ZyVersa Therapeutics Highlights Published Data Demonstrating the Potential of Inflammasome Inhibition to Protect Pancreatic Islet Beta Cells and Attenuate Progression from Obesity to Insulin Resistance and Type 2 Diabetes

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- During obesity, inflammasome-driven inflammation results in significant loss of pancreatic islet beta cell mass, severely impairing the insulin secreting capacity of the remaining beta cells.
- Preserving pancreatic islet beta cell function is key to prevention of insulin resistance and development of type 2 diabetes.
- The published data showed that inflammasome NLRP3 inhibition was protective of pancreatic islet beta cells, restoring their function and improving metabolic status in an obesity DIO mouse model.
- Data from this article support ZyVersa's development of Inflammasome ASC Inhibitor IC 100 for obesity and its associated comorbidities to be used as an add-on to incretin therapy.

WESTON, Fla., Nov. 05, 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 an article published in the peer-reviewed *International Journal of Nanomedicine* titled Small Intestinal Endocrine Cell Derived Exosomal ACE2 Protects Islet β-Cell Function by Inhibiting the Activation of NLRP3 Inflammasome and Reducing β-Cell Pyroptosis. Through investigation on how exosomes derived from gut microbiota can transport signals to remotely regulate pancreatic islet β-cell function, the researchers documented that:

- Inflammasome-driven inflammation resulted in severely damaged pancreatic islets.
- Damaged Islets demonstrated disrupted cellular arrangement and visible vascular thickening, leading to islet cell loss and metabolic dysfunction.
- Inflammasome inhibition reduced the inflammation and pancreatic islet damage, and attenuated the metabolic dysfunction.

"This data supports the potential of Inflammasome ASC Inhibitor IC 100, as a key component of obesity care when added to incretins used for weight loss. According to the International Obesity Collaborative, obesity care is about health, not weight. It consists of evidence-based options that address the comorbidities of obesity, such as diabetes, hypertension, and hyperlipidemia, and improve well-being," said Stephen C. Glover, ZyVersa's Co-founder, Chairman, CEO and President. "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 activated in obesity. More importantly, IC 100 uniquely disrupts the function of ASC specks to attenuate the chronic, systemic inflammation leading to obesity comorbidities. We look forward to progressing IC 100's obesity development program into phase 1 around mid-2025."

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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