January 4, 2024

Sigyn Therapeutics Releases Letter to Shareholders

SAN DIEGO, CA, Jan. 04, 2024 (GLOBE NEWSWIRE) -- via NewMediaWire -- Sigyn Therapeutics, Inc. (“Sigyn” or the “Company”) (OTCQB: SIGY), a development-stage medical technology company, today announced the release of a shareholder letter authored by Chairman and Chief Executive Officer, Jim Joyce.

Dear Fellow Shareholder,

As a small organization operating in a world with short-term expectations, we have not wavered from making decisions and sacrifices that support our long-term objective to build an enduring organization whose therapies save lives. The goal of this letter is to help you better understand our opportunities, our challenges, and decision-making processes.

Over the past eighteen months, we set the stage for first-in-human studies of Sigyn Therapy™ and quietly built a foundation for therapeutic devices to enhance the performance of cancer therapies. More specifically, we leveraged industry relationships to redefine our lead treatment indication for Sigyn Therapy™ and we designed novel devices that offer to overcome the delivery limitations of chemotherapy and immunotherapeutic antibodies to treat cancer. As you will learn, these critically important drug agents are inadequately delivered to intended cancer targets.

Our decision process to develop a new therapy is guided by various factors but must include two prerequisites: 1.) the candidate therapy must offer to overcome a clearly defined limitation in healthcare, and 2.) the successful clinical advancement of the candidate would establish a potential competitive advantage that could disrupt the business model of established therapeutic organizations. I urge you to read the entirety of this letter with the hope you concur our product candidates meet these development prerequisites.

However, I first want to provide an update on our proposed underwritten financing. At present, we have an S-1 registration statement on file with the U.S. Securities and Exchange Commission (SEC) (available at www.sec.gov) to support a financing whose proceeds will advance our clinical programs and potentially allow us to meet the exchange listing requirements of the Nasdaq Capital Market. While our S-1 is on file, we remain in a quiet period that limits the information we can release until the SEC staff declares our registration statement to be effective. However, we are permitted to publish factual information that is material to our business.

This process seems to overshadow the extent to which we transformed our business since the initial submission of our S-1 to the SEC. In that submission, our endeavors were solely predicated on the development and clinical advancement of Sigyn Therapy™. As reflected in recent S-1 amendments, our endeavors today are comprised of Sigyn Therapy™ to

address pathogen-associated inflammatory disorders, the ImmunePrep^{TM} platform to enhance the performance of immunotherapeutic antibodies, ChemoPrep^{TM} to improve the delivery of chemotherapy, and ChemoPure^{TM} to reduce chemotoxicity. Furthermore, our clinical plan to advance Sigyn Therapy^{TM} has evolved to become more expansive and enrollable, with clinical sites and principal investigators now in place for first-in-human studies.

With support from industry colleagues and the steadfast dedication of our team, we established a lineup of therapeutic candidates that is unique within our industry.

The ImmunePrep^{TM} Platform

Immunotherapeutic antibodies to treat cancer are among the most valued assets in global medicine. However, these drugs suffer from a severe limitation. They are poorly delivered to cancer cell targets and as a result, a majority of patients don't respond to therapy. FACT!

Only a fraction of an antibody dose reaches its cancer cell target, yet a significant portion of the same dose can be sequestered from delivery by circulating decoys that display the target (antigen) binding site of the antibody. Amazingly, with more than 1,000 therapeutic antibodies being evaluated in human studies, there was no strategy to reduce the circulating presence of decoys that block the delivery of these drugs.

In response, we designed the ImmunePrep^{TM} platform. Mechanistically, ImmunePrep^{TM} is intended to leverage the use of therapeutic antibodies to create extracorporeal blood purification devices that sweep antibody decoys from the bloodstream prior to the subsequent infusion (normal delivery) of the same therapeutic antibody. We believe this reverse decoy mechanism will increase the availability of antibodies to interact with their intended targets and simultaneously, ImmunePrep^{TM} devices are expected to extract disease targets from the bloodstream to further improve patient benefit. Our regulatory strategy is initially directed toward the development of ImmunePrep^{TM} products that incorporate market-cleared antibodies already demonstrated to be safe and effective in human studies.

Regarding my statement of therapeutic antibodies being among the most valued assets in global medicine, consider that Pfizer's $43 billion acquisition of Seagen, Inc. and Amgen's $27.8 billion acquisition of Horizon Therapeutics were the highest valued M&A deals of 2023. In both cases, transaction values were driven by market-cleared antibody assets.

Perhaps more revealing were the values placed on clinical-stage (pre-revenue) therapeutic antibody candidates. In this regard, consider Merck's $10.8 billion acquisition of Prometheus Biosciences and Roche's $7 billion acquisition of a clinical-stage antibody from Roivant Sciences.

In the backdrop of these M&A transactions, the immune checkpoint antibody Keytruda (Merck) became the world's best-selling (non-vaccine) drug in 2023 with anticipated revenues of ~$24 billion.

ImmunePrep^{TM} is a development-stage platform that introduces a device strategy to synergistically enhance the performance of these highly valued drug assets.

ChemoPrep™ & ChemoPure™

Recent scientific publications have reported that only 1% of chemotherapy is successfully delivered to the tumor cell targets of cancer patients. In response, we began to investigate strategies to overcome the delivery limitations of the most commonly administered drug to treat cancer. Inversely, we recognized if 99% of chemotherapy was missing its therapeutic target, then there was an additional need to remove off-target chemotherapy from the bloodstream to reduce toxicity and limit organ damage.

