

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 OR 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): May 20, 2024

SONNET BIOTHERAPEUTICS HOLDINGS, INC.

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction
of incorporation)

001-35570

(Commission
File Number)

20-2932652

(IRS Employer
Identification No.)

**100 Overlook Center, Suite 102
Princeton, New Jersey**

(Address of principal executive office)

08540

(Zip Code)

Registrant's telephone number, including area code: **(609) 375-2227**

Not Applicable

(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- ☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- ☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- ☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- ☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, \$0.0001 par value per share	SONN	The Nasdaq Capital Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD.

On May 20, 2024, Sonnet BioTherapeutics Holdings, Inc. (the "Company") issued a press release announcing updated clinical data for its candidate immunotherapeutic recombinant drug, SON-1010, as monotherapy or combined with atezolizumab (in collaboration with Genentech, a member of the Roche Group), and an increase of the target dose of SON-1010 during dose escalation in both of the Company's current Phase 1 clinical trials. A copy of the press release is attached hereto as Exhibit 99.1.

The information in this Current Report on Form 8-K under Item 7.01, including the information contained in Exhibit 99.1, is being furnished to the Securities and Exchange Commission (the "SEC"), and shall not be deemed to be "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, and shall not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by a specific reference in such filing.

Item 8.01 Other Events.

On May 20, 2024, the Company announced updated clinical data for SON-1010 as a monotherapy and combined with atezolizumab (Tecentriq®), an anti-PD-L1, and an increase in the target dose of SON-1010 during dose escalation in both of the Company's current Phase 1 clinical trials. The Company's SON-1010 studies have together enrolled 61 subjects, to date, as dose escalation continues in SB101 and SB221 at higher levels. Patients have received up to 25 cycles of SON-1010 as monotherapy and 10 cycles of SON-1010 with atezolizumab without dose-limiting toxicity at any dose level. The Company's cytokine data revealed about 10-fold extended half-life for SON-1010 compared with rhIL-12 that induces prolonged and controlled IFNγ responses, with no evidence of cytokine release syndrome at any dose.

The safety of SON-1010 dosing has been formally reviewed in two current Phase 1 clinical trials and the Company is now increasing the target dose of SON-1010 during dose

escalation. SON-1010 is a proprietary version of recombinant human interleukin-12 (rhIL-12), configured using the Company’s Fully Human Albumin Binding (FHAB®) platform, which extends the half-life and activity of the IL-12 component due to binding native albumin in the serum and targets the tumor microenvironment (TME) by strongly binding gp60 and Secreted Protein Acidic and Rich in Cysteine (SPARC). SB101 is a Phase 1 multiple-ascending dose (MAD) trial in adult patients with advanced solid tumors (NCT05352750) that commenced in Q2 2022 and is currently enrolling the sixth dose cohort. SB221 is a Phase 1b/2a dose-escalation and proof-of-concept study of the combination of SON-1010 with atezolizumab (in collaboration with Genentech, a member of the Roche Group), in a study focused on platinum-resistant ovarian cancer (PROC) (NCT05756907) that started in Q4 2023, now enrolling the fourth dose cohort. In addition, SON-1010 was studied in SB102, which was a Phase 1 single-ascending dose (SAD) trial in healthy volunteers (NCT05408572) that started in Q3 2022, the results were recently published (Kenney, et al, Frontiers in Immunology, 2024).

Safety in both of the active cancer trials has been reviewed by their respective Safety Review Committees at each step during dose escalation. Both trials use a ‘desensitizing’ first dose to take advantage of the known tachyphylaxis with rhIL-12, which minimizes toxicity and allows higher maintenance doses. No dose-limiting toxicities or related serious adverse events have occurred to date. The safety and toxicity profile that has developed is typical for a Phase 1 oncology trial, with the majority of adverse events (AEs) being reported as mild. All have been transient, with no evidence of cytokine release syndrome. Of the 25 cancer patients dosed to date and evaluable for follow-up at this latest cutoff, 15 (60%) had stable disease at their first follow-up scan, 8 of whom were progressing at study entry. At four months follow-up, 8 of 23 evaluable patients remained stable at the second CT scan, suggesting clinical benefit of SON-1010 in 35% of the patients.

