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Sonnet BioTherapeutics Expands Clinical Evaluation of SON-1010 Dose Escalation with Atezolizumab in Ovarian Cancer

Sonnet's lead product, SON-1010 (IL12-F_HAB), is being evaluated in combination with atezolizumab (Tecentriq®) in patients with advanced platinum-resistant ovarian cancer (PROC) (SB221)

Topline safety, cytokine, and efficacy data suggest a strong potential for clinical benefit using the current maximum dose of SON-1010

A second patient with PROC in the E6 combination cohort recently had a confirmed PR, so 2 out of 3 total patients had a tumor response at that dose

After completing enrollment of the expansion group at that top dose, a new E7 cohort has been added to examine the safety and effectiveness of a 25% higher maintenance dose of SON-1010

PRINCETON, N.J., Aug. 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), today announced the expansion of its clinical study of patients with platinum-resistant ovarian cancer (PROC) (SB221). SB221 is a Phase 1b/2a dose-escalation and proof-of-concept study of the combination of SON-1010 (IL12-F_HAB®) with atezolizumab (Tecentriq®), which is provided by Genentech, a member of the Roche Group. Enrollment of the expansion group using the highest maintenance dose from the monotherapy study (the E6 dose of 1200 ng/kg) has been completed, providing an opportunity to study the safety of the combination in a larger population and get a preliminary efficacy readout later this year. A second partial response (PR) based on GCIG criteria was recently observed at the 2-month timepoint and confirmed by RECIST criteria 2 months later in a patient with PROC at that dose. Thus, 2 of the 3 patients (66%) at the E6 dose of SON-1010 had a significant tumor response. Given the strong safety profile at the top dose, the Safety Review Committee (SRC) recommended adding an E7 cohort using a maintenance dose of 1500 ng/kg to study its safety and effectiveness before proceeding to the randomized Phase 2a portion, which will evaluate patients with PROC at one of the two highest doses compared to the standard of care.

Dose escalation results from the SB101 study (previously disclosed), Sonnet's monotherapy trial of SON-1010 in patients with advanced solid tumors, showed a clinical benefit rate in 5 of 6 patients (83%) at the 1200 ng/kg dose, including one patient with soft tissue sarcoma (STS) who had a PR. That study is also being expanded, using SON-1010 alternating with trabectedin (Yondelis®) in patients with STS. In the SB221 study, SON-1010 combined with

atezolizumab has also shown acceptable safety signals and clinical benefit during dose escalation, with controlled induction of IFN. “We are very pleased with the progress of the SB221 study and look forward to investigating the effect of a higher dose of SON-1010, with the hope that it could maximize efficacy without inducing cytokine toxicity,” said Richard Kenney, M.D., Sonnet's Chief Medical Officer. “Top line readouts from this combination study are expected in the fourth quarter of 2025.”

Robert Wenham, M.D., Chair of GYN Oncology at Moffitt Cancer Center, Key Opinion Leader and lead investigator for the SB221 study added, “The strong but controlled induction of IFN is particularly important, as that is necessary for immunotherapeutic control of tumors, but it also induces PD-L1 expression on tumor cells, which contributed to our interest in the combination of SON-1010 with atezolizumab. PROC patients typically have low response rates to currently approved therapies. While more data are needed from the expansion group, the two PRs at the E6 dose are very exciting and represent some of the best data to date in support of a pure combination immunotherapy approach. Other emerging data recently verified a role for IO with chemotherapy in this setting, so I am looking to the future for how we might change the face of this disease with a new drug like SON-1010.”

“The primary goal for the first part of this study was to establish the maximum dose of SON-1010 in combination with atezolizumab as an immune checkpoint inhibitor (ICI), and to provide better evidence of efficacy in the expansion group,” said Raghu Rao, Sonnet’s Interim Chief Executive Officer. “We will follow the patients currently being treated at the E6 dose to assess longer-term safety and tumor responses, and look forward to studying a 25% higher dose in the E7 cohort before selecting the best dose and moving to Part 2. Sonnet continues to seek partnership opportunities to help support the 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.

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 and breast 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.

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 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.

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. 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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