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Sigyn Therapeutics Announces First-In-Human Clinical Strategy to Address Inflammation and Endotoxemia in End-Stage Renal Disease Patients

SAN DIEGO, CA, Sept. 14, 2022 (GLOBE NEWSWIRE) -- via NewMediaWire – Sigyn Therapeutics, Inc. (OTCQB: SIGY), a development-stage company focused on the creation of therapeutic solutions that address unmet needs in global health, announced today that it plans to pursue first-in-human feasibility studies of Sigyn Therapy in End-Stage Renal Disease (ESRD) patients suffering from excess inflammation and/or endotoxemia.

Inflammation and endotoxemia are prevalent conditions associated with increased mortality in dialysis dependent ESRD patients. According to the United States Renal Data System (USRDS), there are more than 550,000 individuals with ESRD, which results in approximately 85 million dialysis treatments being administered in the United States each year. At present, there are no approved drugs to treat ESRD related inflammation and endotoxemia. In this regard, Sigyn Therapy offers a candidate strategy to improve the health and quality-of-life of ESRD patients.

In the Company's proposed study, Sigyn Therapy will be combined in series with enrolled subjects regularly scheduled dialysis treatment. Sigyn Therapy is broad-spectrum blood purification technology that isolates and extracts pathogen sources of life-threatening inflammation in concert with the depletion of proinflammatory cytokines from the bloodstream.

"In recent months, we identified and initiated an evaluation of ESRD inflammation and endotoxemia as a candidate indication to demonstrate initial safety of Sigyn Therapy in human studies," stated Sigyn Therapeutics founder and CEO Jim Joyce. "From a clinical execution perspective, we concluded it would be advantageous to incorporate Sigyn Therapy in series with normally scheduled dialysis treatments of enrolled ESRD patients with established blood access. We also believe that the high incidence of ESRD inflammation and endotoxemia may optimize patient enrollment in a non-intensive care environment and allow for the collection of secondary data endpoints that will contribute to the potential advancement of Sigyn Therapy in other indications," concluded Joyce.

In addition to evaluating the safety of Sigyn Therapy in health compromised ESRD patients, the Company plans to quantify changes in circulating levels of endotoxin (gram-negative bacterial toxin) and inflammatory cytokines including, tumor necrosis factor-a (TNF-a), interleukin-1b (IL-1-b), and interleukin-6 (IL-6) before and after each administration of Sigyn Therapy. Previously conducted *in vitro* studies have validated the ability of Sigyn Therapy to address each of these therapeutic targets, which are also associated with sepsis (leading cause of hospital deaths worldwide), community-acquired pneumonia (a leading cause of

death among infectious diseases) and emerging pandemic threats.

Based on its disclosed intent to enroll ESRD patients, the Company is updating an Investigational Device Exemption (IDE) that it drafted for submission to the U.S. Food and Drug Administration ("FDA") related to the potential initiation of human feasibility studies. However, there is no assurance that human feasibility or pivotal studies will demonstrate Sigyn Therapy to be a safe and efficacious treatment for any candidate treatment indication. The Company further reported that it has downgraded its clinical interest in treating hepatic encephalopathy and other liver-associated disorders at this time.

Summary of Candidate Treatment Indications

Candidate treatment indications for Sigyn Therapy are primarily comprised of pathogen-associated inflammatory disorders that are not addressed with approved drug therapies.

ESRD Inflammation & Endotoxemia

According to the USRDS, more than 550,000 individuals suffer from end-stage renal disease (ESRD), which results in approximately 85 million kidney dialysis treatments being administered in the United States each year. Persistent inflammation is a hallmark feature of ESRD dialysis patients as reflected by the excess production of inflammatory cytokines, including tumor necrosis factor-a (TNF-a), interleukin-1b (IL-1b) and interleukin-6 (IL-6), which contribute to increased all-cause mortality. ESRD inflammation can also induce intestinal permeability, which allows endotoxin (gram-negative bacterial toxin) to translocate from the gut and into the bloodstream. Beyond fueling further inflammation, endotoxin is a potent activator of sepsis, which can lead to multiple organ failure and death.

At present, there are no approved drugs to treat excessive inflammation and endotoxemia that commonly occurs in end-stage renal disease patients.

