ZyVersa Unveils Groundbreaking Potential of Inflammasome Inhibitors in Combination with GLP-1 Agonists to Address Unmet Medical Needs of People Living with Obesity; Provides R&D Update

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WESTON, Fla., May 07, 2025 (GLOBE NEWSWIRE) -- ZyVersa Therapeutics, Inc. (Nasdaq: ZVSA), a clinical-stage biopharmaceutical company specializing in first-in-class therapies for inflammatory and renal diseases, announces significant developments for Inflammasome ASC Inhibitor IC 100. CEO Stephen C. Glover issued a shareholder letter detailing the company's strategy to position IC 100 as a complementary therapy to GLP-1 agonists to treat obesity-associated cardiometabolic complications.

Obesity: A Global Health Crisis with Unmet Medical Needs

Obesity has reached pandemic proportions, affecting over 40% of Americans, with a projected increase to 51% of the global population within 12 years if current trends continue. This condition is intricately linked to various chronic diseases, including type 2 diabetes, cardiovascular disease, non-alcoholic fatty liver disease, and certain cancers. The economic impact is staggering, with global costs projected to exceed $4.32 trillion annually by 2035 without improved prevention and treatment options.

While GLP-1 agonists have revolutionized obesity treatment by promoting substantial weight loss and improving metabolic parameters, significant unmet medical needs remain.

- Muscle loss is common, with patients losing 20% to 40% of muscle along with their fat loss
- GLP-1 agonist discontinuation rates are high, leading to rebound weight gain
    - Around 65% of non-diabetic patients discontinue GLP-1 agonist treatment within a year and 85% within 2 years - a key driver is GI side effects, which affect 40% - 70% of patients
- Importantly, GLP-1 agonists do not fully address the inflammasome-driven chronic, systemic inflammation affecting the hypothalamus that drives obesity, as well as adipose tissue, liver, pancreas, muscle, and gut that dysregulate metabolism in these tissues leading to comorbid conditions

Inflammasome Inhibitors, Opportunity to Address Unmet Needs in Combination With GLP-1 Agonists

Available inflammasome inhibitor preclinical data in diet-induced obesity animal models provide proof-of-concept for inflammasome inhibitors as promising therapeutic options for obesity and its associated cardiometabolic conditions when used as add-on therapy to GLP-1 agonists.

- Reduced inflammatory, cardiovascular, and metabolic biomarkers versus monotherapy with either drug
- Enhanced weight and fat loss, with preserved lean mass versus monotherapy with either drug
- Continuing weight loss with inflammasome inhibitor monotherapy following cessation of GLP-1 agonist monotherapy or GLP-1 agonist/inflammasome inhibitor combination therapy

There is also potential to reduce the dose of GLP-1 agonists with add-on inflammasome inhibitor treatment to help alleviate GI side effects and thus improve duration of anti-obesity therapy.

IC 100: Targeting the Source of Inflammation

While most inflammasome inhibitors in development are small molecules targeting NLRP3, IC 100 was designed to uniquely inhibit ASC and ASC specks to attenuate not only initiation of the inflammatory cascade, but more importantly to attenuate the perpetuation and spread of inflammation contributing to development of obesity-associated cardiometabolic comorbidities.

By targeting ASC, IC 100 also inhibits activation of multiple types of inflammasomes that are associated with obesity and its associated complications:

- Obesity: AIM2, NLRP3
- Insulin Resistance: AIM2, NLRP1, NLRP3, NLRC4, NLRP6
- Diabetic Nephropathy: AIM2, NLRP3

Preclinical data available to date demonstrate IC 100’s potential to address cardiometabolic comorbidities:

- In an ApoE knockout model of atherosclerosis, IC 100 demonstrated a reduction in inflammation and plaque in the aorta
- In an obese animal model of diabetic kidney disease, IC 100 lowered fasting blood glucose levels, suggestive of reduced insulin sensitivity

- In multiple studies in numerous disease states, including CNS and peripheral diseases, IC 100 blocked proinflammatory cytokines, IL-1β, IL-18, and IL-6 that drive inflammation

Strategic Development Plans and Milestones

ZyVersa has outlined a comprehensive development plan for IC 100, with key milestones anticipated over the next 12 months:

- H1-2025: Initiate preclinical study in diet-induced obesity (DIO) mouse model to evaluate IC 100's efficacy as monotherapy and in combination with semaglutide
- H2-2025: Submit an Investigational New Drug (IND) application for IC 100
- H1-2026: Commence Phase 1 clinical trials in overweight subjects (BMI 27–30) with cardiometabolic risk factors to assess safety and biomarkers of cardiometabolic risk

These studies aim to demonstrate that IC 100, when added to GLP-1 agonist therapy, can reduce the underlying inflammation of obesity, with potential to reduce progression to associated cardiometabolic comorbidities, while augmenting weight loss.

Collaborations and Scientific Advisory Support

To support the development of IC 100, ZyVersa has formed a Scientific Advisory Board comprising leading experts in obesity, metabolic diseases, and inflammasome biology. This board will provide strategic guidance as the company advances IC 100 through clinical development.

Additionally, ZyVersa has engaged in preclinical collaborations to explore the potential of IC 100 in treating Parkinson's disease, further expanding the therapeutic applications of this novel inflammasome ASC inhibitor.

Conclusion

With the development of IC 100, ZyVersa Therapeutics is poised to make significant strides in the comprehensive treatment of obesity and its associated cardiometabolic complications. By targeting the root cause of chronic inflammation, IC 100 has the potential to complement existing therapies, offering a more holistic approach to managing obesity and improving patient outcomes. The company's strategic development plan, coupled with expert collaborations, underscores its commitment to addressing the unmet medical needs in this critical area of healthcare**.**

We look forward to updating you on our value-building near-term results from our IC 100 development program. Thank you for your continued support.

Sincerely,
Stephen C. Glover
Co-Founder, Chairman, Chief Executive Officer, and President
ZyVersa Therapeutics

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 peripheral 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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Corporate, IR, and Media Contact
Karen Cashmere

Chief Commercial Officer
kcashmere@zyversa.com
786-251-9641