

**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): April 18, 2023

**SONNET BIOTHERAPEUTICS HOLDINGS, INC.**

(Exact Name of Registrant as Specified in Charter)

<b>Delaware</b> (State or Other Jurisdiction of Incorporation)	<b>001-35570</b> (Commission File Number)	<b>20-2932652</b> (IRS Employer Identification No.)
<b>100 Overlook Center, Suite 102 Princeton, New Jersey</b> (Address of Principal Executive Offices)		<b>08540</b> (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 (see General Instruction A.2. below):

- 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:

<b>Title of each Class</b>	<b>Trading Symbol(s)</b>	<b>Name of each exchange on which registered</b>
Common Stock, \$0.0001 par value per share	SONN	The Nasdaq Stock 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 (17 CFR §230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR §240.12b-2).

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 April 18, 2023, Sonnet BioTherapeutics Holdings, Inc. (the "Company" or "Sonnet") issued a press release announcing 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 enrolling the final dose cohort in the cancer trial. 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, 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 April 18, 2023, the Company issued a press release announcing 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 enrolling the final dose cohort in the cancer trial. SON-1010 is a proprietary version of human interleukin-12 (IL-12), configured using Sonnet's Fully Human Albumin Binding (FHAB<sup>®</sup>) platform. SB101 is a single-ascending dose (SAD) trial for adult patients with advanced solid tumors (NCT05352750) that commenced in Q2 2022 and is currently enrolling the final dose cohort. SB102 is a SAD trial in healthy volunteers (NCT05408572) that started in Q3 2022, and the safety review of the last cohort was recently completed. Updated SB101 data was presented in a poster presentation today at AACR, and data from both studies will be discussed by the Company in a webinar today at 5:00 pm ET.

Of the 15 patients from the first five cohorts of SB101 evaluable for follow-up at this latest cutoff, 9 had stable disease at the first follow-up scan, 4 of which were already progressing at study entry. At four months follow-up, 5 of 14 patients remained stable at the second scan, suggesting clinical benefit of SON-1010 in 36% of patients. The very first patient dosed, with an aggressive endometrial sarcoma, had target tumor shrinkage with complete resolution of ascites at one point and has been clinically stable for nearly a year. Dosing in the first 3 cohorts was performed every 4 weeks, but is now being done every 3 weeks in the new cohorts to enhance safety at higher doses.

SON-1010 has been safe and tolerable at all doses tested to date. Adverse events have generally been mild/moderate and transient in nature, with no study discontinuations for safety reasons. In addition, adverse effects have been less numerous and less intense with subsequent doses. The geometric half-life ( $t_{1/2}$ ) of SON-1010 was 113 hours in SB101 and 122 hours in SB102, compared to 12 hours for recombinant IL-12 observed in prior studies. Comparison of the PK curves between the two studies suggests that SON-1010 may be targeting tumors, as it was designed to do. Cytokine analysis following each dose revealed controlled and prolonged induction of interferon gamma (IFN $\gamma$ ) that peaked at 24 to 48 hours and returned to baseline after 2 to 4 weeks. A small increase in IL-10 was observed with each dose as expected in response to IFN $\gamma$ . There was either a minimal or no signal for IL-1 $\beta$ , IL-6, IL-8, and TNF $\alpha$  and no indication of any potential for cytokine release syndrome (CRS) at these doses.

On April 18, 2023, the Company presented the presentation attached hereto as exhibit 99.2 and incorporated by reference into this Item 8.01.

#### Item 9.01. Financial Statements and Exhibits.

(d) The following exhibit is furnished with this report:

<u>Exhibit No.</u>	<u>Description</u>
99.1	<a href="#">Press Release issued by Sonnet BioTherapeutics Holdings, Inc., dated April 18, 2023.</a>
99.2	<a href="#">Presentation by Sonnet BioTherapeutics Holdings, Inc., dated April 18, 2023.</a>
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

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#### SIGNATURES

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: April 18, 2023

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

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## Sonnet BioTherapeutics Announces Updated Clinical Data for SON-1010 at the 2023 American Association for Cancer Research (AACR) Annual Meeting

