ZyVersa Therapeutics Announces New Peer-Reviewed Publication Reinforcing the Rationale for Inhibiting ASC Specks with IC 100 to Attenuate Spread of Inflammation into Surrounding Tissues

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- The paper, published in *Pharmaceuticals*, demonstrates that pyrin inflammasome-mediated inflammation induced by traumatic brain injury (TBI) contributes to cardiovascular co-morbidities through systemic release of proinflammatory mediators that activate AIM2 inflammasomes in the heart leading to damaging inflammation.
- Marks the third publication in 2023 supporting the potential need to attenuate the spread of inflammation to surrounding tissues to minimize the potential for co-morbidities in certain diseases.
- ZyVersa is developing Inflammasome ASC Inhibitor IC 100 to inhibit multiple types of inflammasomes and their associated ASC specks that trigger damaging inflammation and its spread to surrounding tissues.

WESTON, Fla., Oct. 04, 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 that world renowned inflammasome researchers from the University of Miami Miller School of Medicine and inventors of Inflammasome ASC Inhibitor IC 100 have published a scientific paper in the peer-reviewed journal, *Pharmaceuticals,* highlighting how inflammation in the brain mediated by traumatic injury can trigger inflammation in the heart.

In the paper titled, "Neural–Cardiac Inflammasome Axis after Traumatic Brain Injury," the authors conducted a study in animal models of TBI and evaluated serum from patients following TBI and from healthy controls. Data indicate that pyrin inflammasome-mediated inflammation induced by TBI contributes to cardiovascular co-morbidities through systemic release of proinflammatory mediators that activate AIM2 inflammasomes in the heart leading to damaging inflammation. The role of inflammasome activation in the development of TBI-induced cardiovascular co-morbidities was substantiated by increased ASC speck formation in the brains and hearts of TBI mouse models.

"A heightened systemic inflammatory response is often induced after TBI, but the underlying pathomechanisms that contribute to co-morbidities remain poorly understood. Here, we investigated whether extracellular vesicles (EVs) containing inflammasome proteins are released after severe controlled cortical impact in C57BL/6 mice and cause activation of inflammasomes in the heart that result in tissue damage," said Dr. Robert W. Keane, Professor, Physiology and Biophysics, Neurological Surgery and Microbiology, and Immunology, University of Miami Miller School of Medicine. "TBI resulted in the release of EVs into the serum, which contain a cargo of inflammasome-, complement- and cardiovascular-related signaling proteins, and adoptive transfer of EVs from TBI patients resulted in inflammasome activation in cardiovascular cells."

"Importantly, here, we also found an increase in ASC specks in the brain and the heart of TBI mice, suggesting that these prion-like ASC structures play a significant role in the inflammatory pathogenesis observed after TBI in the brain and systemically. Moreover, this finding emphasizes the potential benefit of therapies targeting ASC specks after CNS injury," stated Dr. Juan Pablo de Rivero Vaccari, Associate Professor, Department of Neurological Surgery, University of Miami Miller School of Medicine. To review the paper, Click Here.

"This research published in the Journal, *Pharmaceuticals*, along with recent research published in the Journal of Clinical Investigation and Translational Research reinforces the importance of attenuating extracellular propagation of IL-1β to minimize induction and perpetuation of inflammation in surrounding tissues and organs," commented Stephen C. Glover, ZyVersa's Co-founder, Chairman, CEO, and President. "ZyVersa's Inflammasome ASC inhibitor IC 100 is designed to inhibit formation of multiple types of inflammasomes to attenuate initiation of the inflammatory cascade, and to inhibit their associated ASC specks to reduce perpetuation of damaging inflammation."

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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