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Sonnet BioTherapeutics Reports Encouraging Data from Phase 1b/2a Clinical Trial of SON-080 in Chemotherapy-Induced Peripheral Neuropathy (CIPN) That Support Advancement into Phase 2 Study

- Data indicates that SON-080 was well-tolerated at both doses, with no evidence of a pro-inflammatory cytokine response
- Pain and quality of life survey results suggest the potential for rapid improvement of peripheral neuropathy symptoms and post-dosing durability with both doses, compared to placebo controls
- Sonnet intends to seek a partnership to support initiation of a Phase 2 clinical trial of SON-080 in Diabetic Peripheral Neuropathy (DPN), a mechanistically synergistic and larger, high-value indication with unmet medical need
- Management highlights data findings in a Virtual Investor "What This Means" segment

PRINCETON, N.J., July 24, 2024 (GLOBE NEWSWIRE) -- Sonnet BioTherapeutics Holdings, Inc. (the "Company" or "Sonnet") (NASDAQ:SONN), a clinical-stage company developing targeted immunotherapeutic drugs, today announced encouraging data from the Phase 1b portion of its Phase 1b/2a clinical trial evaluating SON-080 for the treatment of CIPN (the "SB211 study"). The SB211 study is a double-blind, randomized, controlled trial of SON-080 conducted at two sites in Australia in patients with persistent CIPN using a new proprietary version of recombinant human Interleukin-6 (rhIL-6) that builds upon previous work with atexakin alfa. The goal of the Phase 1b portion of the SB211 study was to confirm safety and tolerability before continued development in Phase 2. As previously announced in March 2024, a data and safety monitoring board reviewed the unblinded safety and tolerability of SON-080 in the first nine patients and concluded that the symptoms were tolerable in the initial patients and the study could proceed to Phase 2. Additionally, the Company participated in a Virtual Investor "What This Means" segment to further discuss the Phase 1b data and highlight what this means for its development program moving forward. Click here to access the segment.

CIPN is a common side effect of many chemotherapeutic drugs that induce peripheral nerve damage. CIPN can last for weeks to years after treatment has ended and patients with CIPN often experience discomfort that can result in persistent, unbearable pain, as well as motor and autonomic dysfunction that may limit the duration of their cancer treatment. Conventional pain medications and opioids are often ineffective against peripheral neuropathy, creating a significant unmet need for new treatment options. Low dose IL-6 has

been shown to stimulate peripheral nerve growth in preclinical models, thereby ameliorating motor and sensory functions and normalizing the associated pain or sensation disturbance of neuropathy.

“We believe this highly encouraging data bridges the large atexakin alfa historical safety database in cancer patients and is foundational in advancing the development of SON-080 to a Phase 2 study evaluating the neuroprotective and neuro-regenerative effects in DPN,” said Pankaj Mohan, Ph.D., Sonnet Founder and Chief Executive Officer. “IL-6 is often dysregulated in diabetic patients, suggesting there is disease modifying potential for the application of rhIL-6 in DPN. Given the high prevalence of neuropathy in diabetes and the commensurate industry interest in this market, we have prioritized DPN as the best potential indication for Phase 2 development. We intend to seek a partnership to move the asset forward towards commercialization."

A total of 9 patients were randomized between two different SON-080 dose groups and placebo in this portion of the study. The treatment period was 12 weeks long and patients were followed-up for an additional 12 weeks.

The Phase 1b data demonstrated SON-080 was well-tolerated at both 20 µg and 60 µg/dose, which was about 10-fold lower than the maximum tolerated dose (MTD) for IL-6 that was established in previous clinical evaluations. Injection site erythema was the most prominent treatment-related adverse event irrespective of the dose of SON-080, and was transient and mild in all but one case at each dose, where it was moderate. Fatigue was reported occasionally and was more prominent at the higher dose. One patient who developed severe fatigue and stopped dosing after one month was in the low-dose group. Headache, dizziness, and chills were reported infrequently in the high-dose group; all were mild apart from a single moderate event with each symptom. All other adverse events were infrequent and mild.

"These data suggest possible benefits in humans with various types of peripheral neuropathy due to cancer and diabetes. Interleukin-6 has been extensively studied in cancer patients in the past, so the use of SON-080 in CIPN was expected to provide a similar adverse event profile at low doses," commented Richard Kenney, M.D., Sonnet's Chief Medical Officer. "We now have a further understanding of the adverse event profile and the opportunity to look at preliminary efficacy trends. We look forward to initiating a Phase 2 study with a partner in the much larger DPN indication."

The Quality-of-Life Questionnaire-CIPN twenty-item scale (QLQ-CIPN20), a validated survey designed to assess cancer patients’ experience of symptoms and functional limitations related to CIPN, was used as the primary indicator of response. While the number of patients in each group was small, a trend toward improved scores within a month of starting therapy was seen for both dose groups as compared to placebo in the overall scores. This greater improvement with SON-080 persisted after the 12 weeks of therapy had stopped, while the placebo group scores returned to baseline. These results are in line with the preclinical model insights with low dose IL-6, although further work with larger clinical groups is needed to substantiate this trend.

Multiple cytokines were studied as part of the safety evaluation. There was no demonstrable drug effect on any of these inflammatory cytokine serum levels during or after therapy with SON-080. However, there was a dose-related increase in serum amyloid alpha that

persisted during therapy, which returned to baseline once treatment was stopped. An expert consultant concluded that the degree of amyloid elevation seen in this study for 12 weeks should be benign.

For more information about the SB211 study, visit clinicaltrials.gov and reference identifier NCT05435742.

About SON-080 as a Therapeutic Drug Candidate

SB211 studied a low dose of rhIL-6 called SON-080 that has an amino acid sequence identical to the native molecule. The trial targets serum levels similar to those induced with moderate exercise, which triggers the natural healing of nerves, muscle, and bone. As a pleiotropic cytokine, native IL-6 participates in several physiological processes, including tissue repair, glucose homeostasis, and the innate immune response at lower levels, but it can result in acute pathological inflammation at higher serum levels. Preclinical models of CIPN and DPN show that low dose rhIL-6 has the potential to stimulate nerve regrowth to re-establish normal sensations, thereby reducing pain and normalizing some of the physiological conditions that had deteriorated due to nerve degeneration. Early versions of rhIL-6, including Serono's atexakin alfa and others, have been tested in hundreds of patients with cancer, diabetes, idiopathic aplastic anemia, and in healthy controls, showing a maximum tolerated dose of 10 µg/kg three times a week (TIW). The IL-6-related fever, nausea, and vomiting that were prominent adverse events at doses over 2.5 µg/kg TIW were substantially reduced at lower doses.

About the SB211 Phase 1b/2a Trial

The SB211 study was primarily designed to evaluate the safety, PK, PD, and initial efficacy of two dose levels of SON-080 compared to placebo. The drug is self-administered subcutaneously three times a week in patients with CIPN lasting at least 3 months after chemotherapy. The study was conducted at multiple sites in Australia, in a blinded fashion, comparing SON-080 to placebo. The primary endpoint explores the safety and tolerability of SON-080, with key secondary endpoints intended to measure PK, PD, and immunogenicity. Preliminary efficacy is being explored using standardized quality of life and pain questionnaires over the course of the trial.

About Sonnet BioTherapeutics Holdings, Inc.

Sonnet BioTherapeutics is an oncology-focused biotechnology company with a proprietary platform for innovating biologic drugs of 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 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 Section21E of the Securities Exchange Act of 1934 and Private Securities Litigation Reform Act, as amended, including those relating to 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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