ZyVersa Therapeutics Announces Publication of an Article in the Journal of Neuroinflammation Addressing the Role of ASC Specks in Propagation of Alpha-Synuclein Pathology in Parkinson's Disease

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- *Parkinson's disease ("PD"), the second leading cause of neurodegeneration in the world, is characterized by progressive degeneration of nigrostriatal dopaminergic neurons and intracellular accumulation of aggregates containing misfolded fibrillar alpha-synuclein ("α-synuclein") in the remaining neurons*
- The authors observed a direct relationship between levels of ASC protein and misfolded α-synuclein aggregates in PD mice brains, and concluded that ASC specks contribute to the propagation of inflammasome-associated α-synuclein pathology in PD, which forms the basis for targeting ASC as a potential therapy for PD

WESTON, Fla., April 25, 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 publication of an article in the peer-reviewed *Journal of Neuroinflammation* supporting the potential of ASC specks as a therapeutic target for Parkinson's disease.

In the paper titled, "ASC specks exacerbate α-synuclein pathology via amplifying NLRP3 inflammasome activities," the authors reported data on the interplay between ASC speck formation, NLRP3 inflammasome activation, and pathological progression in a PD model (induced by human A53T mutant α-synuclein preformed fibrils, "PFFs"). Following is a summary of key findings:

- There was a direct relationship between α-synuclein pathology and ASC expression
- ASC specks enhanced NLRP3 inflammasome activation and reactive microgliosis
- ASC specks accelerated dopaminergic neuron degeneration and dyskinesia (uncontrolled, involuntary movement)
- Knockdown of endogenous ASC markedly suppressed microglial inflammasome activation and neuronal α-synuclein aggregation under the challenge of PFFs

The authors stated, "There is a clear association between ASC specks assembly, NLRP3 inflammasome activation, and PD pathological progression, especially with regards to α-synuclein accumulation. These findings imply that targeting ASC is a promising therapeutic approach for PD." To read the article Click Here.

Stephen C. Glover, ZyVersa's Co-founder, Chairman, CEO and President, stated: "The research on the role of ASC Specks in propagation of alpha-synuclein pathology in Parkinson's disease published in the *Journal of Neuroinflammation* provides additional support for the therapeutic potential of ZyVersa's proprietary monoclonal antibody Inflammasome ASC Inhibitor IC 100, in neurological diseases. IC 100 preclinical studies demonstrate reduced inflammatory activity and/or improved outcomes in, age-related inflammation, Alzheimer's disease, multiple sclerosis, spinal cord injury, and two different models of brain injury."

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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