



## ZyVersa Therapeutics Announces Publication in the Journal, *Hepatology*, Highlighting the Role of NLRP3 Inflammasome-Mediated IL-18 in Development of Liver Fibrosis

Jul 17, 2023

- Liver fibrosis is a progressive form of chronic liver injury mediated by persistent NLRP3 inflammasome activation in liver cells called hepatic stellate cells (“HSCs”), which leads to the development of cirrhosis and liver cancer
- Inflammasome NLRP3 activation leads to production of the proinflammatory cytokines, IL-1 $\beta$  and IL-18, and IL-18 activates HSCs resulting in liver fibrosis
- 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 through ongoing production of IL-1 $\beta$  and IL-18

WESTON, Fla., July 17, 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, *Hepatology*, demonstrating the role of NLRP3 inflammasome-mediated IL-18 in the development of liver fibrosis.

In the paper titled, “Interleukin -18 signaling promotes activation of hepatic stellate cells in mouse liver fibrosis,” the authors evaluated serum levels of IL-18 in patients diagnosed with liver fibrosis/cirrhosis, and they conducted studies in three different mouse models of liver fibrosis. Following are key findings reported in the paper:

- Levels of circulating IL-18 and IL-18 binding protein were elevated in patients with liver fibrosis/cirrhosis in comparison to healthy controls
- Data in liver fibrosis mouse models provided strong evidence that IL-18 signaling and its downstream effects have a pivotal role in the development of liver fibrosis (fibrogenesis)
- The pivotal role of IL-18 signaling in liver fibrosis was confirmed in IL-18 deficient mice, which showed protection from fibrotic liver changes

The authors stated, “Our results highlight the pivotal role of IL-18 signaling in liver fibrogenesis through the activation of HSCs *in vitro* and *in vivo* in three different mouse models.” To read the article, [Click Here](#).

“The research published in the *Hepatology* demonstrated that NLRP3 inflammasome-mediated activation of IL-18 has a pivotal role in liver fibrosis, providing support for inflammasome inhibition as a promising treatment. Unlike NLRP3 inhibitors, which only inhibit formation of the NLRP3 inflammasome to block initiation of the inflammatory cascade, Inflammasome ASC inhibitor IC 100 inhibits formation of multiple types of inflammasomes, and it uniquely inhibits ASC specks to block perpetuation of damaging inflammation,” commented Stephen C. Glover, ZyVersa’s Co-founder, Chairman, CEO and President. 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, NLRP4, AIM2, Pyrin. Intracellularly, IC 100 binds to ASC monomers, inhibiting inflammasome formation, thereby blocking activation of IL-1 $\beta$  early in the inflammatory cascade. IC 100 also binds to ASC in ASC Specks, both intracellularly and extracellularly, further blocking activation of IL-1 $\beta$  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](http://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.

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