ZyVersa Therapeutics Announces a Publication in the Peer-Reviewed Journal, Aging, Linking Inflammasome NLRP3 Activation with Age-Related Structural Changes in the Kidney and Reduced Kidney Function

Oct 18, 2023

- *Chronic kidney disease is most common in people 65 years and older.*
- *NLRP3 inflammasomes signaling in the kidneys' filtration system ("glomerular podocytes") occurs as early as middle age, leading to scarring, podocyte loss, and impaired function, which may be a critical contributor to a lower threshold for developing kidney disease in older people.*
- *Age-related inflammasome signaling and its effects are compounded in the presence of kidney disease, leading to poorer outcomes.*
- *ZyVersa is developing Inflammasome ASC Inhibitor IC 100 which can inhibit up to 12 different inflammasomes (including NLRP3 inflammasomes) and their associated ASC specks which perpetuate damaging inflammation.*

WESTON, Fla., Oct. 18, 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, *Aging,* demonstrating that inflammasome NLRP3 activation is associated with an age-related decline in kidney health, which is compounded in the presence of kidney disease resulting in worsening outcomes.

In the paper titled, "Inhibiting NLRP3 signaling in aging podocytes improves their life-and health-span," the authors conducted studies in various mouse models, human kidney tissues, and human kidney organoids. Data demonstrate a critical role for NLRP3 inflammasomes in age-related kidney deterioration, which is exacerbated in the presence of kidney disease. Following are key findings reported in the paper:

- Glomerular NLRP3 levels in human kidney tissue were associated with pathological changes in the kidneys' filtration system: higher levels of glomerular scarring (glomerulosclerosis) and enlargement (hypertrophy), and reduced podocyte density.
- Glomerular NLRP3 inflammasome levels were higher in aged mice with experimental focal segmental glomerulosclerosis (FSGS) compared to age-matched mice without disease, indicating that FSGS injury augments the age-dependent increase of NLRP3 signaling.
- NLRP3 inflammasome signaling and its effects on podocytes may be a critical contributor to a lower threshold for developing kidney disease in older people.
- Reduction in NLRP3 signaling, either pharmacologically or by gene deletion, in human kidney organoids and in middle-aged mice decreased age-associated podocyte injury.

The authors stated, "By showing that in aged mice with experimental FSGS, injury augments the age-dependent increase of NLRP3 signaling, it makes this pathway an intriguing therapeutic target for podocyte (kidney) diseases in the elderly." To read the article, Click Here.

"The research published in the Journal , *Aging,* demonstrates that age-related NLRP3 inflammasome signaling in the kidneys' filtration system leads to scarring and podocyte loss, which are exacerbated when superimposed by kidney disease, leading to poorer outcomes," commented Stephen C. Glover, ZyVersa's Co-founder, Chairman, CEO and President. "This research provides support for inflammasome inhibition as a promising treatment option for kidney disease, which is most common in the elderly. ZyVersa is developing Inflammasome ASC inhibitor IC 100. Unlike NLRP3 inhibitors, designed to inhibit formation of the NLRP3 inflammasome to block initiation of the inflammatory cascade, IC 100 was designed to inhibit formation of multiple types of inflammasomes, and to uniquely inhibit their associated ASC specks to block perpetuation of damaging inflammation." 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 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.

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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