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Sonnet BioTherapeutics Receives Notice of Allowance for U.S. Patent Covering Composition of Matter of Specific Amino Acid Substitutions of its IL-18 Binding Protein Resistant Variant Protein

Company advancing development of its modified version of Interleukin-18 (IL-18$^{Binding\ Protein\ Resistant}$ or IL-18^{BPR}) that exhibits wild-type binding to the IL-18 receptor (IL-18Rc), coupled with undetectable binding to the inhibitory IL-18 Binding Protein (IL-18BP) thus making IL-18^{BPR} more effective in vitro

Sonnet's variant human IL-18^{BPR} is a key cytokine which comprises substitutions at the following amino acid positions: Y1, M51, M60, S105 and D110, relative to human wildtype IL-18

Patent opens up potential licensing opportunities for rights to IL-18^{BPR} independent of Sonnet's F_HAB platform patent estate

Management releases "What This Means" segment discussing the allowed patent;Access here

PRINCETON, N.J., March 19, 2025 (GLOBE NEWSWIRE) -- Sonnet BioTherapeutics Holdings, Inc. (the "Company" or "Sonnet") (NASDAQ: SONN), a clinical-stage company developing targeted immunotherapeutic drugs, today announced that the United States Patent and Trademark Office (USPTO) has issued a Notice of Allowance to the Company for a second patent in the IL-18 variant protein field which discloses the amino acid sequence of its variant human IL-18^{BPR} protein. The allowed patent claims cover variant human IL-18 (hIL-18) proteins, including but not limited to hIL-18 proteins having amino acid substitutions at the following positions: Y1W, Y1K, M51Y, M51S, M60W, S105E, and D110Y, relative to human wildtype IL-18. Additionally, the Company announced the release of a Virtual Investor "What This Means" segment to discuss the allowed patent, which is now availablehere.

"I believe that Sonnet has become of one of the few companies that hold proprietary rights to IL-18^{BPR} which could be a highly valuable cytokine for cancer patients. This patent covers the composition of matter of the amino acid sequence of our human IL-18^{BPR} variant protein which bolsters our intellectual property position and provides further validation to our approach that when IL-18^{BPR} is synergistically combined with IL-12, we believe we will have the potential to develop an important therapeutic asset for oncology and cell-based therapy. Additionally, we feel that this patent enables us to explore opportunities for IL-18^{BPR} to be

licensed independent of our F_HAB platform. We continue to believe that novel bifunctional molecules such as SON-1411, when combined with our proprietary F_HAB platform, have the potential to demonstrate improved tumor targeting, extended half-life and an enhanced therapeutic window," said Pankaj Mohan, Ph.D., Sonnet Founder and Chief Executive Officer.

Sonnet previously reported the generation of two novel drug candidates, SON-1411 (IL18^{BPR}-F_HAB-IL12) and SON-1400 (IL18^{BPR}-F_HAB), each containing a variant version of recombinant human interleukin-18 (IL-18^{BPR}). SON-1411 is a proprietary bifunctional fusion protein consisting of IL-18^{BPR} combined with single-chain wild-type IL-12, linked to Sonnet's Fully Human Albumin Binding (F_HAB®) platform while SON-1400 is a monofunctional fusion protein comprising the same IL-18^{BPR} domain linked to the F_HAB. F_HAB extends the half-life and biological activity of linked molecules by binding native albumin in the serum and targets the tumor microenvironment (TME) through high affinity binding to glycoprotein 60 (gp60) and the Secreted Protein Acidic and Rich in Cysteine (SPARC).

"SON-1411 (IL18^{BPR}-F_HAB-IL12) is a bifunctional combination of IL-12 and the F_HAB domain with a human variant of human interleukin-18 ("IL-18^{BPR}"), which was modified to resist an inhibitory interaction with IL-18 binding protein (IL-18BP). IL-18 is involved in activating both innate and adaptive immune responses; however, IL-18 clinical therapies have been hampered by a lack of efficacy due to the inhibitory activity of the IL-18BP," commented John Cini, Ph.D., Sonnet Chief Scientific Officer.

About SON-1411

SON-1411 is a candidate immunotherapeutic recombinant drug that is closely related to and will replace SON-1410, which links an unmodified single-chain human IL18 and an unmodified IL-12 with the albumin-binding domain of the single-chain antibody fragment A10m3. The only difference between SON-1410 and SON-1411 is that in the latter, the IL-18 domain has been modified via mutagenesis to retain wildtype binding to the IL-18 receptor (IL-18 Rc) while inhibiting or abolishing binding to the IL-18 binding protein (IL-18 BP). The A10m3 scFv was selected to bind both at normal pH, as well as at the acidic pH that is 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 IL-18 and IL-12, as well as a variety of potent immunomodulators that can be added 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 for this approach. SON-1411 is designed to deliver IL-18^{BPR} and IL-12 to local tumor tissue, turning 'cold' tumors 'hot' by stimulating IFNγ, which activates innate and adaptive immune cell responses and increases the production of Programed Death Ligand 1 (PD-L1) on tumor cells.

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 advanced solid tumors, certain types of sarcoma, and platinum-resistant ovarian cancer (PROC). SON-1010 is being evaluated in an ongoing Phase 1/2a study through a Master Clinical Trial and Supply Agreement with Roche in combination with atezolizumab (Tecentriq®) for the treatment of PROC. The Company is also evaluating its second product candidate, SON-1210, an IL12-F_HAB-IL15 bifunctional for solid tumors, in collaboration with the Innovative Immuno-Oncology Consortium (IIOC), and plans to commence an investigator-initiated and funded Phase 1/2a study for the treatment of locally-advanced or metastatic pancreatic ductal adenocarcinoma (PDAC).

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. In October 2024, Sonnet announced a 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 in India.

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 impact of the second patent in the IL-18 variant protein field, 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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