- The SB101 and SB102 Phase 1 studies have together dosed 46 subjects to date as SB101 dose escalation continues
- Cytokine data reveals extended PK profile for SON-1010
  - Induces prolonged and controlled IFN $\gamma$  response
  - No evidence of cytokine release syndrome
- Clinical benefit was seen in 36% of patients (5/14) with advanced solid tumors

PRINCETON, NJ / ACCESSWIRE / April 18, 2023 / 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 enrolling the final dose cohort in the cancer trial. SON-1010 is a proprietary version of human interleukin-12 (IL-12), configured using Sonnet’s Fully Human Albumin Binding (F<sub>H</sub>AB<sup>®</sup>) platform. SB101 is a single-ascending dose (SAD) trial for adult patients with advanced solid tumors (NCT05352750) that commenced in Q2 2022 and is currently enrolling the final dose cohort. SB102 is a SAD trial in healthy volunteers (NCT05408572) that started in Q3 2022, and the safety review of the last cohort was recently completed. Updated SB101 data was presented in a poster presentation today at AACR, and data from both studies will be discussed by the Company in a webinar today at 5:00 pm ET.

“We have now dosed 15 cancer patients at increasing drug levels in the SB101 study and have completed dosing in 31 healthy volunteers in SB102,” said Richard Kenney, M.D., Sonnet’s Chief Medical Officer. “No dose-limiting toxicities have occurred to date and the formal safety reviews after each cohort have revealed a safety and toxicity profile that is typical for a Phase 1 oncology trial, with the majority of adverse events being reported as mild, and all are transient, with no evidence of Cytokine Release Syndrome observed. The SB102 study has allowed us to generate clean data for the initial pharmacokinetic (PK) analysis, which enabled us to simulate the effect of multiple doses with the help of a continual reassessment model of PK.”

Of the 15 patients from the first five cohorts of SB101 evaluable for follow-up at this latest cutoff, 9 had stable disease at the first follow-up scan, 4 of which were already progressing at study entry. At four months follow-up, 5 of 14 patients remained stable at the second scan, suggesting clinical benefit of SON-1010 in 36% of patients. The very first patient dosed, with an aggressive endometrial sarcoma, had target tumor shrinkage with complete resolution of ascites at one point and has been clinically stable for nearly a year. Dosing in the first 3 cohorts was performed every 4 weeks, but is now being done every 3 weeks in the new cohorts to enhance safety at higher doses.

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“We study cancer patients to give us a sense of the safety and activity at higher doses, while the use of healthy volunteers lets us rapidly get clean PK and PD data without the background of prior cancer treatment,” said Pankaj Mohan, Ph.D., Sonnet Founder and Chief Executive Officer. “We are very pleased with the data we are seeing with these early dose levels, with safety and tolerability being well within expected levels, as well as displaying early signs of SON-1010’s extended PK and clinical activity. 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. Based on these data, we are excited to study the impact of SON-1010 in patients with platinum-resistant ovarian cancer, both as monotherapy at the highest dose in the current cancer study and in our next clinical study in combination with the Roche checkpoint inhibitor atezolizumab (Tecentriq<sup>®</sup>). We believe these results set a positive tone for our ongoing business development initiatives, and we are comfortable that our cash on the balance sheet will give us operating runway into the 2024 calendar year.”

### Webcast

Investors and analysts are invited to join a webcast presentation of the SON-1010 results conducted by CEO Pankaj Mohan, Ph.D. and CMO Richard Kenney, M.D. today, April 18<sup>th</sup>, at 5 pm ET. The webcast at 5:00 pm ET, with an accompanying presentation, will be accessible under News & Events, IR Calendar in the Investors section of the company’s website. The archived audio webcast will be available on Sonnet’s website following the call.

To participate in the webcast, please see the following details:

- Webcast Link: [https://event.webcasts.com/starthere.jsp?ei=1607729&tp\\_key=f6d5c78778](https://event.webcasts.com/starthere.jsp?ei=1607729&tp_key=f6d5c78778)
- Toll Free: 1-877-869-3847
- International: +1-201-689-8261
- Conference ID: 13737737

### 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 an acidic pH typically found in the tumor microenvironment (TME). The F<sub>H</sub>AB 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 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 $\gamma$ , which activates innate and adaptive immune cells 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 is being 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 FHAB platform.

