March 26, 2025

Sonnet BioTherapeutics Successfully Completes First Safety Review of SON-1010 in Combination with Trabectedin in Certain Sarcomas

SON-1010 is being studied as a combination therapy with trabectedin (Yondelis®), the first FDA-approved treatment for two types of advanced soft tissue sarcoma after failure of standard chemotherapy, due to the potential for immune mechanism synergies and enhancement of progression-free survival (PFS)

The Safety Review Committee found no unexpected toxicities in early dosing of SON-1010 in the first 7 patients at the maximum tolerated dose (MTD), paving the way for full enrollment of up to 18 patients

The annual review showed extended safety of SON-1010 monotherapy at the MTD with clinical benefit in 83% of patients at that dose, including confirmed partial response (PR) in a patient with clear cell sarcoma

Potential to improve upon the $2.1B trabectedin global market opportunity[1] and treatment of sarcomas, an area of significant unmet medical need

Management releases "What This Means" segment discussing the Safety Review Committee findings; Access here

PRINCETON, N.J., March 26, 2025 (GLOBE NEWSWIRE) -- Sonnet BioTherapeutics Holdings, Inc. (NASDAQ:SONN) (the "Company" or "Sonnet"), a clinical-stage company developing targeted immunotherapeutic drugs, today announced positive findings from the first safety review of the expansion cohort in its Phase 1 SB101 clinical trial evaluating 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, in combination with trabectedin (Yondelis®) in adult patients with advanced leiomyosarcoma (LMS) or liposarcoma (LPS). The expansion cohort builds on the successful completion of monotherapy dose escalation and assignment of the SON-1010 maximum tolerated (MTD) dose of 1200 ng/kg. Additionally, the Company announced the release of a Virtual Investor "What This Means" segment to discuss the first safety review findings, which is now available here.

The SB101 Safety Review Committee (SRC) met to evaluate the initial status of the patients in the expansion cohort, all of whom are receiving the SON-1010/trabectedin combination, as enrollment continues. After an average treatment of slightly over two months, one patient progressed and the other six are tolerating treatment. Adverse events (AEs) considered to

be related to either drug have all been mild or moderate, suggesting that the two drugs do not appear to be adversely impacting each other. The annual review including all 30 patients dosed to date showed that common AEs considered related to SON-1010 monotherapy or in combination included fatigue, fever, chills, and myalgia in 15% or more; moderate fatigue was the only related AE in 2 or more of the patients treated with trabectedin to date. Full enrollment of the combination cohort will provide an opportunity to evaluate statistical evidence of benefit in the response using the standard RECIST paradigm, which may also confirm synergy. Meanwhile, five of the six patients in the SON-1010 high-dose monotherapy group (83%) showed stable disease at 4 months and four continue on trial at 6 months with no new safety concerns. The partial response (PR) in one of those patients persists, confirming the potential for benefit of SON-1010 monotherapy at the MTD in this small cohort. Overall, 13 of the 24 patients studied during SON-1010 dose escalation (54%) had evidence of monotherapy clinical benefit.

“Our physicians are always working to improve the outcomes in sarcoma and very pleased to continue to support the expanded SB101 trial,” commented Dr. Sant Chawla, Principal Investigator at the Sarcoma Oncology Center in Santa Monica, California. “We have a wealth of experience with trabectedin and believe that SON-1010 has the ability to improve its therapeutic effectiveness, given that SON-1010 as a clinical trial monotherapy has already demonstrated clinical benefit in advanced sarcoma patients, including a partial response. LPS and LMS are the most common types of sarcoma, which are difficult diseases to treat. While the approval of trabectedin in the US has helped, there is room for improvement in all types of STS and the drug appears to have utility in the relapsed ovarian cancer setting as well. The safety of SON-1010 in combination with trabectedin is encouraging at this stage and we look forward to the results from the larger group of patients for further clinical trials.”

The primary outcome measures for the Phase 1 SB101 trial are the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of SON-1010 and to establish the MTD. Sonnet has treated 7 patients over 2 months on average and expects to enroll up to 18 patients with unresectable, metastatic LMS or LPS in this open-label, single-arm expansion cohort. Patients are being treated with SON-1010 in combination with the standard 21-day trabectedin cycles, alternating the dosing of the two drugs. Trabectedin, the first approved chemotherapeutic drug for advanced soft-tissue sarcomas (STS) after failure of primary therapy, works by preventing tumor cells from proliferating but has also been shown to have pro-inflammatory immune effects in the tumor microenvironment (TME) that may be enhanced by the IL-12 activity in SON-1010. Trabectedin is approved in 76 countries globally for the treatment of advanced STS as a single-agent, and in 69 countries for relapsed ovarian cancer in combination with doxorubicin HCl liposome injection.

“The goal for the expansion cohort is to assess combination therapy in earlier-stage patients with STS, which provides an exciting opportunity to evaluate the potential for SON-1010 to turn ‘cold’ tumors ‘hot’ and improve the response of trabectedin in a licensed chemotherapy indication,” added Pankaj Mohan, Ph.D., Sonnet Founder and Chief Executive Officer. “We believe the results of this expansion cohort will position SON-1010 for a larger Phase 2 study that could establish the combination of SON-1010 and trabectedin as a new and potentially improved treatment for STS at an earlier stage. Furthermore, the global market opportunity for trabectedin is $2.1B and sarcoma still represents an unmet medical need, which we believe opens up another potential opportunity for partnering.”

For more information about the Phase 1 SB101 trial in adult patients with advanced solid tumors visit www.clinicaltrials.gov and reference identifier NCT05352750.

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 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 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 Phase 1 SB101 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 the 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, established the MTD at 1200 ng/kg using subcutaneous injections of SON-1010 every 3 to 4 weeks. The primary endpoint explores the safety and tolerability of SON-1010, with key secondary endpoints intended to measure PK, 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 F_HAB platform.

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, including the expansion cohort in its Phase 1 SB101 clinical trial which combines SON-1010 with trabectedin, 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, including potential partnerships, 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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[1] https://www.cognitivemarketresearch.com/trabectedin-market-report

Source: Sonnet BioTherapeutics Holdings, Inc.