

December 3, 2025



Sigyn CEO Note: Nature Publication Reinforces Rationale for CardioDialysis™ to Address Cardiovascular Disease in Dialysis Patients

SAN DIEGO, CA - December 3, 2025 ([NEWMEDIAWIRE](#)) - Sigyn Therapeutics, Inc. ("Sigyn" or the "Company") (OTCQB: SIGY), a developer of dialysis-like therapies to address cardiovascular disease and cancer, today released the following note authored by its CEO/Inventor, Jim Joyce.

Dear Readers,

On November 20, 2025, the scientific journal Nature published a review article entitled "Still Searching for the Right Target for Cardioprotection in Haemodialysis," which further reinforced our recent introduction of CardioDialysis(TM) to address cardiovascular disease in end-stage renal disease (ESRD) patients.

Consistent with our findings, the article reported ESRD dialysis patients have up to a 20-fold greater risk of death from cardiovascular disease as compared to the general population. This is a staggering statistic when considering that cardiovascular disease is already the leading cause of death worldwide. The review article also reported that drugs to treat cardiovascular disease have not improved survival or reduced cardiovascular events in dialysis patients.

Consistent with our CardioDialysis(TM) clinical strategy, the authors believe future research should focus on targeting inflammatory pathways that are activated when blood interacts with dialysis membranes. We refer to this as dialysis-induced inflammation, which is known to accelerate cardiovascular disease progression.

In conclusion, the authors state that future drug studies should focus on specific inflammatory targets to lower the risk of dialysis-related cardiovascular disease. At this point, our beliefs diverge from those of the authors as CardioDialysis(TM) performs critically important functions that are beyond the reach of drugs. Instead of targeting a single inflammatory molecule, CardioDialysis(TM) aims to address a broad-spectrum of inflammatory molecules that fuel cardiovascular disease progression while simultaneously lowering levels of cholesterol-transporting lipoproteins that contribute to heart attacks, strokes, and other Major Adverse Cardiovascular Events (MACE). Beyond these broad-spectrum attributes, CardioDialysis(TM) can be conveniently administered to ESRD patients during their regularly scheduled dialysis treatments.

The following link will provide access to the featured review article in Nature.
<https://www.nature.com/articles/s41581-025-01035-z>

To learn more about CardioDialysis(TM), I encourage you to continue reading below.

Sincerely, Jim

About CardioDialysis(TM)

CardioDialysis(TM) is an emerging candidate to treat cardiovascular disease, the leading cause of death worldwide. CardioDialysis(TM) establishes an adjunct strategy to enhance the benefit of cardiovascular drugs without adding further drug toxicity. The technology also introduces a non-pharmacological option for patients who are unresponsive to cholesterol-lowering drugs.

CardioDialysis(TM) aims to reduce the circulating presence of inflammatory molecules that fuel cardiovascular disease progression while simultaneously lowering levels of cholesterol-transporting lipoproteins that contribute to heart attacks, strokes, and other Major Adverse Cardiovascular Events (MACE).

Based on its broad-spectrum mechanism, CardioDialysis(TM) is positioned to reduce the incidence of MACE by overcoming the inherent limitations of single-target drugs. The annual market for MACE-reducing therapies is reported to exceed \$100 billion.

Initial Clinical and Commercialization Focus

The initial clinical and commercialization focus of *CardioDialysis(TM)* is directed toward the treatment of cardiovascular disease in end-stage renal disease (ESRD) patients. According to the U.S. Renal Data System (USRDS), cardiovascular disease is attributed to 67% of ESRD patient deaths and its incidence is up to 20 times higher in ESRD dialysis patients as compared to the general population.

Beyond high mortality rates, cardiovascular disease is a well-defined, yet substantial market opportunity, given an estimated 550,000 ESRD patients receive ~85 million dialysis treatments in the U.S. each year. To optimize potential market penetration within the dialysis industry, CardioDialysis(TM) can be administered to ESRD patients during their regularly scheduled dialysis treatments.

A Medical Device Precedent to Treat Cardiovascular Disease

CardioDialysis(TM) targets multiple key therapeutic pathways, including cholesterol-transporting lipoproteins that play a central role in the development and progression of cardiovascular disease.

Lipoprotein Apheresis (LA) is an established FDA-approved precedent that has proven the ability of blood purification to significantly reduce Major Adverse Cardiovascular Events (MACE) by lowering levels of lipoprotein(a) and low-density lipoprotein cholesterol (LDL-C) in the bloodstream. In a recent review article published by the American Heart Association, Lipoprotein Apheresis was observed to lower the incidence of MACE by 59% to 95% across 11 studies encompassing 1,387 treated patients. In contrast, pharmaceutical statins (Lipitor, Crestor, and Zocor) to lower LDL-C levels are reported to reduce MACE by 20% to 45%.

Unfortunately, the clinical adoption of Lipoprotein Apheresis has been constrained by a limited delivery infrastructure, with fewer than 60 specialized apheresis centers providing

access to the therapy in the United States.

Leveraging the Global Infrastructure of Dialysis Machines

CardioDialysis(TM) is not constrained by delivery infrastructure as it can be deployed on dialysis machines already located in hospitals and clinics around the world. An estimated 150,000 dialysis machines are already located in more than 7,500 kidney dialysis clinics in the U.S. alone. By leveraging this infrastructure, Sigyn Therapeutics envisions a possibility to transform current kidney dialysis clinics into future Renal and CardioDialysis(TM) treatment centers.

