ZyVersa Therapeutics Announces Publication Reinforcing the Rationale for Inhibiting ASC with IC 100 to Potentially Attenuate Cardiac Comorbidities in Patients with Alzheimer's Disease

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- This publication, authored by leading experts in inflammasome-mediated inflammation and neurology at University of Miami Miller School of Medicine, demonstrates that multiple inflammasome triggers (NLRP1 and pyrin) govern the inflammatory response in Alzheimer's Disease (AD), and that release of inflammasome laden extracellular vesicles (EV) into the blood induce significant inflammation in cardiovascular cells.
- ZyVersa is developing Inflammasome ASC Inhibitor IC 100 to inhibit multiple types of inflammasomes, including NLRP1 and pyrin, and their associated ASC specks that trigger damaging inflammation and its spread to surrounding tissues.
- AD, a progressive neurodegenerative disease affecting 6.7 million people in the US, is associated with many comorbidities, especially heart disease and stroke, resulting in increased morbidity and mortality.

WESTON, Fla., April 29, 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, announces that acclaimed 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, *Frontiers in Molecular Neuroscience,* highlighting how inflammasome-mediated inflammation in Alzheimer's disease can trigger inflammation in the heart.

The paper titled, "*Extracellular vesicles mediate inflammasome signaling in the brain and heart of Alzheimer's disease mice* ," summarizes research evaluating serum and tissue cultures from an AD mouse model, and experiments of adoptive transfer of EV from AD patients into cardiovascular cells. Following is a summary of key findings:

- NLRP1, pyrin, caspase-1, and ASC were significantly elevated in the cortex of AD mice.
- In AD mice, there was a heightened level of inflammatory proteins circulating in the body via EVs containing an inflammasome protein cargo.
- Inflammasome activation was demonstrated in the heart of AD mice, associated with an increase in ASC oligomerization into specks.
- In adoptive transfer experiments, EVs released from AD patients induced significant inflammation in cardiovascular cells when compared to EVs from healthy individuals.

"Our data provide evidence that there is a neural-cardiac axis mediated by EVs in AD. Therefore, inflammasomes may provide a novel therapeutic target for the treatment of cardiac comorbidities in AD and beyond," said Juan Pablo de Rivero Vaccari, Associated Professor of Neurological Surgery and The Miami Project to Cure Paralysis at the University of Miami.

"This research reinforces the importance of attenuating activation of multiple types of inflammasomes that govern the inflammatory response in AD and mediating systemic inflammatory signals in EVs to control the spread of damaging inflammation to cardiovascular and other cells," 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 spread and 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, 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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Corporate, Media, and IR Contact:
Karen Cashmere
Chief Commercial Officer
kcashmere@zyversa.com
786-251-9641