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Sonnet's SON-1010 Demonstrates a Strong Safety Profile in Combination with Atezolizumab for Treatment of Platinum-Resistant Ovarian Cancer, Including a Partial Response at the Highest Dose

Topline safety data in SB221 study suggest clinical benefit of SON-1010 in combination with atezolizumab (Tecentriq®)

The maximum tolerated dose (MTD) of SON-1010 was set at 1200 ng/kg in combination with atezolizumab in patients with platinum-resistant ovarian cancer (PROC), without dose-limiting toxicity or evidence of cytokine release syndrome at any dose level

Stable disease (SD) at four months post-initiation of dosing was seen in 5 of 15 evaluable patients (33%), with 4 continuing beyond 6 months

One patient with PROC who was dosed at the MTD had a partial response (PR) by RECIST criteria (44% decrease from baseline) and >2x decrease in the CA 125 biomarker

Sonnet management and the lead PI for the SB221 study discuss the safety data in a "What This Means" webinar; Access here

PRINCETON, N.J., April 04, 2025 (GLOBE NEWSWIRE) -- Sonnet BioTherapeutics Holdings, Inc. (NASDAQ:SONN) (the "Company" or "Sonnet"), a clinical-stage company developing immunotherapeutic drugs targeting the tumor microenvironment (TME), announced today positive safety results of SON-1010 (IL12-F_HAB) at the highest dose combined with atezolizumab in the Phase 1b/2a clinical trial in adult patients with advanced solid tumors or platinum-resistant ovarian cancer (PROC) (the SB221 study). Based on positive feedback from a formal evaluation by the Safety Review Committee (SRC) for the SB221 study, the study can now advance to the expansion phase, which will study the preliminary effect of the combination at the MTD, before proceeding to a Phase 2a randomized comparison with the standard of care in patients with PROC. Additionally, the Company announced the release of a "What This Means" webinar discussing the interim SB221 safety data, now available here.

The SB221 study was designed to assess the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of increasing doses of SON-1010 administered with atezolizumab. The primary goal for the first part of the study was to establish the MTD in combination with the immune checkpoint inhibitor (ICI). A total of 19 subjects were treated during dose escalation and one patient with PROC had a partial response at the highest dose.

The SB221 SRC review at the completion of dose expansion in combination with atezolizumab concluded that fatigue, fevers, and gastrointestinal symptoms were the most common adverse effects; no dose-limiting toxicity or cytokine release syndrome were seen. The only related serious adverse event (SAE) during dose escalation was Grade 2 pneumonitis, which is a known adverse event with atezolizumab. One patient with PROC had a 44% tumor size reduction, indicating a partial response (PR), along with a more than 2-fold reduction in the CA 125 ovarian cancer biomarker. SON-1010 monotherapy in the SB101 study led to a PR at the same MTD in a patient with sarcoma.

“Platinum resistant ovarian cancer patients remain a very difficult group to treat, and these patients continue to have low response rates to currently approved therapies,” said Robert Wenham, M.D., Chair of the Department of GYN Oncology at Moffitt Cancer Center and the study’s lead Principal Investigator. “It has been difficult to show efficacy using existing immune drugs like checkpoint inhibitors. This patient’s tumor reduction using an ICI in combination with a novel extended PK IL-12 immune therapeutic is exciting. We are looking forward to entering the next stage of the SB221 trial.”

SON-1010 may work best with an ICI, particularly with immunologically ‘cold’ tumors that are high in secreted protein acidic and rich in cysteine (SPARC), such as ovarian cancer. Binding to native albumin in the serum extends the half-life and bioactivity of the IL-12 component, which also allows targeting of and retention in the TME by strong binding to gp60 and SPARC. Safety has been a concern since the initial Phase 2 study of rhIL-12 in the late 1990’s, where daily dosing led to severe adverse effects. While safer dosing strategies have since been developed with rhIL-12, the promise of improved tumor control in humans has not been achieved using doses that are also demonstrated to be safe. Linking the IL-12 to a fully human single chain variable fragment (scFv) that binds albumin and extends the half-life may finally allow higher doses that are potentially more effective to be given safely. The preclinical and mechanistic characterization of SON-1010, the Company’s proprietary version of recombinant human interleukin-12 (rhIL-12) configured using genetic fusion to Sonnet's Fully Human Albumin Binding (F_HAB®) platform, was recently published here.

