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Sonnet BioTherapeutics Announces a Publication Demonstrating Safety and Tolerability of SON-1010 in Healthy Volunteers

PRINCETON, NJ / ACCESSWIRE / February 29, 2024 /Sonnet BioTherapeutics Holdings, Inc., (NASDAQ:SONN) a clinical-stage company developing targeted immunotherapeutic drugs for cancer, announced today the publication of clinical data on SON-1010 in *Frontiers in Immunology*. SON-1010, Sonnet's lead proprietary monofunctional compound, combines the company's fully-human albumin-binding (F_HAB) construct with single-chain interleukin 12 (IL-12). The paper, entitled "A phase I trial of SON-1010, a tumor-targeted, interleukin-12-linked, albumin-binding cytokine, shows favorable pharmacokinetics, pharmacodynamics, and safety in healthy volunteers", demonstrated safety and tolerability up to 300 ng/kg as a single ascending dose. In the B16F10 melanoma model, a single dose of SON-1010 results in a marked reduction of tumor growth that was concomitant with increased IFNg, along with augmented immune cell numbers and activity in the tumor microenvironment (TME). The study of SON-1010 in healthy volunteers, called SB102 (NCT05408572), was first announced in July 2022 and was done in parallel with the ongoing SB101 study in cancer patients (NCT05352750). The results from SB102 provide the initial 'desensitizing dose' for further dose escalation of the maintenance dose in SB101, to establish the maximum tolerated dose for this molecule.

"The publication of these data is an important milestone for Sonnet that provides additional scientific validation of our FHAB technology." said Pankaj Mohan, Ph.D., Founder and CEO of Sonnet. "The SB102 study was designed to elucidate the PK and PD of SON-1010 in normal, healthy volunteers, and shows that the drug is safe in the dose range tested, while also providing an appreciably extended half-life. When combined with checkpoint inhibitors, we hypothesize that the targeted immune enhancing components of the SON-1010 mechanism have the potential to turn cold tumors hot. We also believe that our pipeline, which includes compounds with bifunctional combinations of Interleukins 15 and 18, could potentially prove useful in combination with cell-based therapies. We are diligently pursuing these applications, as well."

While doses above 100 ng/kg were tolerated, participants generally experienced more treatment-emergent adverse effects (TEAEs) than those receiving the lowest dose of 50 ng/kg. All TEAEs were transient and were consistent with published experience using recombinant IL-12. More precise pharmacokinetic (PK) and pharmacodynamic (PD) data can be obtained using this non-genotoxic cancer therapy in healthy individuals, without a background of immunosuppression. PK analysis showed two-compartment elimination in SB102 with a mean half-life of 104 hours, compared with one-compartment elimination in SB101, which correlated with prolonged but controlled and dose-related increases in IFNg.

This is evidence for target-mediated drug disposition (TMDD), which implies delivery to and retention of SON-1010 in tumor tissue. There were minimal responses with other cytokines and no evidence of cytokine release syndrome.

"IL-12 has been studied in healthy volunteers in the past and has shown great promise in animal models of cancer treatment for decades, yet developmental progress in human trials has typically been hindered by toxicity before the therapeutic dose can be reached." said Richard Kenney, M.D., Sonnet's Chief Medical Officer. "Extending the PK by binding to the neonatal Fc receptor (FcRn), combined with targeting retention in the TME through binding to gp60 and SPARC, contributes to TME localization of SON-1010. This may be the key to enhancing the therapeutic window and inducing successful immune responses in the TME, as the PD will also be extended to allow better activation of immune cell penetration and replacement of immune inhibitors."

The manuscript can be accessed through the following link:

https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2024.1362775/full

About SON-1010

SON-1010 is an immunotherapeutic drug candidate that links unmodified single-chain human IL-12 with the albumin-binding domain of the single-chain antibody fragment F_HAB. 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 IL-12. A variety of other potent immunomodulators can be combined with the platform to orchestrate a robust immune response to many cancers and pathogens. 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, colorectal cancer, head and neck cancer, sarcoma, and some gynecological cancers are particularly relevant for this approach. SON-1010 is designed to deliver IL-12 to local tumor tissue, with the intention of turning ‘cold' tumors ‘hot' by stimulating IFNg, 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 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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