ZyVersa Therapeutics Announces Published Data Demonstrating That Plasma Levels of Inflammasome ASC Show Promise as Biomarker of Early Cognitive Changes in Older Adults

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- This data supports the potential of plasma ASC levels as a biomarker for early stages of cognitive decline, based on elevated ASC levels in older adults (>60 years) who were cognitively normal at baseline but demonstrated cognitive decline one year later (N_I) compared to ASC levels in those who:
    1. Were cognitively normal at both baseline and 1 year later (N_N), and
    2. Were cognitively impaired at both baseline and one year later (I_I)
- Inflammasome-induced neuroinflammation has been associated with early stages of cognitive decline in dementia associated with Alzheimer's and Parkinson's diseases.
- Excessive inflammasome activation leads to cell death (pyroptosis) and systemic release of cell contents, including ASC that can be measured in the plasma.

WESTON, Fla., July 29, 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 that leading inflammasome researchers from the University of Miami Miller School of Medicine and inventors of Inflammasome ASC Inhibitor IC 100 have published a scientific paper in the peer-reviewed *International Journal of Molecular Sciences* demonstrating that plasma levels of inflammasome ASC show promise as a biomarker of early cognitive decline in older adults.

"Elevations in plasma ASC in early cognitive decline reinforce the role of inflammasome-induced inflammation in the development of neurodegenerative conditions such as Alzheimer's and Parkinson's diseases," stated Stephen C. Glover, ZyVersa's Co-founder, Chairman, CEO, and President. "ZyVersa is developing Inflammasome ASC Inhibitor IC 100 to inhibit multiple types of inflammasomes and their associated ASC specks that trigger damaging inflammation pathogenic in neurological and other inflammatory diseases, such as obesity and its metabolic complications, our lead indication."

The paper titled, The Inflammasome Adaptor Protein ASC in Plasma as a Biomarker of Early Cognitive Changes, summarizes biomarker assessments in older adults at baseline and at one-year follow-up. Following is a summary of key findings:

- Plasma ASC levels were elevated in older adults (>60 years) who were cognitively normal at baseline but demonstrated cognitive decline one year later (N_I) compared to ASC levels in those who remained cognitively normal one-year post-baseline assessment (N_N). The increase in ASC levels was even higher in people who were 70 years or older.
- Likewise, plasma ASC levels in the N_I group were elevated compared to ASC levels in older adults who demonstrated cognitive impairment at both baseline and one year later (I_I), indicating that plasma ASC levels are increased in the early stages of cognitive decline. Again, the increase in ASC levels was even higher in people who were 70 years or older.
- In the group over 70 years old, area under the curve (AUC) for plasma levels of ASC in group N_I versus group N_N was 0.81, indicating excellent ability to differentiate between people with cognitive decline at one year versus those who were cognitively normal both at baseline and at one year. AUC is used to determine the diagnostic power of a biomarker.

"Dementia affects 57 million people worldwide, and the incidence is expected to double by 2040. There is an unmet need to develop minimally invasive, reliable biomarkers to diagnose early brain impairments so that emerging interventions can be applied before brain degeneration," said Dr. Juan Pablo de Rivero Vaccari, Associate Professor of Neurological Surgery and The Miami Project to Cure Paralysis and Distinguished Faculty of the Center for Cognitive Neuroscience and Aging at the University of Miami Miller School of Medicine. "Our data indicate that plasma levels of ASC are a strong early indicator of the eventual development of cognitive impairment, especially in persons older than 70 years."

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, 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 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. The lead indication for IC 100 is obesity and its associated metabolic complications. To review a white paper summarizing the mechanism of action and preclinical data for IC 100, Click Here.

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 inflammatory or kidney diseases with high unmet medical needs. We are well positioned in the rapidly emerging inflammasome space with a highly differentiated monoclonal antibody, Inflammasome ASC Inhibitor IC 100, and in kidney disease with phase 2 Cholesterol Efflux Mediator™ VAR 200. The lead indication for IC 100 is obesity and its associated metabolic complications, and for VAR 200, focal segmental glomerulosclerosis (FSGS). Each therapeutic area offers a "pipeline within a product," with potential for numerous indications. The total accessible market is over $100 billion. 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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