April 18, 2023

Sonnet BioTherapeutics Announces Updated Clinical Data for SON-1010 at the 2023 American Association for Cancer Research (AACR) Annual Meeting

- **The SB101 and SB102 Phase 1 studies have together dosed 46 subjects to date as SB101 dose escalation continues**
- **Cytokine data reveals extended PK profile for SON-1010**
  - **Induces prolonged and controlled IFNγ response**
  - **No evidence of cytokine release syndrome**
- **Clinical benefit was seen in 36% of patients (5/14) with advanced solid tumors**

PRINCETON, NJ / ACCESSWIRE / April 18, 2022 /Sonnet BioTherapeutics Holdings, Inc. (NASDAQ:SONN) (the "Company" or "Sonnet"), a clinical-stage company developing targeted immunotherapeutic drugs, announced today that the safety of SON-1010 dosing has been formally reviewed in both of the current Phase 1 clinical trials, and the Company is now enrolling the final dose cohort in the cancer trial. SON-1010 is a proprietary version of human interleukin-12 (IL-12), configured using Sonnet's Fully Human Albumin Binding ($F_HAB^®$) platform. SB101 is a single-ascending dose (SAD) trial for adult patients with advanced solid tumors (NCT05352750) that commenced in Q2 2022 and is currently enrolling the final dose cohort. SB102 is a SAD trial in healthy volunteers (NCT05408572) that started in Q3 2022, and the safety review of the last cohort was recently completed. Updated SB101 data was presented in a poster presentation today at AACR, and data from both studies will be discussed by the Company in a webinar today at 5:00 pm ET.

"We have now dosed 15 cancer patients at increasing drug levels in the SB101 study and have completed dosing in 31 healthy volunteers in SB102," said Richard Kenney, M.D., Sonnet's Chief Medical Officer. "No dose-limiting toxicities have occurred to date and the formal safety reviews after each cohort have revealed a safety and toxicity profile that is typical for a Phase 1 oncology trial, with the majority of adverse events being reported as mild, and all are transient, with no evidence of Cytokine Release Syndrome observed. The SB102 study has allowed us to generate clean data for the initial pharmacokinetic (PK) analysis, which enabled us to simulate the effect of multiple doses with the help of a continual reassessment model of PK."

Of the 15 patients from the first five cohorts of SB101 evaluable for follow-up at this latest cutoff, 9 had stable disease at the first follow-up scan, 4 of which were already progressing at study entry. At four months follow-up, 5 of 14 patients remained stable at the second scan, suggesting clinical benefit of SON-1010 in 36% of patients. The very first patient dosed, with an aggressive endometrial sarcoma, had target tumor shrinkage with complete resolution of ascites at one point and has been clinically stable for nearly a year. Dosing in

the first 3 cohorts was performed every 4 weeks, but is now being done every 3 weeks in the new cohorts to enhance safety at higher doses.

SON-1010 has been safe and tolerable at all doses tested to date. Adverse events have generally been mild/moderate and transient in nature, with no study discontinuations for safety reasons. In addition, adverse effects have been less numerous and less intense with subsequent doses. The geomean half-life ($t_{½}$) of SON-1010 was 113 hours in SB101 and 122 hours in SB102, compared to 12 hours for recombinant IL-12 observed in prior studies. Comparison of the PK curves between the two studies suggests that SON-1010 may be targeting tumors, as it was designed to do. Cytokine analysis following each dose revealed controlled and prolonged induction of interferon gamma (IFNγ) that peaked at 24 to 48 hours and returned to baseline after 2 to 4 weeks. A small increase in IL-10 was observed with each dose as expected in response to IFNγ. There was either a minimal or no signal for IL-1β, IL-6, IL-8, and TNFα and no indication of any potential for cytokine release syndrome (CRS) at these doses.

"We study cancer patients to give us a sense of the safety and activity at higher doses, while the use of healthy volunteers lets us rapidly get clean PK and PD data without the background of prior cancer treatment," said Pankaj Mohan, Ph.D., Sonnet Founder and Chief Executive Officer. "We are very pleased with the data we are seeing with these early dose levels, with safety and tolerability being well within expected levels, as well as displaying early signs of SON-1010's extended PK and clinical activity. It is important to note that many of these patients have been fighting their cancers for a very long time and have exhausted all approved treatment regimens available to them, so seeing tumor shrinkage at any dose is both difficult to achieve and encouraging for future results. Based on these data, we are excited to study the impact of SON-1010 in patients with platinum-resistant ovarian cancer, both as monotherapy at the highest dose in the current cancer study and in our next clinical study in combination with the Roche checkpoint inhibitor atezolizmab (Tecentriq®). We believe these results set a positive tone for our ongoing business development initiatives, and we are comfortable that our cash on the balance sheet will give us operating runway into the 2024 calendar year."