These thoughts, along with some pre-clinical data evolved into a patent submission entitled: *"Systems and Methods to Enhance Chemotherapy Delivery and Reduce Toxicity."* This pending patent underlies our therapeutic system comprised of ChemoPrep™ which is intended to enhance the tumor site delivery of chemotherapy and ChemoPure™ to reduce its toxicity.

To enhance chemotherapy delivery, we designed ChemoPrep™ to reduce the circulating presence of tumor-derived exosomes (cancer exosomes) that interfere with chemotherapy delivery and contribute to treatment resistance. As might be expected, high concentrations of cancer exosomes in the bloodstream correspond with poor treatment outcomes, whereas low concentrations are associated with more favorable outcomes. As compared to non-cancer subjects, exosome populations are reported to be 10x to 500x higher in the bloodstream of cancer patients.

There is a compelling scientific rationale to reduce the circulating presence of cancer exosomes prior to chemotherapy administration. In this regard, we envision the possibility of improving chemotherapy delivery with lower doses. Such an achievement could contribute to addressing ongoing drug shortages that have limited the availability of chemotherapy to cancer patients.

Post-chemotherapy administration, ChemoPure™ is intended to reduce treatment toxicity by depleting the presence of off-target chemotherapy from the bloodstream. A reduction in chemotoxicity may also alleviate treatment-related fatigue and temper the long-term health consequences associated with chemotherapy administration.

Sigyn Therapy™

We are advancing Sigyn Therapy™ to treat pathogen-associated inflammatory disorders that are not addressed with FDA approved drugs. Our candidate treatment indications include community-acquired pneumonia, drug-resistant viral & bacterial infections, endotoxemia, and sepsis, the leading cause of hospital deaths in the United States.

Our technology has the following attributes and capabilities:

- Sigyn Therapy™ incorporates a formulation of adsorbent components that have more than 200,000 square meters (~50 acres) of surface area on which to adsorb and remove therapeutic targets from the bloodstream.
- *In vitro* studies have demonstrated the ability of Sigyn Therapy™ to reduce life-threatening pathogen and inflammatory disease targets from human blood plasma. In

these studies, twelve relevant targets, including viral pathogens, bacterial toxins, and inflammatory cytokines were validated. Subsequent animal studies have been conducted at the University of Michigan. GO WOLVERINES!

- Sigyn Therapy™ is highly efficient as the entire circulatory system of a patient can pass through the device ~15-times during a four-hour treatment.

- To allow for potential broad-market deployment, we designed Sigyn Therapy™ for use on the established infrastructure of dialysis and continuous renal replacement machines already located in hospitals and clinics around the world.

We believe the successful clinical advancement of Sigyn Therapy™ could offer a strategic competitive advantage within the dialysis industry. As such, the treatment protocol of first-in-human studies calls for the enrollment of dialysis dependent end-stage renal disease (ESRD) patients with endotoxemia and concurrent inflammation. These are untreatable conditions associated with cardiovascular disease, the leading cause of ESRD patient deaths. Endotoxemia and inflammation also underlie other common causes of ESRD mortality, including viral and bacterial infections that induce sepsis.

A strategy that extended the lives of ESRD patients should be of considerable value to the dialysis industry. Consider that there are more than 550,000 individuals with ESRD in the United States, which results in approximately 85 million dialysis treatments being administered each year. Once on dialysis, the five-year survival rate of an ESRD patient is just 42%. A large percentage of ESRD patients suffer from endotoxemia and/or chronic inflammation. Most are treated by either Fresenius Medical Care or DaVita Kidney Care.

In 2022, Fresenius generated $14.5 billion in revenues through the administration of 31.8 million dialysis treatments to the 208,310 ESRD patients in their North American network. During the same year, DaVita generated $11.6 billion in revenues based on administering 30 million dialysis treatments to the 199,400 ESRD patients in their North American network.

Based on 2022 numbers, extending the life of Fresenius network patients by just one month would be worth ~ $1.2 billion in added revenues to Fresenius, whereas DaVita would add almost $1 billion in revenues per month of extended life of their patients. Fresenius and DaVita also lose revenues when their patients are hospitalized, which is a common occurrence. In this regard, each week of reduced hospitalization is worth ~ $300 million in added revenues for Fresenius and ~$240 million for DaVita.

Our business and clinical strategy to enroll ESRD patients was established with feedback from dialysis industry executives. Furthermore, we leveraged our industry relationships to craft the protocol of our first-in-human clinical studies, to establish multiple clinical site locations, and identify our principal investigators.

To support our proposed study, we have drafted an Investigational Device Exemption (IDE) for submission to the FDA that calls for the enrollment of 12-15 ESRD patients with endotoxemia and concurrent inflammation. In the proposed study, Sigyn Therapy™ will be combined in series with each enrolled subjects normally scheduled dialysis treatments. While our primary objective is to demonstrate treatment safety, we will also quantify changes in endotoxin and inflammatory cytokine levels that result from Sigyn Therapy™ administration. The successful completion of this study would then set the stage for us to pursue pivotal

efficacy studies necessary for market approval.

In closing, we have created an expansive lineup of therapeutic candidates with support from industry colleagues and the steadfast dedication of our team. A team that is not naïve to the challenges of advancing medical devices through FDA. A team focused on building an enduring organization whose therapies save lives.

On behalf of Sigyn's board of directors and employees, I thank you for your support and belief in our endeavors.

James A. Joyce

Chairman and Chief Executive Officer

January 4, 2024

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, 2022, 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.

Contact:

Jim Joyce
Chairman, CEO
Phone: 619.353.0800
Email: jj@SigynTherapeutics.com

Source: Sigyn Therapeutics, Inc.