ZyVersa Therapeutics Announces Publication in the Journal Circulation That Demonstrates the Role of Inflammasome Activation in Hypertrophic Heart Disease Induced by Mechanical Stress

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- *Mechanical stress on the heart, such as high blood pressure, initiates NLRP3-induced inflammation through heart-brain interactions, causing heart enlargement (hypertrophic heart disease)*
- Mechanical stress on the heart triggers neural signals that contribute to NLRP3 inflammasome activation and subsequent release of IL-1β to initiate inflammation in the stressed heart
- ZyVersa is developing Inflammasome ASC Inhibitor IC 100, which can inhibit up to 12 different inflammasomes (including NLRP3 inflammasomes) and their associated ASC specks which perpetuate damaging inflammation

WESTON, Fla., July 10, 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 *Circulation* demonstrating the role of inflammasome NLRP3 activation in hypertrophic heart disease induced by mechanical stress.

In the paper titled, "NLRP3 Inflammasome Activation Through Heart-Brain Interaction Initiates Cardiac Inflammation and Hypertrophy During Pressure Overload," data are reported from *in vivo* studies in various animal models, and *in vitro* experiments using primary rat neonate cardiomyocytes and fibroblasts, and a human microvascular endothelial cell line. The objective was to determine the regulatory mechanism of inflammation and its role in the stressed heart. Key findings are as follows:

- Neural signals contribute to NLRP3 inflammasome activation in cardiac nonimmune cells that initiate inflammation in the stressed heart through IL-1β production
- Pressure overload to the heart's left ventricle activates sympathetic efferent nerves (SENs) to secrete extracellular ATP, which activates NLRP3 inflammasomes in cardiomyocytes, fibroblasts, and vascular endothelial cells, leading to L-1β production and initiation of the inflammatory cascade that causes cardiac adaptive hypertrophy in response to mechanical stress
- Cardiac afferent nerve signals also contribute to ATP secretion from SEN terminals and inflammasome activation
- The above findings reveal that cardiac inflammation and hypertrophy are controlled through NLRP3 activation through heart-brain interactions

To read the article, Click Here.

"The research published in *Circulation* demonstrating that mechanical stress on the heart, such as high blood pressure, initiates NLRP3-induced inflammation through heart-brain interactions causing hypertrophic heart disease, provides support for Inflammasome ASC Inhibitor IC 100 as a potential therapeutic candidate for a condition that affects approximately 1 in 500 people. Hypertrophic heart disease puts people at greater risk of heart failure, stroke, and cardiac arrhythmias, including sudden cardiac death. Our preclinical data demonstrate that IC 100 has broad penetration, including the heart and central nervous system, where it can inhibit formation of NLRP3 and other types of inflammasomes to block initiation of the inflammatory cascade. Likewise, IC 100 uniquely inhibits ASC specks to block perpetuation of damaging inflammation," 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.

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