ZyVersa Therapeutics Highlights Data Demonstrating a Critical Need for Therapies to Address Kidney Lipotoxicity to Alleviate Diabetic Kidney Disease (DKD) and Its Progression

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- Data show that diabetes-associated metabolic issues lead to kidney lipid accumulation, resulting in inflammation and fibrosis that cause progressive kidney damage and disease progression.
- Earlier data by Kanbay et al (Eur J Clin Invest. 2022) demonstrate that fatty kidney is an independent risk factor for chronic kidney disease (CKD), not just DKD, and reinforce that lipid accumulation promotes release of pro-inflammatory cytokines leading to inflammation, fibrosis, and CKD progression.
- ZyVersa is developing Cholesterol Efflux Mediator™ VAR 200 to mediate removal of damaging excess lipids from the kidneys' filtration system. VAR 200 directly removes cholesterol and lipids from kidney cells, and it upregulates cholesterol transporters, ABCA1 and ABCG1 for active removal.
- A phase 2a clinical trial in patients with DKD has been initiated and is actively screening patients for enrollment. Future studies are planned for patients with rare kidney diseases, focal segmental glomerulosclerosis (FSGS), VAR 200's lead indication, and Alport Syndrome.
- The global drug market for kidney diseases was $18 Billion in 2024, with $30 Billion projected by 2034 (Precedence Research).

WESTON, Fla., Aug. 14, 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, highlights key data on the role of lipotoxicity in the development and progression of DKD from a review article, Targeting lipid metabolic reprogramming to alleviate diabetic kidney disease: molecular insights and therapeutic strategies, recently published in *Frontiers in Immunology.* This article, which summarized 172 papers, demonstrated that under diabetic conditions, kidney cells undergo significant lipid metabolic abnormalities resulting in accumulation of lipids that trigger inflammation and fibrosis leading to DKD progression.

"This large body of evidence from 2 review papers demonstrates the critical need for therapies to treat kidney lipotoxicity, a crucial factor in the pathology of DKD and other kidney diseases, such as FSGS and Alport syndrome," commented Stephen C. Glover, ZyVersa's Co-founder, Chairman, CEO, and President. "Currently, over 130,000 patients with kidney disease progress to renal failure each year in the US, and more than 800,000 patients are living with renal failure requiring dialysis or transplant to sustain life. We are hopeful that by alleviating lipotoxicity with Cholesterol Efflux Mediator™ VAR 200, kidney injury and disease progression will be reduced, lowering these statistics and improving patients' quality of life. The first patient in our VAR 200 Phase 2a trial in patients with DKD is expected to start therapy by end of this quarter, with an initial data read-out in the second half of the year."

Overview of Key Findings

Metabolic issues associated with diabetes, especially insulin resistance and high blood glucose, lead to abnormal lipid metabolism resulting in kidney lipid accumulation, inflammation, and fibrosis.

Multiple impaired pathways contribute to lipid accumulation:

- Insulin resistance increases release of free fatty acids and uptake by kidney cells
- Activation of fatty acid synthesis pathways leads to excessive lipid production
- Impaired cholesterol efflux (removal) resulting from reduced function of cholesterol transporters, ABCA1 and ABCG1, leads to cholesterol and lipid accumulation
- Impaired fatty acid oxidation, reduces ability to break down and use stored lipids

Of the above pathways, impaired cholesterol efflux is a key factor in DKD pathology. It exacerbates lipid accumulation, especially in podocytes, the key component of the kidney's filtration system, causing structural damage and impaired filtration resulting in protein leaking into the urine, DKD progression, and ultimately kidney failure, if the lipotoxicity is not addressed.

Lipid overload can trigger an inflammasome-induced inflammatory response in kidney cells. Free fatty acids activate inflammasomes initiating an inflammatory cascade via release of IL-1β. Inflammasome activation also induces upregulation of lipid synthesis-related genes while inhibiting expression of lipid efflux transporters like ABCA1, further increasing lipid accumulation. This creates a vicious cycle, causing continuous decline in renal function and ultimately causes irreversible damage.

Currently, no drugs specifically target kidney lipotoxicity.

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.

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