Webcast

Investors and analysts are invited to join a webcast presentation of the SON-1010 results conducted by CEO Pankaj Mohan, Ph.D. and CMO Richard Kenney, M.D. today, April 18th, at 5 pm ET. The webcast at 5:00 pm ET, with an accompanying presentation, will be accessible under News & Events, IR Calendar in the Investors section of the company's website. The archived audio webcast will be available on Sonnet's website following the call.

To participate in the webcast, please see the following details:

- Webcast Link: https://event.webcasts.com/starthere.jsp?ei=1607729&tp_key=f6d5c78778
- Toll Free: 1-877-869-3847
- International: +1-201-689-8261
- Conference ID: 13737737

About SON-1010

SON-1010 is a candidate immunotherapeutic recombinant drug that links unmodified single-chain human IL-12 with the albumin-binding domain of the single-chain antibody fragment A10m3. This was selected to bind both at normal pH, as well as at an acidic pH typically found in the tumor microenvironment (TME). The F_HAB technology targets tumor and lymphatic tissue, providing a mechanism for dose sparing and an opportunity to improve the safety and efficacy profile of not only IL-12, but a variety of potent immunomodulators using the platform. Interleukin-12 can orchestrate a robust immune response to many cancers and pathogens. Given the types of proteins induced in the TME, such as the Secreted Protein and Rich in Cysteine (SPARC) and glycoprotein 60 (GP60), several types of cancer such as non-small cell lung cancer, melanoma, head and neck cancer, sarcoma, and some gynecological cancers are particularly relevant for this approach. SON-1010 is designed to deliver IL-12 to local tumor tissue, turning ‘cold' tumors ‘hot' by stimulating IFNγ, which activates innate and adaptive immune cells and increases the production of Programed Death Ligand 1 (PD-L1) on tumor cells.

About the SB101 Phase 1 Trial

This first-in-human study is primarily designed to evaluate the safety of multiple ascending doses of SON-1010 in cancer patients and is being conducted at several sites across the United States. While the optimal dose is unknown at this stage, the potential to target tumors, the extended PK mechanism and our preclinical data suggest the therapeutic dose may be lower compared to native human IL-12. The study, utilizing a standard 3+3 oncology design in at least five cohorts, should establish the MTD and the recommended Phase 2 dose (RP2D) using monthly subcutaneous injections of SON-1010. The primary endpoint explores the safety and tolerability of SON-1010, with key secondary endpoints intended to measure pharmacokinetics (PK), pharmacodynamics (PD), immunogenicity, and anti-tumor activity. This study will form the basis for potential combinations with other types of immunotherapies and the future development of bispecific candidates using the FHAB platform.

About the SB102 Phase 1 Trial

The SB102 study is designed to robustly evaluate the safety, PK and PD of single ascending doses of SON-1010, using larger groups of healthy volunteers, and was conducted at a single site in Australia. The study was done in a blinded fashion, comparing a single dose of SON-1010 to placebo utilizing five cohorts. Both PK and PD were be closely followed during dose escalation in this double-blind, placebo-controlled study, along with an assessment of the cellular immune responses at each dose using sophisticated fluorescence activated cell sorting (FACS) analysis. The primary endpoint explores the safety and tolerability of SON-1010, with key secondary endpoints intended to measure PK, PD, and immunogenicity.

About Sonnet BioTherapeutics Holdings, Inc.

Sonnet BioTherapeutics is an oncology-focused biotechnology company with a proprietary platform for innovating biologic drugs of single or bispecific, bifunctional action. Known as FHAB (Fully Human Albumin Binding), the technology utilizes a fully human single chain antibody fragment (scFv) that binds to and "hitch-hikes" on human serum albumin (HSA) for transport to target tissues. Sonnet's FHAB was designed to specifically target tumor and lymphatic tissue, with an improved therapeutic window for optimizing the safety and efficacy of immune modulating biologic drugs. FHAB is the foundation of a modular, plug-and-play

construct for potentiating a range of large molecule therapeutic classes, including cytokines, peptides, antibodies, and vaccines.

Forward-Looking Statements

This press release contains certain 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 and Private Securities Litigation Reform Act, as amended, including those relating to the Company's product development, clinical and regulatory timelines, market opportunity, competitive position, possible or assumed future results of operations, business strategies, potential growth opportunities and other statements that are predictive in nature. These forward-looking statements are based on current expectations, estimates, forecasts and projections about the industry and markets in which we operate and management's current beliefs and assumptions.

These statements may be identified by the use of forward-looking expressions, including, but not limited to, "expect," "anticipate," "intend," "plan," "believe," "estimate," "potential, "predict," "project," "should," "would" and similar expressions and the negatives of those terms. These statements relate to future events or our financial performance and involve known and unknown risks, uncertainties, and other factors which may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Such factors include those set forth in the Company's filings with the Securities and Exchange Commission. Prospective investors are cautioned not to place undue reliance on such forward-looking statements, which speak only as of the date of this press release. The Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

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