ZyVersa Therapeutics Announces Peer-Reviewed Publication in Nature Reviews Nephrology Substantiating VAR 200's Rationale for Mediating Transport of Cholesterol and Lipids Out of Kidney Cells to Attenuate Progression of Kidney Disease

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- This review paper summarizes numerous research studies that address the role of kidney cholesterol and lipid accumulation in the development and progression of chronic kidney disease (CKD).
- ZyVersa's Cholesterol Efflux Mediator ™VAR 200 is in development to reduce renal cholesterol and lipid accumulation that damages the kidneys' filtration system in patients with glomerular diseases, including diabetic kidney disease, focal segmental glomerulosclerosis, and Alport Syndrome.

WESTON, Fla., Oct. 11, 2023 (GLOBE NEWSWIRE) -- ZyVersa Therapeutics, Inc. (Nasdaq: ZVSA, or "ZyVersa"), a clinical stage specialty biopharmaceutical company developing first-in-class drugs for treatment of renal and inflammatory diseases, announces publication of a paper in the peer-reviewed journal, *Nature Reviews Nephrology*, that summarizes data highlighting how lipid accumulation in the kidneys contributes to CKD development and disease progression.

In the review paper titled, "Kidney lipid dysmetabolism and lipid droplet accumulation in chronic kidney disease," the following key points were made:

- Lipids and lipid-related enzymes have a major role in modulating the function of the kidney's filtration system, and lipid accumulation can drive CKD irrespective of circulating lipid levels and use of systemic lipid lowering drugs like statins.
- Although several lipid types, including cholesterol, triglycerides, fatty acids, and phospholipids, are dysregulated in the kidney and contribute to CKD progression, dysregulation of cholesterol metabolism is one of the hallmarks of kidney injury in CKD. Cholesterol accumulation occurs in association with impaired transport of cholesterol out of the kidney.
- Accumulation of fatty acids triggers kidney cell damage by promoting inflammation and fibrosis.

The paper includes a brief overview of Cholesterol Efflux Mediator ™VAR 200 (hydroxy-propyl-beta-cyclodextrin), highlighting that it reduced cholesterol accumulation and cell death (apoptosis) in podocytes *in vitro*, and provided protection from kidney disease progression in mouse models of diabetic kidney disease, FSGS, and Alport Syndrome. The authors concluded this section by stating that VAR 200, which is in development for patients affected by several forms of kidney disease, provides therapeutic potential for diseases characterized by ABCA1 deficiency. To read the article, Click Here.

"The numerous studies summarized in the paper published in *Nature Reviews Nephrology* reinforce the importance of addressing kidney accumulation of cholesterol and lipids to help attenuate progression of chronic kidney disease, which affects over 35 million adults in the United States," 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, and more than 800,000 patients are living with renal failure requiring dialysis or transplant to sustain life. We are hopeful that protection against kidney injury, fibrosis, and disease progression seen with VAR 200 in animal models of diabetic kidney disease, FSGS, and Alport Syndrome will translate to humans. Our first clinical trial with VAR 200 in patients with diabetic kidney disease is planned to begin in early 2024." To review a white paper summarizing the preclinical research with VAR 200, Click Here.

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

Media Contacts
Tiberend Strategic Advisors, Inc.
Casey McDonald
cmcdonald@tiberend.com
646-577-8520

Dave Schemelia
dschemelia@tiberend.com
609-468-9325