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Sonnet BioTherapeutics Announces Publication Demonstrating Suitability of SON-1210, the First Albumin-binding Bifunctional IL-12/IL-15 Fusion Protein, for Solid Tumor Immunotherapy

PRINCETON, NJ / ACCESSWIRE / December 21, 2023 /Sonnet BioTherapeutics Holdings, Inc., (NASDAQ:SONN) a clinical-stage company developing targeted immunotherapeutic drugs for cancer, announced today the publication of extensive preclinical data on SON-1210 in *Frontiers in Immunology*. SON-1210, Sonnet's lead proprietary bifunctional compound, combines the company's F_HAB construct with a novel single-chain IL-12 and fully human Interleukin 15 (IL-15). The paper, entitled "SON-1210 - a novel bifunctional IL-12 / IL-15 fusion protein that improves cytokine half-life, targets tumors, and enhances therapeutic efficacy", demonstrated the robust binding affinity of SON-1210 to albumin and the anticipated *in vitro* activity and tumor model efficacy that might be expected from the body of research on native IL-12 and IL-15. In the B16F10 melanoma model, a single dose resulted in a marked reduction of tumor growth that was concomitant with increased IFN γ and augmented immune cell numbers and activity in the tumor microenvironment. Repeat doses in non-human primates displayed excellent safety and tolerability and were similarly accompanied by increased IFN γ levels.

"We are pleased to share these encouraging preclinical findings, which support the advancement of SON-1210 into future clinical development." said Pankaj Mohan, Ph.D., Founder and CEO of Sonnet. "These data support the impact of our proprietary engineering of SON-1210 to provide opportunity to target the tumor microenvironment (TME), redirect the immune response, and control tumor growth, positioning us to advance our mission to realize the full potential of this therapeutic class for cancer patients."

The manuscript can be accessed through the following link:

<https://www.frontiersin.org/articles/10.3389/fimmu.2023.1326927/full>

About SON-1210

SON-1210 is an immunotherapeutic bifunctional drug candidate that links unmodified single-chain human IL-12 and human IL-15 with the albumin-binding domain of the single-chain antibody fragment F_HAB separating the two cytokines with linkers to avoid steric hindrance. The F_HAB single chain was selected to bind well at normal pH, as well as at an acidic pH that is typically found in the tumor microenvironment (TME). The F_HAB technology targets tumor and lymphatic tissue, providing a mechanism for dose-sparing, enhanced pK, and an

opportunity to improve the safety and efficacy profile of not only IL-12 and IL-15, but a variety of other potent immunomodulators using the platform. We believe the two cytokines can orchestrate a robust immune response to many cancers and pathogens, particularly when presented together on the same molecule. Given the types of proteins induced in the TME, such as Secreted Protein Acidic and Rich in Cysteine (SPARC), 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-1210 is designed to deliver IL-12 and IL-15 to local tumor tissue, with the intention of turning 'cold' tumors 'hot' by stimulating IFN γ , which activates both innate and adaptive immune cells in the TME, as well as increasing the production of Programed Death Ligand 1 (PD-L1) on tumor cells.

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 Section 21E 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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