ZyVersa Therapeutics Announces Article Published in Biomaterials Addressing the Critical Role of Inflammasome Activation in Neuroinflammation Resulting from Intracortical Implants

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- *Deep brain stimulation devices are intracortical implants used to treat disabling symptoms of neurological conditions such as Parkinson's disease, epilepsy, essential tremor, and dystonia*
  - *Microelectrodes ("ME") are implanted in the brain and connected to a pulse generator that delivers electrical stimulation to block abnormal nerve signals in areas in the brain that control movement*
- *Data demonstrate that continuous activation of multiple types of inflammasome at the ME-tissue interface result in persistent neuroinflammation that could potentially lead to device failure and neuronal cell loss*

WESTON, Fla., April 19, 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, is pleased to announce that world renowned inflammasome researchers and inventors of ZyVersa's Inflammasome ASC Inhibitor IC 100 from the University of Miami Miller School of Medicine have published a scientific paper in the peer-reviewed journal*, Biomaterials*.

In the paper titled, "Activation of inflammasomes and their effects on neuroinflammation at the microelectrode-tissue interface in intracortical implants," the researchers reported:

- Glial cell activation was demonstrated at the site of ME implant
- Multiple types of inflammasome sensor molecules (NLRP1, NLRP3, AIM2, and NLRC4) were upregulated following ME implant injury
- NLRP1 and NLRP3, which were upregulated by 48 hours and remained distinctly elevated at 4 weeks, play a vital role in activation of inflammasome complexes during acute and sub-chronic periods following ME-induced injury
- In addition to sensor molecules, ASC and Caspase-1 were persistently elevated throughout the implant duration
- IL-1β and IL-18 expression was upregulated soon after ME implantation and remained elevated
- Sustained presence of gasdermin D provides evidence of elevated pyroptosis ("cell death") occurring at the injury site, which coincided with a decrease in neuronal density

"Deep brain stimulation is an important therapeutic option to help maintain quality of life in patients with movement disorders whose symptoms are not effectively controlled by medication," stated Dr. Abhishek Prasad, Associate Professor, the Department of Biomedical Engineering at the University of Miami Miller School of Medicine. "Our results not only demonstrate that continuous activation of inflammasomes contribute to neuroinflammation at the ME-tissue interface, but also reveal the therapeutic potential of targeting inflammasomes to attenuate the foreign body response to cortical implants."

"The research published in *Biomaterials* provides additional support for the therapeutic potential of ZyVersa's proprietary monoclonal antibody inflammasome ASC inhibitor, IC 100, in neurological injury and disease," indicated Stephen C. Glover, ZyVersa's Co-founder, Chairman, CEO and President. "Preclinical studies have demonstrated reduced inflammatory activity and/or improved outcomes in two different models of brain injury, spinal cord injury, age-related inflammation Alzheimer's disease, and multiple sclerosis."

To review the publication, 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 attenuates 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 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

developed to ameliorate renal lipid accumulation that damages the kidneys' filtration system in patients with glomerular 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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