ZyVersa Therapeutics Announces Article Published in Metabolism Pointing to Glomerular Cholesterol Accumulation as Key Factor Exacerbating Renal Injury and Dysfunction in Diabetic Kidney Disease

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- *Published data demonstrate that a deficiency in cholesterol transporter ABCA1 increases deposition of cellular cholesterol, contributing to inflammation, cell death (apoptosis), and damage to the kidney's filtration barrier in type 2 diabetic mice and in human renal glomerular endothelial cells cultured to simulate type 2 diabetes*
- *ZyVersa's Cholesterol Transport Mediator™ VAR 200 is in development to reduce renal cholesterol and lipid accumulation that damages the kidneys' filtration system in patients with glomerular diseases (diabetic kidney disease, focal segmental glomerulosclerosis, and Alport Syndrome)*
- *VAR 200 mediates transport of excess cholesterol out of kidney cells passively and by upregulating cholesterol transporter ABCA1*

WESTON, Fla., May 15, 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, *Metabolism,* which supports the mechanism of action of Cholesterol Efflux Mediator™ VAR 200 in development to treat kidney diseases.

In the paper titled, "ABCA1 deficiency-mediated glomerular cholesterol accumulation exacerbates glomerular endothelial injury and dysfunction in diabetic kidney disease," the authors reported that ABCA1 deficiency contributes to injury and dysfunction of the kidney's filtration system (glomerular endothelium) in early diabetic kidney disease ("DKD"). They proposed that ABCA1 transporter deficiency results in glomerular cholesterol/lipid accumulation leading to inflammation and cell death. This causes structural and functional damage to the kidney's filtration system and in turn, protein spillage into the urine (proteinuria) and DKD progression.

The authors concluded that therapies which effectively reduce elevated glomerular cholesterol levels have potential to combat early DKD. To read the article, Click Here.

"The research published in *Metabolism* demonstrating that deposition of glomerular cholesterol contributes to structural damage and dysfunction of the kidney's filtration system in models of type 2 diabetes is consistent with data from VAR 200's preclinical program. Our preclinical program showed similar results not only in models of DKD, but also in models of two orphan kidney diseases, focal segmental glomerular sclerosis (FSGS) and Alport Syndrome. More importantly, by mediating cholesterol transport out of the glomeruli through passive transport and upregulation of ABCA1 transporters, VAR 200 protected against glomerular injury and fibrosis, and significantly reduced protein spillage into the urine in all three kidney diseases," commented Stephen C. Glover, ZyVersa's Co-founder, Chairman, CEO and President. "Given the unmet needs for effective treatments for kidney disease, we are hopeful that VAR 200 will demonstrate similar results in patients with kidney disease in studies planned to initiate late this year," continued Mr. Glover.

About Cholesterol Efflux Mediator™VAR 200

Cholesterol Efflux Mediator™ VAR 200 (2-hydroxypropyl-beta-cyclodextrin, 2HPβCD) is a phase 2a-ready drug in development to ameliorate renal lipid accumulation that damages the kidneys' filtration system, leading to kidney disease progression. VAR 200 passively and actively removes excess lipids from the kidney.

Preclinical studies with VAR 200 in animal models of FSGS, Alport syndrome, and diabetic kidney disease demonstrate that removal of excess cholesterol and lipids from kidney podocytes protects against structural damage and reduces excretion of protein in the urine (proteinuria).

The lead indication for VAR 200 is orphan kidney disease focal segmental glomerulosclerosis (FSGS). VAR 200 has potential to treat other glomerular diseases, including orphan Alport syndrome and diabetic kidney disease.

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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