ZyVersa Therapeutics Announces Publication Showing AIM2 and NLRP3 Inflammasomes Promote Atherosclerosis in Diabetes, Supporting IC 100's Rationale for Targeting ASC to Inhibit Multiple Inflammasome Pathways

Dec 6, 2023

- *Atherosclerosis, an inflammatory disease characterized by buildup of cholesterol, lipids, and other substances (plaque) in arteries leading to heart attack and stroke, is accelerated in patients with diabetes.*
- *The study published in Diabetes demonstrates that AIM2 and NLRP3 inflammasome activation leads to development of atherosclerotic lesions in diabetic mice.*
- *ZyVersa is developing Inflammasome ASC Inhibitor IC 100, which inhibits multiple inflammasome pathways (including NLRP3 and AIM2) to attenuate initiation and perpetuation of damaging inflammation that is pathogenic in numerous diseases.*

WESTON, Fla., Dec. 06, 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, *Diabetes,* demonstrating that AIM2 and NLRP3 inflammasome activation contributes to development of atherosclerosis in two different animal models of type 1 diabetes.

In the paper titled, "Hematopoietic NLRP3 and AIM2 inflammasomes promote diabetes-accelerated atherosclerosis, but increased necrosis is independent of pyroptosis," the authors studied mouse models of type 1 diabetes and atherosclerosis. Following are key findings reported in the paper:

- Diabetic animals demonstrated activation of inflammasome pathways, based on increased levels of plasma IL-1β and IL-18, and elevated levels of cleaved caspase- 1 in the peritoneal cavity fluid.
    - Each of the two different type 1 diabetes models exhibited similar levels of plasma IL- 1β and IL-18 and similar aortic lesion sizes and severity.
- Diabetic mice deficient in NLRP3 and/or AIM2 had reduced aortic lesion size compared to diabetic controls, indicating that NLRP3 and AIM2 inflammasome activation contributes to atherosclerotic lesion development.
- Results are consistent with other animal model studies showing deficiencies in essential inflammasome components, such as NLRP3, AIM2, ASC, and caspase-1, appear to protect against atherosclerosis.

To read the article, Click Here.

"The research published in *Diabetes* reinforces that inhibition of multiple types of inflammasomes, not just NLRP3, may be required to effectively control inflammation in diseases, such as atherosclerosis, in which activation of more than one type of inflammasome is pathogenic," commented Stephen C. Glover, ZyVersa's Co-founder, Chairman, CEO and President. "ZyVersa's Inflammasome ASC inhibitor IC 100 is designed to inhibit formation of multiple types of inflammasomes and their associated ASC specks to attenuate initiation and perpetuation of damaging inflammation contributing to numerous diseases." 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 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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