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Sonnet BioTherapeutics Announces Publication Detailing the Discovery and Development of SON-1010, an Albumin-Binding IL-12 Fusion Protein, Demonstrating Its Mechanism of Action

Pankaj Mohan, CEO of Sonnet discusses what this publication means in a Virtual Investor "What This Means" segment; access here

PRINCETON, NJ, Dec. 04, 2024 (GLOBE NEWSWIRE) -- Sonnet BioTherapeutics Holdings, Inc. (the "Company" or "Sonnet") (NASDAQ: SONN), a clinical-stage company developing innovative targeted immunotherapeutic drugs, today announced the publication of extensive discovery, development and preclinical data on SON-1010 demonstrating its mechanism of action in *Frontiers in Immunology*. SON-1010, Sonnet's lead proprietary drug candidate, combines the Company's fully human albumin-binding (F_HAB®) construct with a native single-chain IL-12 sequence to simplify delivery of the cytokine systemically. The paper entitled, "*SON-1010: An Albumin-binding IL-12 Fusion Protein with Improved Cytokine Half-life Targets Tumors and Enhances Therapeutic Efficacy*," details the identification of single-chain variable fragments (scFv) from a human phage display library that bound human, mouse, and cynomolgus macaque serum albumin, both at physiologic and acidic conditions. The composition of matter patent claims on the F_HAB domain and SON-1010 fusion protein have been issued in a number of major markets, including but not limited to the U.S., China, Japan, Russia and New Zealand, and expire between 2038 and 2039. Additionally, the Company announced the release of a "What This Means" segment to discuss the publication which is now available here.

The extensive discovery program included putting the scFv domains through a series of steps to identify strongly binding molecules that bind tightly over a 5.8 to 7.2 pH range and do not interfere with the normal physiology of albumin to bind the neonatal Fc receptor (FcRn). This resulted in having prolonged half-life in serum and binding to SPARC/GP60, which allows albumin to target the tumor microenvironment (TME). A final molecule was selected and a single mutation was introduced that minimizes the potential for immunogenicity. This F_HAB domain was characterized, and manufacturing processes were developed to prepare Sonnet's first drug candidate for the clinic. Once identified, the murine form of mIL12-F_HAB was shown to be much more efficient at blocking tumor growth compared to murine IL-12, while stimulating significant and prolonged IFNγ production with minimal toxicity. Biodistribution studies in mice confirmed tumor delivery and toxicological studies in non-human primates allowed the initiation of the clinical trials.

"We are pleased to share these findings, which is the first time we have fully described the

extensive research that was required to discover and develop our signature F_HAB platform," said Pankaj Mohan, Ph.D., Founder and CEO of Sonnet. "This work lays the foundation for all of the products on our platform that are designed to safely extend the half-life of cytokines and deliver them to the tumor, where they can convert the immunological response from 'cold' to 'hot' and potentially realize the promise of immunotherapy."

"IL-12 and related compounds have been extensively studied in cancer and immunotherapy indications. However, recombinant interleukins have had limited clinical success owing to their short circulating half-life, inefficient TME targeting, and requirement for frequent dosing, often leading to substantial systemic toxicities," added John Cini, Ph.D. Co-Founder and CSO of Sonnet. "We believe we have addressed these issues with our discovered platform, having utilized a molecule that can be applied in any solid tumor type that concentrates albumin, such as sarcoma, gynecologic, and gastrointestinal cancers. We intend to explore new compounds as well, as funds become available."

The Company is currently conducting a Phase 1 clinical trial of SON-1010 (IL12-F_HAB) as a monotherapy in adult patients with advanced solid tumors (SB101; NCT05352750). The Company expects to report safety data from this study in Q4 2024. 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).

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 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). The Company is also evaluating its second program, 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.

The Company's SON-080 program is a low dose of rhIL-6 in development for Chemotherapy-Induced Peripheral Neuropathy (CIPN) and Diabetic Peripheral Neuropathy (DPN). SON-080 demonstrated encouraging results in a Phase 1b/2a clinical trial, being well tolerated with no evidence of a pro-inflammatory cytokine response. Sonnet is currently

seeking partnership opportunities to support a Phase 2 trial. In October 2024, Sonnet announced an India license agreement with Alkem Laboratories, Inc. who will assume responsibility for advancing development of the SON-080 program into a Phase 2 study in DPN.

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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