ZyVersa Therapeutics Announces a Publication in Journal of the American Heart Association Linking NLRP3 Inflammasomes with Calcification in Arteries of Patients with Peripheral Arterial Disease (PAD)

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- *PAD, characterized by vascular inflammation and associated calcification, affects 8.5 million people in the United States and contributes to more than 50,000 limb amputations annually, yet there are no specific pharmacologic treatments*
- ZyVersa is developing Inflammasome ASC Inhibitor IC 100 for numerous inflammatory diseases

WESTON, Fla., June 20, 2023 (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 publication of an article in the peer-reviewed *Journal of the American Heart Association* addressing the role of NLRP3 inflammasomes in PAD. ZyVersa's Inflammasome ASC Inhibitor IC 100 inhibits the inflammasome adaptor protein ASC, a component of multiple types of inflammasomes including NLRP3 inflammasomes.

In the paper titled, "NLRP3 Inflammasome Activation in Peripheral Arterial Disease," the authors evaluated human peripheral arteries from patients undergoing limb amputation and serum collected prior to surgery. Data demonstrated an association between NLRP3, macrophage accumulation, and calcification in arteries of patients with PAD, suggesting that NLRP3 inflammasome activation may be a driver of the disease. Following are key findings reported in the paper:

- NLRP3 protein was significantly increased in vessels from patients with PAD compared with control vessels, and it was present in macrophages in the vicinity of calcification, along with IL-1β and caspase-1
- Likewise, serum NRLP3 protein levels and IL-1β were significantly increased in PAD patients compared to controls, suggesting activation of NLRP3 Inflammasomes both locally and systemically

The authors stated, "Given that PAD is associated with increased risk of cardiac comorbidity and cardiac and cerebrovascular ischemic events, further studies are now needed to determine the clinical implication of pharmacologically reducing vascular inflammation in this cohort before surgical intervention. Inhibition of the NLRP3 inflammasome activation or downstream signaling cascade may be beneficial to the reduction of inflammatory-driven PAD." To read the article, Click Here.

"The research published in the *Journal of the American Heart Association* demonstrating that NLRP3 inflammasome activation is associated with calcification in arteries of patients with PAD, along with research referenced by the authors on the potential role of NLRP1 activation in PAD, provides support for inhibiting multiple types of inflammasomes by targeting inflammasome ASC, the mechanism of action of IC 100." commented Stephen C. Glover, ZyVersa's Co-founder, Chairman, CEO and President. 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, 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.

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

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