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Sonnet BioTherapeutics Announces Successful Completion of Two IND-Enabling Toxicology Studies with SON-1210 in Non-Human Primates

- ***SON-1210 elicited no serious adverse events in repeat, subcutaneous dosing in a GLP toxicology study***
- ***SON-1210 was well-tolerated using dosing levels at least 50x higher than the highest anticipated human clinical dose level***
- ***Data show controlled induction of IFNg with no signs of cytokine release syndrome or off-target toxicity***

PRINCETON, NJ / ACCESSWIRE / February 1, 2023 /Sonnet BioTherapeutics Holdings, Inc. (NASDAQ:SONN) (the "Company" or "Sonnet"), a clinical-stage company developing targeted immunotherapeutic drugs, announced today that two IND-enabling toxicology studies have been completed in non-human primates (NHPs) using its lead bifunctional therapeutic candidate. SON-1210 is a proprietary, bispecific version of human Interleukins 12 (IL-12) and 15 (IL-15), configured using Sonnet's Fully Human Albumin Binding ($F_HAB^®$) platform.

"We continue to be very excited about the progress of our pipeline development activities and in particular, the potential of our bifunctional F_HAB compounds that target the tumor microenvironment by binding albumin, which was designed to enhance the pharmacokinetic profile in humans", commented John Cini, PhD, Sonnet's co-founder and Chief Scientific Officer. "To that end, SON-1210 is Sonnet's most advanced bifunctional asset and secondary lead F_HAB-derived compound that is evolving towards clinical development. The data generated from these IND-enabling toxicology studies represent an important milestone in this process and we remain confident in our technology platform."

Pankaj Mohan, PhD, Sonnet's founder and Chief Executive Officer added, "Data analysis and reporting for both of these studies will enable the preparation of regulatory filings to begin during the first half of 2023 for first-in-human trials of SON-1210. Collectively, these datasets demonstrate that SON-1210 is well-tolerated with subcutaneous dosing and support advancing this asset into Phase I clinical trials."

The first of two studies, a non-GLP toxicology study, was designed to elucidate the maximum tolerated dose (MTD) of SON-1210 in a dose-escalation format in four cohorts of NHPs. The second study was a GLP repeat-dose toxicology study that employed three dose levels of SON-1210 or a vehicle control, each dosed three times every two weeks. The GLP study included a six-week recovery period for the high dose and vehicle control groups following the completion of the dosing phase.

There were no SON-1210-related increases in toxicity, including liver enzymes, in the GLP study apart from the expected, and mild, on-target changes in hematology and clinical chemistry parameters that resolved completely within 14 to 21 days post-dosing. A significant increase in interferon gamma (IFNg), which was transient in nature, was noted as early as one day following administration, with no apparent increase in other proinflammatory cytokines. IFNg is a well-known pharmacodynamic biomarker that is required for anti-tumor efficacy in preclinical models. Other signs of cytokine imbalance, or uncontrolled increase of pro-inflammatory cytokines (including TNF-α, IL-1β, and IL-6) were notably absent from all dose levels tested in the study.

About SON-1210

SON-1210 is an immunotherapeutic bispecific, 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 equally well at normal pH, as well as at an acidic pH 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 Interleukin 12 can 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, 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 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 bispecific, 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 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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