ZyVersa Therapeutics Highlights Published Data Demonstrating NLRP3 Inflammasome Inhibition Has Potential to Decrease Atherosclerotic Lesions in Patients with Diabetes

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- *Atherosclerosis (AS) and its sequelae are the most common cause of death in diabetic patients and one of the reasons why diabetes has entered the top 10 causes of death worldwide.*
- *The published data show that inhibiting the NLRP3 inflammasome pathway significantly reduces atherosclerotic lesions and improves hyperglycemic-induced plaque instability.*
- *ZyVersa is developing IC 100, a monoclonal antibody targeting inflammasome ASC and ASC specks from multiple types of inflammasomes, including NLRP3, to block initiation and perpetuation of damaging inflammation that promotes atherosclerosis and its progression, among numerous other inflammatory diseases.*

WESTON, Fla., April 04, 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, highlights data from a peer-reviewed article published in *Biochemical and Biophysical Research Communications*. This article demonstrates that NLRP3 inhibition results in improved glucose tolerance and markedly smaller and more stable atherosclerotic lesions in a diabetic mouse model.

In the paper titled, "High glucose levels accelerate atherosclerosis via NLRP3-IL/ MAPK/ NF-κB-related inflammation pathways," the authors evaluated serum and coronary artery tissues from patients with coronary artery disease (CAD), with and without diabetes and they conducted a study in diabetic mouse models. Key findings include:

- Patients with comorbid CAD and diabetes had higher serum levels and expression of NLRP3 in their coronary arteries, and increased serum levels of IL-1β and IL-6 than those with CAD only.
- Diabetic mouse models showed a significantly higher atherosclerotic plaque/vessel area ratio than non-diabetic mice, which was markedly reduced with NLRP3 inhibition and the resulting reduction in levels of proinflammatory cytokines and inflammation.

The authors concluded, "Our research offers new understanding of the pathological mechanisms of diabetes-accelerated AS and provide a novel and promising target for treating diabetes-accelerated AS." To review the publication, Click Here.

"We are excited about the data published in *Biochemical and Biophysical Research Communications* demonstrating that inhibiting inflammasome NLPR3 pathways has potential to attenuate the development and progression of AS in patients with diabetes, a leading cause of morbidity and mortality," commented Stephen C. Glover, ZyVersa's Co-founder, Chairman, CEO, and President. "We look forward to seeing our preclinical data with Inflammasome ASC Inhibitor IC 100 in an animal model of atherosclerosis in the first half of this year. We believe that by inhibiting multiple types of inflammasomes and disrupting the structure and function of their associated ASC specks to attenuate initiation and perpetuation of inflammation, that IC 100 has promise to effectively control AS development and progression." To review a white paper summarizing the mechanism of action and preclinical data for IC 100, Click Here.

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.

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 renal and inflammatory diseases who have significant unmet medical needs. The Company is currently advancing a therapeutic development pipeline with multiple programs built around its two proprietary technologies – Cholesterol Efflux Mediator™ VAR 200 for treatment of kidney diseases, and Inflammasome ASC Inhibitor IC 100, targeting damaging inflammation associated with numerous CNS and other inflammatory diseases. 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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