#### **About the SB102 Phase 1 Trial**

The SB102 study is designed to robustly evaluate the safety, PK and PD of single ascending doses of SON-1010, using larger groups of healthy volunteers, and was conducted at a single site in Australia. The study was done in a blinded fashion, comparing a single dose of SON-1010 to placebo utilizing five cohorts. Both PK and PD were be closely followed during dose escalation in this double-blind, placebo-controlled study, along with an assessment of the cellular immune responses at each dose using sophisticated fluorescence activated cell sorting (FACS) analysis. The primary endpoint explores the safety and tolerability of SON-1010, with key secondary endpoints intended to measure PK, PD, and immunogenicity.

#### **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 FHAB (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 FHAB 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. FHAB 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.

Sonnet BioTherapeutics Investor Contact

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[mmorabito@soleburystrat.com](mailto:mmorabito@soleburystrat.com)

SOURCE: Sonnet BioTherapeutics, Inc.

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# POWERING A NEW WAVE OF IMMUNE THERAPEUTICS

## SON-1010 Clinical Update Presentation

April 18, 2023



*This presentation contains forward looking statements that do not guarantee future performance.*

### FORWARD LOOKING STATEMENTS

This presentation contains forward-looking statements about **Sonnet BioTherapeutics** based on management's current expectations which are subject to known and unknown uncertainties and risks. Words such as "anticipated," "initiate," "expect," "intend," "plan," "believe," "seek," "estimate," "may," and variations of these words or similar expressions are intended to identify forward-looking statements. Our actual results could differ materially from those discussed due to a number of factors, including, but not limited to, our ability to raise additional equity and debt financing on favorable terms, the success of our R&D programs, our ability to obtain regulatory approval of our clinical assets and other risk factors.

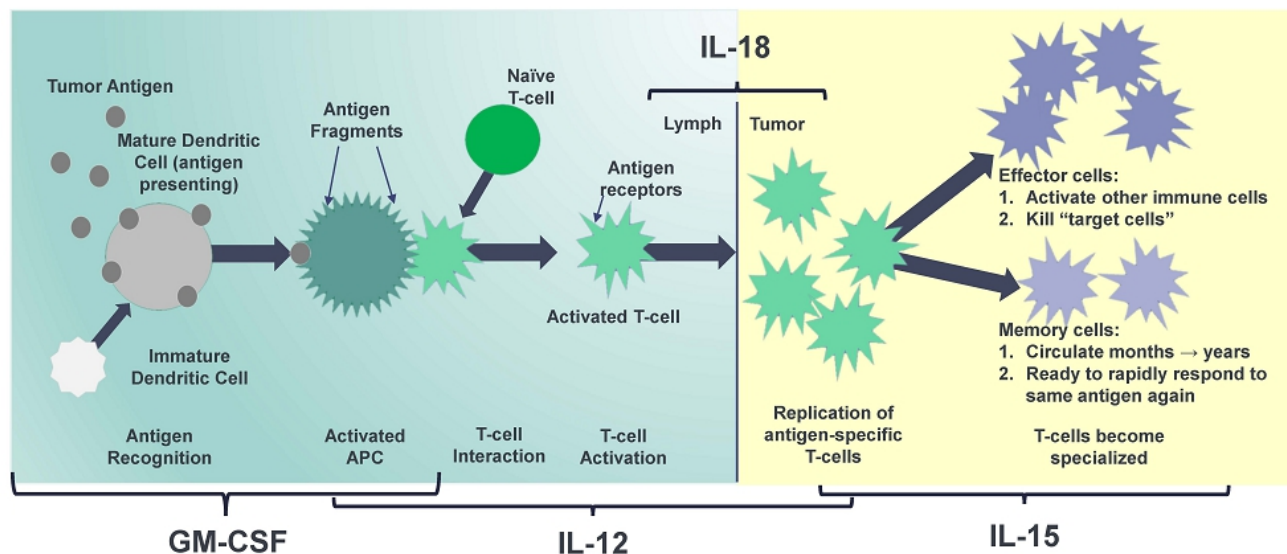
We are providing this information as of the date of this presentation and do not undertake any obligation to update any forward-looking statements contained in this presentation as a result of new information, future events or otherwise. Unless the context requires otherwise, references to "Sonnet," "Company," "we," "us" and "our" refer to **Sonnet BioTherapeutics**.