One patient with progressive endometrial sarcoma receiving SON-1010 monotherapy in SB101 had stable disease (SD) for almost 2 years before progressing – her ascites had resolved and tumors had shrunk at one point but she never reached a partial response (PR) by Response Evaluation Criteria in Solid Tumors (RECIST) rules. Cytokine analysis following each dose in that study revealed controlled and prolonged induction of interferon gamma (IFNγ) that peaked at 24 to 48 hours and returned to baseline within 2 to 4 weeks. A small increase in IL-10 was observed with each dose as expected in response to IFNγ. There was either a minimal or no signal for IL-1β, IL-6, IL-8, and TNFα, and there was no indication of any potential for cytokine release syndrome (CRS) at these doses. One patient in Part 1 of SB221 with uterine sarcomas received 8 cycles of the SON-1010/atezolizumab combination therapy every 3 weeks before progressing; another two have received 8 and 10 cycles, respectively, and are continuing on the study. The stable AE profiles despite dose escalation led the Company to reevaluate the target dose, so the Company has added groups in both studies to evaluate 1200 ng/kg SON-1010 as a maintenance dose (the molar equivalent of 800 ng/kg rhIL-12). Finally, Part 2 of the SB221 combination study has been trimmed to remove the monotherapy arm.

Forward-Looking Statements

This Current Report on Form 8-K contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Exchange 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 the Company’s 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 SEC. Prospective investors are cautioned not to place undue reliance on such forward-looking statements, which speak only as of the date of this Current Report. The Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release dated May 20, 2024
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

SONNET BIOTHERAPEUTICS HOLDINGS, INC.

Date: May 20, 2024

By: /s/ Pankaj Mohan, Ph.D.
Name: Pankaj Mohan, Ph.D.
Title: Chief Executive Officer

Sonnet BioTherapeutics Announces Updated Clinical Data for SON-1010 as Monotherapy or Combined with an anti-PD-L1, along with an Increase in the Dose-Escalation Target

- The SON-1010 studies have together enrolled 61 subjects, to date, as dose escalation continues in SB101 and SB221 at higher levels
- Patients have received up to 25 cycles of SON-1010 as monotherapy and 10 cycles of SON-1010 with atezolizumab (Tecentriq[®]) without dose-limiting toxicity at any dose level
- Cytokine data reveals about 10-fold extended half-life for SON-1010 compared with rhIL-12 that induces prolonged and controlled IFN γ responses, with no evidence of cytokine release syndrome at any dose
- Clinical benefit was seen at four months post-initiation of dosing in 35% of evaluable patients (8/23) with advanced solid tumors

PRINCETON, NJ / ACCESSWIRE / May 20, 2024 / Sonnet BioTherapeutics Holdings, Inc. (NASDAQ:SONN) (the “Company” or “Sonnet”), a clinical-stage company developing targeted immunotherapeutic drugs, announced today that the safety of SON-1010 dosing has been formally reviewed in both of the current Phase 1 clinical trials and the Company is now increasing the target dose of SON-1010 during dose escalation. SON-1010 is a proprietary version of recombinant human interleukin-12 (rhIL-12), configured using Sonnet’s Fully Human Albumin Binding (F_HAB[®]) platform, which extends the half-life and activity of the IL-12 component due to binding native albumin in the serum and targets the tumor microenvironment (TME) by strongly binding gp60 and Secreted Protein Acidic and Rich in Cysteine (SPARC). SB101 is a Phase 1 multiple-ascending dose (MAD) trial in adult patients with advanced solid tumors ([NCT05352750](#)) that commenced in Q2 2022 and is currently enrolling the sixth dose cohort. SB221 is a Phase 1b/2a dose-escalation and proof-of-concept study of the combination of SON-1010 with atezolizumab (in collaboration with Genentech, a member of the Roche Group), in a study focused on platinum-resistant ovarian cancer (PROC) ([NCT05756907](#)) that started in Q4 2023, now enrolling the fourth dose cohort. In addition, SON-1010 was studied in SB102, which was a Phase 1 single-ascending dose (SAD) trial in healthy volunteers ([NCT05408572](#)) that started in Q3 2022; the results were recently published ([Kenney, et al. Frontiers in Immunology, 2024](#)).

