring maximal oxygen consumption rate.
- Attenuated cardiac lipid accumulation that promotes progression of obesity-induced heart failure.

The authors concluded, "Our study confirms that aberrant NLRP3 inflammasome activation in cardiomyocytes worsens obesity-associated cardiomyopathy and implicates inhibition of NLRP3 inflammasome as a potent therapeutic approach for obesity cardiomyopathy."

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.

This press release does not constitute an offer to sell, or the solicitation of an offer to buy, any securities.

Corporate, Media, and IR Contact:

Karen Cashmere
Chief Commercial Officer
kcashmere@zyversa.com
786-251-9641