ZyVersa Therapeutics Highlights Peer-Reviewed Article Linking Inflammasome Activation to Triple-Negative Breast Cancer Brain Metastasis

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- *Up to 40% of women with triple negative breast cancer (TNBC) experience metastasis to their brain, which affects physical function, independence, personality, quality of life, and significantly increases mortality rates.*
- *Published data demonstrate that inflammasome activation increases proliferation of TNBC cells in the brain, which was prevented by inhibition of NLRP3 inflammasomes in both mouse and human models.*
- *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., Jan. 17, 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 publication of an article in the peer-reviewed journal, *Acta Neuropathologica Communications,* demonstrating that inflammasome activation enhances cancer metastasis to the brain in women with TNBC.

In the paper titled, "Inflammasome activation in peritumoral astrocytes is a key player in breast cancer brain metastasis development," the authors evaluated *in vivo* and *in vitro* brain metastasis models, as well as human cultures of astrocytes and TNBC cells. Key findings are as follows:

- Activation of the NLRP3 inflammasome results in excretion of IL-1β in the tumor environment, enhancing proliferation of metastatic cells in the brain.
- Expression of IL-1β correlates with the size of metastatic lesions, being absent in tumor-free brain areas and more intense in the vicinity of large tumors in comparison to smaller ones.
- Inhibition of NLRP3 activation prevented proliferation of TNBC cells in both mouse and human models.

The authors stated, "We are the first to show that peritumoral reactive astrocytes promote the proliferation of TNBC cells in the brain through NLRP3 inflammasome-dependent secretion of IL-1β. Brain metastases are among the most aggressive and the least curable malignant tumors; therefore, we need novel therapies targeting mechanisms that contribute to the proliferation of metastatic cells in the brain." They concluded, "We suggest that inflammasome inhibition might become a therapeutic option in this currently incurable disease."

To read the article, click here.

"The research published in *Acta Neuropathologica Communications* linking inflammasome activation in patients with triple-negative breast cancer to brain metastasis supports a growing body of evidence about the role of dysregulated inflammasome pathways in a broad range of devastating diseases," commented Stephen C. Glover, ZyVersa's Co-founder, Chairman, CEO, and President. "We are excited about the potential to transform the treatment of a multitude of inflammatory diseases with drugs like Inflammasome ASC Inhibitor IC 100. IC 100 uniquely inhibits inflammasome ASC and ASC specks to block initiation 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, 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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