Safety in both of the active cancer trials has been reviewed by their respective Safety Review Committees at each step during dose escalation. Both trials use a ‘desensitizing’ first dose to take advantage of the known tachyphylaxis with rhIL-12, which minimizes toxicity and allows higher maintenance doses. No dose-limiting toxicities or related serious adverse events have occurred to date. The safety and toxicity profile that has developed is typical for a Phase 1 oncology trial, with the majority of adverse events (AEs) being reported as mild. All have been transient, with no evidence of cytokine release syndrome. Of the 25 cancer patients dosed to date and evaluable for follow-up at this latest cutoff, 15 (60%) had stable disease at their first follow-up scan, 8 of whom were progressing at study entry. At four months follow-up, 8 of 23 evaluable patients remained stable at the second CT scan, suggesting clinical benefit of SON-1010 in 35% of the patients.

“We have now dosed 18 cancer patients at increasing SON-1010 drug levels in the SB101 study, completed dosing in 31 healthy volunteers in SB102, and are rapidly filling the dose-escalation cohorts with 12 subjects enrolled in the first four cohorts of the SB221 combination study,” said Richard Kenney, M.D., Sonnet’s Chief Medical Officer. “The overall safety and toxicity profile for SON-1010, primarily including local reactions, headache, myalgia, and fatigue, mimics the published experience with rhIL-12, which prompted us to raise the target dose to enhance potential efficacy. The SB102 study allowed us to generate clean data for the pharmacokinetic (PK) and pharmacodynamic (PD) analyses, enabling simulation of the effect of multiple doses with the help of a continual reassessment model of PK and PD. This modeling suggests target-mediated drug disposition (TMDD), which supports the mechanism of the F_HAB being directed to tumor tissue. The combination of SON-1010 with atezolizumab may benefit from the ability of IL-12 to turn ‘cold’ tumors ‘hot’, which upregulates the amount of PD-L1 in the TME.”

One patient with progressive endometrial sarcoma receiving SON-1010 monotherapy in SB101 had stable disease (SD) for almost 2 years before progressing – her ascites had resolved and tumors had shrunk at one point but she never reached a partial response (PR) by Response Evaluation Criteria in Solid Tumors (RECIST) rules. Cytokine analysis following each dose in that study revealed controlled and prolonged induction of interferon gamma (IFN γ) that peaked at 24 to 48 hours and returned to baseline within 2 to 4 weeks. A small increase in IL-10 was observed with each dose as expected in response to IFN γ . There was either a minimal or no signal for IL-1 β , IL-6, IL-8, and TNF α , and there was no indication of any potential for cytokine release syndrome (CRS) at these doses. One patient in Part 1 of SB221 with uterine sarcomas received 8 cycles of the SON-1010/atezolizumab combination therapy every 3 weeks before progressing; another two have received 8 and 10 cycles, respectively, and are continuing on the study. The stable AE profiles despite dose escalation led us to reevaluate the target dose, so the Company has added groups in both studies to evaluate 1200 ng/kg SON-1010 as a maintenance dose (the molar equivalent of 800 ng/kg rhIL-12). Finally, Part 2 of the SB221 combination study has been trimmed to remove the monotherapy arm.