“We are encouraged by the topline safety data and very pleased with the ovarian cancer PR in the Phase 1b portion of the SB221 study. Given the history of safety concerns with rhIL-12, it is exciting to see higher doses of SON-1010 demonstrating minimal toxicity when used in combination with atezolizumab,” added Richard Kenney, M.D., Sonnet's Chief Medical Officer. “We may finally be able to realize the promising antitumor effect that has been associated with this cytokine in preclinical models for decades. While the clinical benefit we have seen during dose escalation has been reassuring, the PR at the highest dose is particularly important, as this suggests that there may be a synergistic therapeutic effect in combination with checkpoint inhibitors or chemotherapy.”

All enrolled patients have advanced solid tumors and all patients at the higher doses have PROC, including those enrolled in a final 1200 ng/kg dose-escalation cohort. The SB221 trial employed a ‘desensitizing’ first dose of 300 ng/kg to take advantage of the known tachyphylaxis with rhIL-12, with the intention of minimizing toxicity while allowing for higher maintenance doses. The safety and toxicity profile that has developed is typical for a Phase 1 oncology trial, with the majority of adverse events (AEs) being reported as mild and transient and there has been no evidence of cytokine release syndrome. Of the 19 patients

dosed to date, 8 of the 15 evaluable patients (53%) had SD at the first follow-up CT scan and 5 of the 15 evaluable patients (33%) remained stable at four months, suggesting SON-1010 is showing clinical benefit. While the follow-up is still early, four of those 15 patients were still on trial at 6 months, including 3 with SD and one with an unconfirmed PD. As noted, one of the PROC patients in the highest SON-1010 dose cohort had a PR at 2 months.

“This topline safety data release from our atezolizumab combination program is another significant milestone for Sonnet’s clinical development,” concluded Raghu Rao, Sonnet’s Interim Chief Executive Officer. “Safety of this extended PK version of IL-12 has been within expected levels and the comparison with dosing in healthy volunteers provided strong evidence of tumor targeting and accumulation in humans. We have used this trial to establish the MTD of combination with an ICI and will continue to follow the patients currently being treated to assess longer-term safety and tumor responses. Sonnet continues to seek partnership opportunities to help support later stage development of SON-1010.”

For more information about the Phase 1b/2a SB221 study in adult patients with advanced solid tumors or PROC, visit www.clinicaltrials.com and reference identifier NCT05756907. Tecentriq® (atezolizumab) is a registered trademark of Genentech, a member of the Roche Group.

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 single-chain antibody fragment was selected to bind albumin both at normal pH, as well as at the 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 that can be linked 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 SPARC and 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 to this approach. SON-1010 is designed to deliver IL-12 to local tumor tissue, turning ‘cold' tumors ‘hot' by stimulating IFN, which activates innate and adaptive immune cell responses and increases the production of Programed Death Ligand 1 (PD-L1) on tumor cells.

About the SB221 Phase 1b/2a Trial

SB221 is a global Phase 1b/2a multicenter, dose-escalation and randomized proof-of-concept study to assess the safety, tolerability, PK, PD, and efficacy of SON-1010 administered subcutaneously (SC), either alone or in combination with atezolizumab given intravenously (IV). The study is designed in Part 1 to rapidly establish the maximum tolerated dose (MTD) of the combination, starting in patients with advanced solid tumors and moving to PROC in small dose-escalation groups, then to expand the dataset at the recommended Phase 2 dose (RP2D) to show the likelihood of efficacy in PROC using a standard 2-stage design. This would be followed in Part 2 by an assessment in patients with PROC of the potential for improved efficacy of the combination over SON-1010 alone or the

standard of care. Both Sonnet and Roche look forward to this collaboration as an opportunity to improve outcomes for patients with ovarian cancer.

About Sonnet BioTherapeutics Holdings, Inc.

Sonnet is an oncology-focused biotechnology company with a proprietary platform for developing targeted biologic drugs with single or bifunctional 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 platform 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.

Sonnet's lead program, SON-1010, or IL-12-F_HAB, is in development for the treatment of solid tumors, certain types of sarcoma, and ovarian cancer. SON-1010 is being evaluated in an ongoing Phase 1/2a study through a Master Clinical Trial and Supply Agreement, along with ancillary Quality and Safety Agreements, with Roche in combination with atezolizumab (Tecentriq®) for the treatment of platinum-resistant ovarian cancer (PROC) (NCT05756907). The Company is also evaluating its second program using this platform, SON-1210, an IL12-F_HAB-IL15 for solid tumors, in collaboration with the Sarcoma Oncology Center to commence an investigator-initiated and funded Phase 1/2a study for the treatment of pancreatic cancer.

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 outcome of the Company's clinical trials, the Company's cash runway, 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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