ZyVersa Therapeutics Announces Review Article Published in Frontiers in Pharmacology Addressing Microglial Inflammatory Activity as a Pharmacological Target in Mild Cognitive Impairment and Alzheimer's Disease

April 13, 2023

- *During aging, the central nervous system ("CNS") becomes more inflammatory, leading to activation of microglia ("CNS immune cells"), tissue damage, dysfunction, and senescence*
- *The article reviews microglial pathways, including the NLRP3 inflammasome pathway, which are promising drug targets for potential treatment of Alzheimer's disease ("AD") and slowing of cognitive aging*

WESTON, Fla., April 13, 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 a review article in *Frontiers in Pharmacology* addressing the NLRP3 inflammasome pathway as a potential drug target for treating mild cognitive impairment ("MCI") and AD.

In the paper titled, "Microglia: A pharmacological target for the treatment of age-related cognitive decline and Alzheimer's disease," the authors reviewed data associated with microglial pathways that have potential as drug targets for treatment of MCI and AD. Reported data supporting the NLRP3 inflammasome pathway as a drug target are summarized below:

- IL-1β, which is considered toxic to microglia by triggering increased oxidative stress and apoptosis ("cell death"), is elevated in cerebrospinal fluid and brains of patients with AD
- IC 100, an anti-ASC antibody which permeates the blood-brain-barrier and binds to ASC filaments, blocks IL-1β production in human whole blood cell assays
- Inflammasome ASC, which is produced by microglia, binds to amyloid beta ("Aβ") and aids in formation of Aβ oligomers - administration of an anti-ASC antibody in an AD mouse model prevented Aβ from accumulating
- AD mouse models deficient in NLRP3 or caspase-1 demonstrate reduced activation of IL-1β and reduced spatial memory loss
- Administration of a caspase-1 inhibitor in a mouse model of "Aβ" pathology reversed impairment of episodic and spatial memory, while preventing brain inflammation and Aβ build up
- Administration of a compound that inhibits NLRP3 assembly, reduced levels of IL-1β and Aβ which were associated with improved working and recognition memory in an AD mouse model; this compound administered to a Tau-P301S mouse model of AD prevented Tau pathology

The authors stated, "thus far, animal models testing NLRP3 pathway inhibitors suggest that such treatments may have pharmacologic relevance in reducing cognitive aging and AD pathology within patients." To read the article Click Here.

"There is a tremendous unmet need to identify effective therapies to treat the growing number of people with cognitive impairment and Alzheimer's disease, a leading cause of disability and death in the world," stated Stephen C. Glover, ZyVersa's Co-founder, Chairman, CEO, and President. "It is encouraging to see the extensive research underway to identify potential drug targets. We are proud of the original scientific contributions in this area by the inventors of ZyVersa's Inflammasome ASC Inhibitor IC 100, Drs. Robert W. Keane and Juan Pablo de Rivero Vaccari at the University of Miami Miller School of Medicine." To review their latest publication on Alzheimer's disease, 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.

This press release does not constitute an offer to sell, or the solicitation of an offer to buy, any securities.

Corporate and IR Contact:
Karen Cashmere
Chief Commercial Officer
kcashmere@zyversa.com
786-251-9641

Media Contacts
Tiberend Strategic Advisors, Inc.
Casey McDonald
cmcdonald@tiberend.com
646-577-8520

Dave Schemelia
dschemelia@tiberend.com
609-468-9325