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Sonnet BioTherapeutics Announces Interim Data in Two Phase 1 Dose-Escalation Trials of SON-1010

- ***The SB101 and SB102 studies have together dosed 36 subjects to date as dose escalation continues***
- ***Cytokine data show extended pharmacokinetics of SON-1010 with controlled induction of IFNγ and no signs of cytokine release syndrome***
- ***All but one patient remain on study, with evidence of tumor improvement at 6 months in one patient***

PRINCETON, NJ / ACCESSWIRE / November 2, 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 in several cohorts has been formally reviewed in both Phase 1 clinical trials and that dose escalation is continuing as early data becomes available. 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 multiple-dose trial for adult patients with advanced solid tumors (NCT05352750) that commenced in April and has now started treating the fourth dose cohort. SB102 is a single-ascending dose trial in healthy volunteers (NCT05408572) that started in July and is dosing the third cohort. Safety Review Committees found no safety concerns and approved advancing to the next higher dose levels for both studies. The data will be presented at a webinar at 8:30 am ET today. The data will also be presented at an upcoming medical conference.

"We have now dosed 12 cancer patients at increasing drug levels in the SB101 study and 24 healthy volunteers in SB102," said Richard Kenney, M.D., Sonnet's Chief Medical Officer. "No dose-limiting toxicities have occurred to date using this novel approach to enhance the safety of cytokine-based immunotherapy and we are starting to get encouraging data back on the pharmacokinetic (PK) and pharmacodynamic (PD) responses. By linking the IL-12 cytokine to an albumin-binding domain that can target tumor tissue and extend the cytokine half-life in the body, we believe our proprietary F_HAB technology will allow us to use higher doses of cytokines without triggering unacceptable toxicity. This could be the key to inducing a successful local immune response to Il-12 in the tumor microenvironment (TME)."

The clinical dose-escalation strategy was developed based on the ability to use this non-cytotoxic drug in a single-ascending dose (SAD) study in healthy volunteers to rapidly provide clean PK/PD data without interpretation challenges from prior cancer treatment effects. The initial safety and PD data are being used to evaluate the immune response to SON-1010 and predict the effect of further dose escalation. IL-12 has been shown to stimulate the production of interferon-gamma (IFNγ), which is necessary for its antitumor effects. Sonnet is using the known protective effects of IL-12 dose timing to minimize toxicity

and extend the maximum tolerated dose (MTD).

The adverse events have generally been mild/moderate, transient in nature, and have all been tolerable. In addition, they have been less numerous and less intense with subsequent doses. Acute inflammation in both studies was assessed with a Luminex bead assay for multiple cytokine analytes. IL-12p70 (used to measure SON-1010 concentration) was readily quantified and demonstrated extended pharmacokinetics. The resulting increase in IFNγ (showing an IL-12 effect and potential for tumor control) was dose-related, controlled, and prolonged. There was minimal/no signal for IL-1β, IL-6, IL-8, or TNFα and no indication of cytokine release syndrome (CRS). IL-10 was also induced at a low level, as expected. Even though these patients with advanced solid tumors have been heavily pretreated and many had actively progressive disease at study entry, all but one patient remain on study.

Of the 6 patients from the first two cohorts evaluable for follow-up at this latest cutoff, 5 of the 6 had stable disease at the first follow-up scan, with one patient progressing who is now off study. As of the most recent scan, 2 of the 5 stable disease patients remain stable, while the others had tumor growth that may simply represent tumor inflammation or unconfirmed progression. One patient with endometrial stromal sarcoma who was progressing at study entry now has evidence of improvement after 6 months on SON-1010 with smaller tumors and complete resolution of her ascites.

"We are highly encouraged by these data, some of which shows early signs of SON-1010 activity in the tumors at these initial dose levels that are accompanied by a tolerable safety profile," said Pankaj Mohan, Ph.D., Sonnet Founder and Chief Executive Officer. "As the first F_HAB technology-derived candidate dosed in patients, we believe the demonstration of extended PK with SON-1010 represents a significant step forward in Sonnet's approach to immunotherapy with the F_HAB platform. These studies are expected to form the basis for combinations with other immunotherapies that could have synergistic effects on cancer and that we expect will support potential licensing activities."

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 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 will be 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 is being conducted at a single site in Australia. The study is done in a blinded fashion, comparing a single dose of SON-1010 to placebo utilizing five cohorts. Both PK and PD will 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 action. Known as F_HAB (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 F_HAB 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. F_HAB 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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