- ◆ **Next Generation Oncology Platform (F<sub>H</sub>AB)**
  - ❑ Confers both tumor targeting and enhanced pharmacokinetics (PK);
  - ❑ Fully human protein sequence, and thus, no predicted immunogenicity
- ◆ **First immune activator with tumor-targeting functions on a proprietary F<sub>H</sub>AB platform**
- ◆ **Encouraging preclinical data in a cancer model**
  - ❑ Tumor growth inhibition, associated with the induction of IFN $\gamma$  (i.e., potentially better efficacy with lower dosing), in the “immunologically cold” B16F10 melanoma model, with a 30-fold therapeutic index vs. wild-type IL-12
- ◆ **GLP toxicology data**
  - ❑ Up to 50x the human dose is safe in monkeys with NO cytokine release syndrome (CRS)
- ◆ **Clinical data experience for IL12-F<sub>H</sub>AB**
  - ❑ Normal healthy volunteer study – PK was significantly enhanced compared to historical rIL-12
  - ❑ Cancer patient study – demonstrates transient, mild-to-moderate toxicity with NO cytokine release syndrome;
    - ❑ Preliminary clinical benefit in 36% of patients with advanced solid tumors
- ◆ **Broad, global intellectual property, including composition of matter, indications and manufacturing.**
- ◆ **Pipeline includes first-in-class bifunctional oncology products: SON-1210 and SON-1410**
  - ❑ Agreement with Janssen for the evaluation of three Sonnet product candidates
  - ❑ Collaboration with Roche for clinical evaluation of SON-1010 with atezolizumab (Tecentriq®) in ovarian cancer

## Sonnet Pipeline Targets

### Multiple Points of Intervention



Cytokines have shown great promise as cancer therapeutics but suffer from dose-related toxicity and short half-life



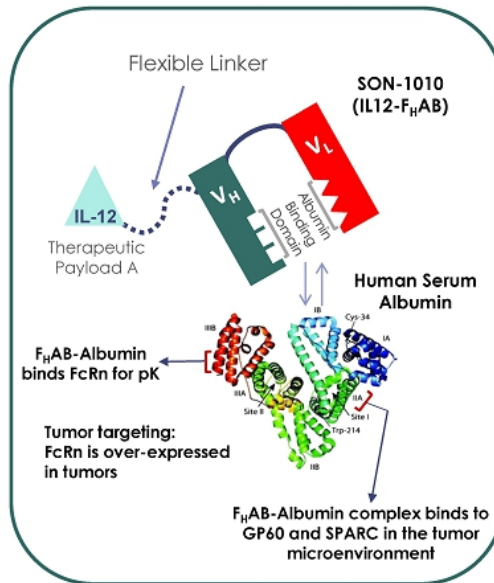
## STRUCTURE/FUNCTION

Sonnet's Fully Human Albumin Binding ( $F_H$ AB) technology utilizes a single chain antibody fragment (scFv) capable of delivering one or two active drug compounds

- Therapeutic payloads attached via flexible linker peptides

Following administration, Sonnet's  $F_H$ AB-derived candidates bind to and "hitch-hike" on endogenous human serum albumin (HSA) for transport to target tissues

- $F_H$ AB has been designed to bind, unbind and rebind to albumin in an on-and-off fashion through a physical bonding mechanism, obviating the need for chemical conjugation



## KEY FEATURES

### Fully Human Construct

- Low/No immunogenicity
- Single- or bifunctional design

### Targeted Delivery

- Potential for greater efficacy with reduced side effects
- GP60- and SPARC-driven uptake
- Accumulation in tumor tissue

