ZyVersa Therapeutics CEO Issues Shareholder Letter Announcing Transformative R&D Trends for Inflammasome Inhibitors, and Provides Update on Inflammasome ASC Inhibitor IC 100's Development Status

Apr 24, 2025

WESTON, Fla., April 24, 2025 (GLOBE NEWSWIRE) -- ZyVersa Therapeutics, Inc. (Nasdaq: ZVSA; "ZyVersa"), a clinical stage specialty biopharmaceutical company developing first-in-class drugs for treatment of patients with renal and inflammatory diseases who have unmet medical needs, announces that Stephen C. Glover, Co-Founder, Chairman, Chief Executive Officer, and President, has issued a Shareholder Letter addressing R&D trends for inflammasome inhibitors in development, and provides an update on the development status of Inflammasome ASC Inhibitor IC 100. The full text of the letter follows.

A MESSAGE FROM OUR CHIEF EXECUTIVE OFFICER

ZyVersa is developing Inflammasome ASC Inhibitor IC 100 for treatment of chronic inflammatory diseases, with initial focus on Obesity-associated cardiometabolic conditions as the lead. Plans for indication expansion include treatments for Parkinson's and Alzheimer's diseases, and Multiple Sclerosis. The global drug market for anti-inflammatory biologics was valued at $105 billion in 2024, and it's projected to reach $186 billion by 2034 (Precedence Research). This growth is driven by the rising incidence of chronic inflammatory diseases associated with population aging, lifestyle changes, and environmental factors.

Because of the large and growing market for drug therapies to treat chronic inflammation, as well as the novel approach of targeting the innate immune system, strategic collaborations and M&A activity tend to occur at early stages of inflammasome inhibitor development. Over the last 5 years, there have been over $7 Billion in deals in this space.

Inflammasome Inhibitor Development Trends

Since discovery of the first inflammasome in 2002, it has become increasingly clear that dysregulated inflammasome activation plays a causative or contributing role in the initiation and progression of various diseases affecting all body systems (cardiovascular, digestive, neurological, respiratory, urogenital, and even blood and lymphatic systems). With such a broad and diverse range of diseases that can be targeted, it is not surprising that the biggest challenge in development of inflammasome inhibitors has been determining which diseases to address first.

Inflammasome inhibitor development is now at an inflection point. Major inflammasome inhibitor developers have completed their preclinical programs and healthy subject phase 1 studies demonstrating product safety and promising signals of efficacy, such as improved biomarkers of inflammation (hsCRP, IL-6, IL-1β, IL-18) and metabolic function (decreased cholesterol, triglycerides, insulin resistance, and HbA1c), leading to identification of initial indications to pursue. Many have initiated phase 1b and phase 2 clinical trials, with some expected to have data read-outs between now and years' end. Phase 2 data read-outs will provide insights regarding the potential role for inflammasome inhibitors for specific indications and will provide direction for future inflammasome inhibitor development.

Following is a summary of diseases in clinical development with NLRP3 inflammasome inhibitors:

- Obesity and cardiovascular risk factors (Ventyx, P2*, Nodthera, P2)
- Recurrent Pericarditis (Ventyx, P2*)
- Cardiovascular risk reduction (Novartis, P1)
- Coronary artery disease (Roche, P1)
- Parkinson's disease (Ventyx, P2 #; Nodthera, P2; Ventus, P2; Roche, P1)
- Obesity-associated osteoarthritis (Ventus, P1)
- Asthma (Roche, P1)
- Low risk myelodysplastic syndrome (Novartis, P1)

*Announced data read-out H2-2025
#Announced data read-out Q2-2025

Inflammasome ASC Inhibitor IC 100's Near-term Value Inflection Milestones

While most inflammasome inhibitor development has targeted small molecule NLRP3 inhibition only, 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 comorbidities. Additionally, by targeting ASC, IC 100 inhibits activation of multiple types of inflammasomes that are associated with development and/or progression of numerous inflammatory diseases, which we believe will lead to better control of inflammation than targeting just one inflammasome (e.g., NLRP3).

Following are highlights of the progress we have achieved in development of Inflammasome ASC Inhibitor IC 100.

- Proof-of-concept study with IC 100 in diet-induced obesity (DIO) mouse model is planned to begin H1-2025. Study will

evaluate the effects of IC 100 on changes in inflammatory and cardiometabolic biomarkers, including insulin resistance which can lead to type 2 diabetes, as well as changes in body weight and body composition in comparison to semaglutide and when administered concurrently with semaglutide. We expect a preliminary read-out in H2-2025.

- Investigational New Drug Application (IND) for IC 100 is anticipated to be submitted H2-2025, followed by initiation of a Phase 1 clinical trial in overweight subjects (BMI 27 to 30) with cardiometabolic risk factors. Safety of three different doses of IC 100 will be evaluated, as well as changes in biomarkers of cardiometabolic risk factors. Results are anticipated in the first half of 2026.
- Preclinical study funded by The Michael J. Fox Foundation (MJFF) to evaluate the potential of IC 100 as a treatment for Parkinson's disease has been completed and a manuscript has been accepted for publication. Stay tuned for an announcement of the published data when available.
- Invited MJFF grant request for funding of a second IC 100 proof-of-concept preclinical study in Parkinson's disease animal model has been submitted; response expected in June 2025.

We look forward to reporting the 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.

This press release does not constitute an offer to sell, or the solicitation of an offer to buy, any securities.

Corporate, IR, and Media Contact
Karen Cashmere
Chief Commercial Officer
kcashmere@zyversa.com
786-251-9641