ZyVersa Therapeutics Highlights Review Article Supporting the Need for Drug Therapies to Treat the Inflammation of Obesity in Addition to Weight Loss Drugs

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- Obesity, due to its associated chronic, systemic inflammation, increases the risk for metabolic diseases, atherosclerosis, various malignant tumors, and numerous immune-mediated disorders.
- With weight loss, less inflammation is expected, but adipose tissue inflammation can persist long after weight loss. One study showed that immediately after weight loss fat breakdown releases fatty acids triggering an increase in adipose tissue (AT) proinflammatory macrophages and inflammation. Over time, there is a gradual decline in inflammatory processes.
- The NLRP3 inflammasome and its release of pro-inflammatory cytokines, IL-1β and IL-18, by AT macrophages is essential in development of obesity-related complications. NLRP3 inhibition in a DIO mouse model protected against cardiovascular complications and fatty liver disease.
- Data from this review article support ZyVersa's development of Inflammasome ASC Inhibitor IC 100 for obesity with associated comorbidities to be used as an add-on to incretin therapy.

WESTON, Fla., Oct. 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, highlights data from a review article published in the peer-reviewed journal, *Life.* The article summarizes data from 345 publications on the role of inflammasome-induced inflammation in obesity and its comorbidities, and it reinforces the need for therapeutic options to better address the inflammation.

"Strong evidence that obesity treatment needs to go beyond weight loss and address the damaging inflammation leading to life-altering comorbidities is driving ZyVersa and other biopharma companies to invest in development of drugs to be used along with incretin therapy to treat inflammation," said Stephen C. Glover, ZyVersa's Co-founder, Chairman, CEO and President. "Studies documenting the key role of inflammasomes in triggering obesity-associated inflammation led ZyVersa to focus on this area for development of Inflammasome ASC Inhibitor IC 100. We are excited about the potential of IC 100 to effectively control the inflammation of obesity. Unlike the NLRP3 inhibitors in development, IC 100 targets ASC to inhibit multiple inflammasomes, including NLRP3 and AIM2, which are associated with obesity. More importantly, IC 100 uniquely disrupts the function of ASC specks to attenuate chronic, systemic inflammation leading to obesity comorbidities. We look forward to progressing IC 100's obesity development program into phase 1 around mid-2025."

In the review article titled, The Interplay between Obesity and Inflammation, the authors concluded:

- Development of adipose tissue inflammation triggers subsequent cardiovascular events and therefore represents a major reason for the treatment of obesity.
- The interplay between obesity and inflammation is complex, involving a variety of cellular and humoral factors, and due to the complexity and particular features of the adipose tissue, the inflammation within may persist for long periods of time.
- Macrophages are the main cellular component driving adipose tissue chronic inflammation. Modulation of macrophages and their release of proinflammatory cytokines, such as NLRP3-driven IL-Iβ and IL-18, can be a key factor in medical intervention in obese patients.
- Understanding the pathophysiological changes in adipose tissue and the interplay with chronic inflammation can assist in the design of future studies and reveal opportunities for the development of more efficient therapies for obesity.

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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