Potential Value of CardioDialysis(TM) to the Dialysis Industry

If successfully advanced, CardioDialysis(TM) could improve and extend the quality of life of ESRD patients who rely on dialysis for survival. Beyond introducing a potential new revenue source to the dialysis industry, CardioDialysis(TM) could provide a pathway to treat cardiovascular disease in the general population.

Extending ESRD patient lives and reducing their hospitalizations would also provide quantifiable value to the dialysis industry, which is dominated by DaVita and Fresenius Medical Care in the United States. When ESRD patients are hospitalized, dialysis organizations lose revenues as in-clinic dialysis treatments are instead administered at out-of-network hospitals. Based on average dialysis revenues of \$400 per treatment, the U.S. dialysis industry could recoup up to \$654 million in lost revenues for each week of reduced ESRD patient hospitalizations. More importantly, the U.S. dialysis industry could increase top-line revenues by ~\$2.8 billion for each month the lives of their patients are extended.

Addressing Unique Cardiovascular Disease Challenges of Dialysis Patients

ESRD patients face unique cardiovascular disease challenges that are beyond the reach of drug therapies. Once they become dialysis dependent, the median length of ESRD patient survival is reported to be 3-5 years. Unlike the general population, clinical studies indicate that ESRD patients receive limited if any clinical benefit from LDL-C reducing statins, the leading class of drugs to treat cardiovascular disease. Additionally, circulating levels of cholesterol-transporting lipoprotein(a) are reported to be two to four times higher in ESRD dialysis patients as compared to the general population.

Compounding these treatment challenges is the unfortunate reality that dialysis treatments induce inflammatory responses that further contribute to the progression of cardiovascular disease. More specifically, circulating levels of endotoxin and inflammatory cytokines are often elevated in response to dialysis treatment.

At present, there are no market-cleared pharmaceutical products to address Lipoprotein(a), endotoxemia, or the broad-spectrum of inflammatory cytokines observed to be elevated in dialysis patients.

In response, CardioDialysis(TM) provides a strategy to reduce circulating LDL-C and Lipoprotein(a) levels, which has been clinically proven to reduce major adverse cardiovascular events (MACE). Simultaneously, CardioDialysis(TM) aims to control dialysis-induced inflammation that further fuels cardiovascular disease progression.

In regard to commercialization strategy, the enrollment of ESRD patients is clinically advantageous as they already have blood access and CardioDialysis(TM) can be conveniently integrated during regularly scheduled dialysis sessions at their dialysis clinic.

About Sigyn Therapeutics(TM)

Sigyn Therapeutics is developing dialysis-like therapies to address cardiovascular disease and cancer. The Company's therapeutic candidates are designed to improve and extend the quality of patient lives, and their successful clinical advancement offers to provide strategic value to the dialysis and biopharmaceutical industry.

Sigyn CardioDialysis(TM) is a first-in-industry medical device to treat cardiovascular disease, the leading cause of death globally. CardioDialysis(TM) aims to reduce the circulating presence of inflammatory molecules that fuel cardiovascular disease progression while simultaneously lowering levels of cholesterol-transporting lipoproteins that contribute to heart attacks, strokes, and other Major Adverse Cardiovascular Events (MACE). Based on its broad-spectrum mechanism, CardioDialysis(TM) offers to reduce the incidence of MACE by overcoming the inherent limitations of single-target drugs.

The Company's development pipeline is comprised of ImmunePrep(TM) to optimize the delivery of immunotherapeutic antibodies to treat cancer; ChemoPrep(TM) to enhance the targeted delivery of chemotherapy; and ChemoPure(TM) to reduce the toxicity of chemotherapy.

To learn more about Sigyn Therapeutics, visit: www.SigynTherapeutics.com

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Cautionary Note Regarding Forward-Looking Statements

This information in this press release contains forward-looking statements of Sigyn Therapeutics, Inc. ("Sigyn") that involve substantial risks and uncertainties. All statements contained in this summary are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 that involve risks and uncertainties. Statements containing words such as "may," "believe," "anticipate," "expect," "intend," "plan," "project," "will," "projections," "estimate," "potentially" or similar expressions constitute forward-looking statements. Such forward-looking statements are subject to significant risks and uncertainties, and actual results may differ materially from the results anticipated in the forward-looking statements. These forward-looking statements are based upon Sigyn's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Factors that may contribute to such differences may include, without limitation, the Company's ability to clinically advance Sigyn Therapy in human studies required for market clearance, the Company's ability to manufacture Sigyn Therapy, the Company's ability to raise capital resources, and other potential risks. The foregoing list of risks and uncertainties is illustrative but is not exhaustive. Additional factors that could cause results to differ materially from those

anticipated in forward-looking statements can be found under the caption "Risk Factors" in the Company's Annual Report on Form 10-K, and in the Company's other filings with the Securities and Exchange Commission, including its quarterly Reports on Form 10-Q. All forward-looking statements contained in this report speak only as of the date on which they were made. Except as may be required by law, the Company does not intend, nor does it undertake any duty, to update this information to reflect future events or circumstances.

View the original release on www.newmediawire.com