ZyVersa Therapeutics Announces Article Published in Peer-Reviewed Biomedical Journal Demonstrating That NLRP3 Inflammasome Inhibition Attenuates Inflammatory Bowel Disease Symptoms in Animal Model

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- *Inflammatory bowel disease (IBD) is a chronic inflammatory disease of the gastrointestinal tract affecting 1 in 100 Americans (around 2.4 million people) that can lead to disabling bowel symptoms and progressive bowel damage.*
- *Study provides direct evidence that NLRP3 signaling is over-activated in IBD, and that its inhibition attenuates intestinal inflammation and tissue damage, leading to significant improvements in IBD symptoms, and restoration of normal intestinal microbial flora.*
- *ZyVersa is developing Inflammasome ASC Inhibitor IC 100 which can inhibit up to 12 different inflammasomes (including NLRP3 inflammasomes) and their associated ASC specks which perpetuate damaging inflammation.*

WESTON, Fla., Nov. 09, 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 *Biomedical Journal* demonstrating that inhibiting NLRP3 inflammasomes in an IBD animal model attenuates intestinal inflammation and tissue damage, leading to significant improvements in IBD symptoms, and restoration of normal intestinal microbial flora.

In the paper titled, "Inhibition of NLRP3 attenuates sodium dextran sulfate-induced inflammatory bowel disease through gut microbiota regulation," the authors evaluated human colon biopsy samples from patients with IBD and healthy controls, and conducted a study in an IBD mouse model. Following are key findings reported in the paper:

- NLRP3 and IL-1β expression is increased in the colon of IBD patients.
- NLRP3 inhibition in the IBD animal model:
  - Inhibited NLRP3 inflammasome signaling in the colon, resulting in significantly reduced levels of the pro-inflammatory cytokines IL-1b, IL-6, and TNF-α.
  - Alleviated severe diarrhea and significantly improved IBD symptoms, based on the disease activity index score.
  - Attenuated histopathological changes indicative of tissue damage (goblet cell reduction, crypt destruction, and epithelial barrier disruption).
  - Restored gut microbiota to normal.

The authors stated, "In conclusion, this study provides direct evidence that NLRP3 signaling is over-activated in IBD patients. The inhibition of NLRP3 reverses the IBD-like symptoms in DSS-induced mice, which the regulatory effects on gut microbiota might mediate. Overall, this present study provides a basis for the clinical application of NLRP3 as a target for IBD treatment." To read the article, Click Here.

"Restoration of quality of life is the ultimate long-term goal in IBD management. Although disease remission can often be achieved with current therapies, bothersome symptoms can still prevail," stated Stephen C. Glover, ZyVersa's Co-founder, Chairman, CEO and President. "The research published in the *Biomedical Journal* provides support for inflammasome inhibition as a promising treatment option for IBD. ZyVersa is developing Inflammasome ASC inhibitor IC 100. Unlike NLRP3 inhibitors, designed to inhibit formation of one inflammasome to block initiation of the inflammatory cascade, IC 100 was designed to inhibit multiple types of inflammasomes and their associated ASC specks to uniquely block both initiation and perpetuation of damaging inflammation, which we believe is necessary to control chronic inflammation." To review a white paper summarizing the mechanism of action and preclinical data for IC 100, 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.

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