Sepsis

Sepsis is defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection. In January of 2020, a report entitled; *"Global, Regional, and National Sepsis Incidence and Mortality,"* was published in the Journal Lancet. The publication reported 48.9 million cases of sepsis and 11 million deaths in 2017. In that same year, an estimated 20.3 million sepsis cases and 2.9 million deaths were among children younger than 5-years old. In the United States, sepsis was reported to be the most common cause of hospital deaths with an annual financial burden that exceeds $24 billion.

At present, there are no approved drugs to treat sepsis, which is commonly induced by a viral or bacterial infection. Sigyn Therapy establishes a strategy to address a broad-spectrum of pathogen sources in concert with controlling dysregulated cytokine production (the cytokine storm), which is a hallmark of sepsis.

Community Acquired Pneumonia

According to the American Thoracic Society, Community Acquired Pneumonia (CAP) is a leading cause of death among infectious diseases, the leading cause of death in children under five years of age, and a catalyst for approximately 50% of sepsis and septic shock cases. In the United States, more than 1.5 million individuals are hospitalized with CAP

each year, resulting in an annual financial burden that exceeds $10 billion.

In a recent study of 2,259 patients hospitalized with pneumonia, ninety seven percent (97%) of cases were either viral or bacterial in origin. Sigyn Therapy offers a broad-spectrum mechanism to deplete the bloodstream presence of viral pathogens and bacterial toxins. Additionally, Sigyn Therapy may assist to control the excess production of inflammatory cytokines that can lead to sepsis.

Emerging Pandemic Threats

Covid-19 affirmed the use of extracorporeal blood purification devices as first-line countermeasures to treat an emerging pandemic threat. On March 24, 2020, the U.S. Department of Health and Human Services (HHS) declared that the emergence of COVID-19 justified the Emergency-Use Authorization (EUA) of drugs, biological products, and medical devices to combat the pandemic. Within a month, the FDA awarded an EUA to four different blood purification therapies. In connection with these authorizations, FDA published a statement that blood purification devices may be effective at treating patients with confirmed COVID-19 by reducing various pathogens, cytokines, and other inflammatory mediators from the bloodstream.

Consistent with FDA's statement, Sigyn Therapy addresses pathogen sources of life-threatening inflammation in concert with the broad-spectrum depletion of cytokines and other inflammatory mediators from the bloodstream. Sigyn Therapy provides a candidate strategy to address future pandemic outbreaks, which are increasingly being fueled by a confluence of global warming, urban crowding, and intercontinental travel.

Sigyn Therapy also aligns with HHS initiatives established through the Public Health Emergency Medical Countermeasure Enterprise (PHEMCE) that support the development of broad-spectrum medical countermeasures that can mitigate the impact of an emerging pandemic, yet also have viability in established disease indications.

About Sigyn Therapeutics™

Sigyn Therapeutics is a development-stage company focused on the creation of therapeutic solutions that address unmet needs in global health.

Sigyn Therapy™ is a broad-spectrum blood purification device designed to address pathogen-associated inflammatory disorders that are not addressed with an approved drug therapy. To accomplish such unmet medical needs, Sigyn Therapy extracts pathogen sources of life-threatening inflammation in concert with dampening down the dysregulated overproduction of inflammatory cytokines.

In vitro blood purification studies have demonstrated the potential of Sigyn Therapy to address a broad-spectrum of relevant therapeutic targets, including endotoxin (gram-negative bacterial toxin); peptidoglycan and lipoteichoic acid (gram-positive bacterial toxins); viral pathogens (including SARS-CoV-2); CytoVesicles (extracellular vesicles that transport inflammatory cytokine cargos); and tumor necrosis factor alpha (TNF alpha), interleukin-1 beta (IL-1b), and interleukin 6 (IL-6), which are inflammatory cytokines that play a prominent role in each Sigyn Therapy treatment indication. Subsequent to these milestone achievements, Sigyn Therapy has been demonstrated to be well tolerated in animal studies.

Based on Sigyn Therapy's ability to isolate and extract viral pathogens, bacterial toxins, and inflammatory cytokines from the bloodstream, candidate treatment indications include pathogen-associated sepsis (leading cause of hospital deaths), community acquired pneumonia (a leading cause of death among infectious diseases), emerging pandemic threats, and inflammation & endotoxemia that commonly occurs in end-stage renal disease patients.

To learn more about our therapeutic endeavors, market opportunities and management team, we encourage to visit our website at: www.SigynTherapeutics.com

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 for the year ended December 31, 2021, 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.

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