“The findings to date in these two trials represent significant progress for the SON-1010 molecule”, said Robert Wenham, M.D., Chair, Department of GYN Oncology at Moffitt Cancer Center and the Lead Principal Investigator for SB221. “Multiple strategies to present IL-12 safely have been tried over the past two decades with little evidence of improved tolerability in humans, yet the preclinical models continue to suggest that induction of IFN γ in the TME can activate an effective anti-tumor response. This also results in the local induction of PD-L1. Adding a cohort to increase the target MTD of SON-1010, an extended PK molecule that is concentrated in the TME, is the right approach at this stage. This will provide a chance to study the safety of SON-1010 monotherapy in SB101, and then in combination with atezolizumab in SB221, along with the clinical effect of the combination on PROC in a limited set of subjects in the expansion cohort later this year. Defining the best dose for SON-1010 is required to allow a direct randomized comparison of the strategy with the standard of care therapy in Part 2.”

“We are very pleased with the data we are seeing at these higher dose levels of SON-1010, with safety and tolerability being well within expected levels, as well as displaying SON-1010 extended PK/PD, tumor targeting, and clinical activity during treatment,” said Pankaj Mohan, Ph.D., Sonnet Founder and Chief Executive Officer. “Research on rhIL-12 in humans has been hindered by toxicity for decades. We believe that the IL-12 component in SON-1010 is presented in a way that is safer, due to the longer half-life, and it is concentrated in the tumor, due to the recurrent binding of the F_HAB-associated albumin to SPARC in the TME. It is important to note that many of these patients have been fighting their cancers for a very long time and have exhausted all approved treatment regimens available to them, so seeing tumor shrinkage at any dose is both difficult to achieve and encouraging for future results. We are excited to continue testing the impact of SON-1010 in combination with atezolizumab at these higher dose levels in patients with PROC, who represent a significant unmet medical need, and we expect to have a further update early next year.”

About SON-1010

SON-1010 is a candidate immunotherapeutic recombinant drug that links unmodified single-chain human IL-12 with the albumin-binding domain of the single-chain antibody fragment A10m3. This was selected to bind both at normal pH, as well as at the acidic pH 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 not only IL-12, but 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 the Secreted Protein and Rich in Cysteine (SPARC) and glycoprotein 60 (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-1010 is designed to deliver IL-12 to local tumor tissue, turning ‘cold’ tumors ‘hot’ by stimulating IFN γ , which activates innate and adaptive immune cell responses and increases the production of Programmed Death Ligand 1 (PD-L1) on tumor cells.

About the SB101 Phase 1 Trial

This first-in-human study is primarily designed to evaluate the safety of multiple ascending doses of SON-1010 in cancer patients and will be conducted at several sites across the United States. While the optimal dose is unknown at this stage, the potential to target tumors, the extended PK mechanism and our preclinical data suggest the therapeutic dose may be lower compared to native human IL-12. The study, utilizing a standard 3+3 oncology design in at least five cohorts, should establish the MTD and the recommended Phase 2 dose (RP2D) using monthly subcutaneous injections of SON-1010. The primary endpoint explores the safety and tolerability of SON-1010, with key secondary endpoints intended to measure pharmacokinetics (PK), pharmacodynamics (PD), immunogenicity, and anti-tumor activity. This study will form the basis for potential combinations with other types of immunotherapies and the future development of bispecific candidates using the F_HAB platform.

About the SB221 Phase 1b/2a Trial

SB221 is a global Phase 1b/2a multicenter, dose-escalation and randomized proof-of-concept study to assess the safety, tolerability, PK, PD, and efficacy of SON-1010 administered subcutaneously (SC), either alone or in combination with atezolizumab given intravenously (IV). The study is designed in Part 1 to rapidly establish the maximum tolerated dose (MTD) of the combination in patients with advanced solid tumors at the lower dose levels. The focus shifts to PROC at higher dose levels using small dose-escalation groups with expansion of the dataset at the recommended Phase 2 dose (RP2D). This would be followed in Part 2 by an assessment in patients with PROC of the potential for improved efficacy of the combination versus the standard of care. Both companies look forward to this collaboration as an opportunity to improve outcomes for patients with ovarian cancer.

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.

Tecentriq[®] (atezolizumab) is a registered trademark of Genentech, a member of the Roche Group.

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 the Company’s 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.

Sonnet BioTherapeutics Investor Contact

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SOURCE: Sonnet BioTherapeutics Holdings, Inc.
