ZyVersa Therapeutics Announces New Publication in Translational Research Showing IC 100 Reduces Inflammasome Activation in Mouse Model for Alzheimer's Disease Following Traumatic Brain Injury

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- *Data published in Translational Research indicate that pyroptotic release of cytokines and ASC Specks from traumatic brain injury (TBI) induces a heightened inflammasome response in Alzheimer's disease (AD), causing worsened cognitive outcomes*
- *Individuals with a history of moderate TBI have a 2.3 times greater risk of developing AD, according to the CDC*

WESTON, Fla., Feb. 23, 2023 (GLOBE NEWSWIRE) -- ZyVersa Therapeutics, Inc. (Nasdaq: ZVSA, or "ZyVersa"), a clinical stage specialty biopharmaceutical company developing first-in-class drugs for treatment of underserved patients with inflammatory and renal diseases, is pleased to announce that world renowned inflammasome researchers from the University of Miami Miller School of Medicine have published a scientific paper in the peer-reviewed journal, *Translational Research.* The article demonstrates that inflammasome activation and pyroptotic release of active cytokines and ASC specks following TBI is synergistic with inflammasome activation that occurs in AD, heightening the inflammatory response and worsening cognitive outcomes. Furthermore, it shows that IC 100, an inflammasome ASC inhibitor, reduces inflammasome activation that triggers the inflammatory response. Click Here to read the article.

"Importantly, we were able to connect TBI-induced inflammasome activation mechanistically to the exacerbated response in AD commonly observed following head injury," stated Dr. W. Dalton Dietrich, III, Professor, Neurological Surgery, Neurology, Biomedical Engineering, and Cell Biology at the University of Miami Miller School of Medicine. "We evaluated if blocking inflammasome activity by inhibiting ASC reduces the elevated inflammatory response in AD mice after TBI. Administration of IC 100 resulted in reduction of the inflammasome-mediated cytokine IL-1β in the injured cortex of AD mice at 1-week post-injury. Considering that the primary injury phase of TBI is traditionally seen during the first week post-injury, this finding demonstrates a reduction in TBI-induced neuroinflammation," continued Dr. Dietrich.

"Inflammasome ASC represents a promising therapeutic target for TBI and AD because of its unique role in heightening and perpetuating inflammation in neighboring cells, as well as its pathological interactions with amyloid beta and phosphorylated tau," said Dr. Juan Pablo de Rivero Vaccari, Associate Professor, Department of Neurological Surgery and The Miami Project to Cure Paralysis, University of Miami Miller School of Medicine, and Distinguished Faculty Member of The Center for Cognitive Neuroscience and Aging, University of Miami Miller School of Medicine.

This data reinforces conclusions from a review article published in *Translational Research* in September 2022. The review article concluded that TBI and AD are linked by activation of multiple types of inflammasomes (NLRP3, NLRP1, and AIM2), leading to chronic inflammation, structural damage, neuronal loss, and behavioral abnormalities. Click Here to read the article.

"The two publications in *Translational Research* support the potential of ZyVersa's proprietary monoclonal antibody inflammasome ASC inhibitor IC 100 in neurological disorders," stated Stephen Glover, Co-founder, Chairman, CEO, and President of ZyVersa Therapeutics. "TBI and Alzheimer's disease are two major causes of death and disability in the United States, and individuals with a history of moderate TBI have a substantially greater risk of developing AD," Mr. Glover said.

About 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, 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 is a clinical stage specialty biopharmaceutical company leveraging advanced, proprietary technologies to develop first-in-class drugs. Our focus is on patients with inflammatory or renal diseases who have significant unmet medical needs. Our development pipeline includes a novel inflammasome ASC inhibitor with potential to treat multiple CNS and other inflammatory diseases. It also includes a phase 2a-ready Cholesterol Efflux Mediator™ VAR 200, for treatment of rare kidney disease, focal segmental glomerulosclerosis (FSGS). VAR 200 has potential to treat other kidney diseases, such as Alport Syndrome and Diabetic Kidney Disease. 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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