### Enhanced pK Characteristics

- Extended dosing intervals
- FcRn binding

### Small Size with Linear Flexibility

- Optimized tumor penetration

### Mammalian Cell Production (CHO)

- Continuous intensive perfusion

### Modular

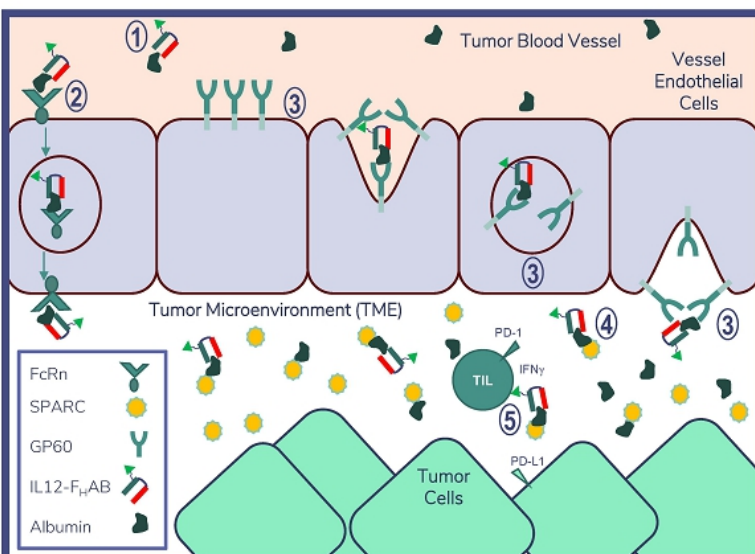
- Off-the-shelf system
- Rapid asset development

For a video displaying the  $F_H$ AB mechanism, please click [here](#)

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# SON-1010 $F_H$ AB: Targeting the Tumor Microenvironment

Mono- or bifunctional cytokine(s) linked to an albumin-binding domain



Albumin is elevated in solid tumors

FcRn over expressed in tumors

GP60 is over-expressed on tumor vessel endothelial lining

Over-expression of SPARC has been shown in many solid tumors

Tumor architectural changes cause EPR that helps maintain the TME

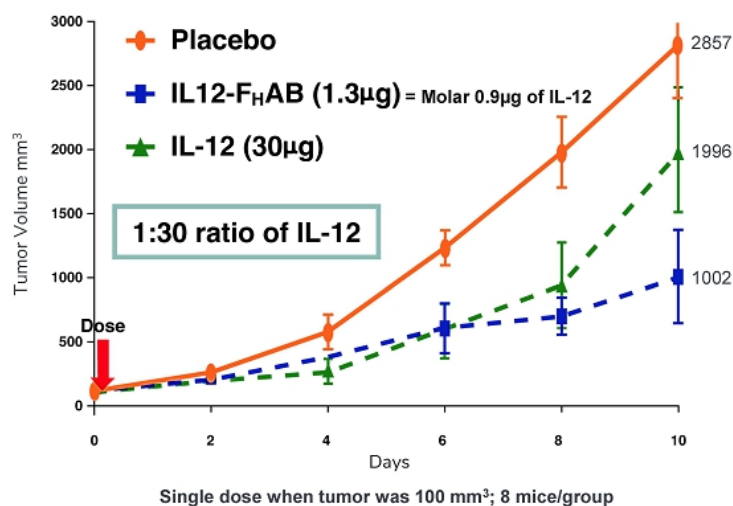
- IL- $F_H$ AB binds Albumin in the blood
  - IL- $F_H$ AB - Albumin binds to FcRn resulting in transport from blood to TME
  - IL- $F_H$ AB - Albumin binds to GP60, resulting in transport from blood to TME
  - IL- $F_H$ AB - Albumin binds to SPARC
  - Cytokine activates local immune cells
- This mechanism of action results in SPARC retaining IL- $F_H$ AB in the TME

Hoogenboezem, Adv Drug Deliv Rev. (2018) 130: 73-89  
Merlot, Front Physiol (2014) 5: 299

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# SON-1010: Reduces Tumor Growth in Mice

IL12-F<sub>H</sub>AB vs IL-12 in B16F10 Melanoma



IL-12 (1µg) and IL12-F<sub>H</sub>AB (1.3µg) are molar equivalent and have similar bioactivity, *in vitro*; however, *in vivo*, F<sub>H</sub>AB is approximately 30-fold more potent than IL-12 (at day 10, 1.3µg IL12- F<sub>H</sub>AB > IL-12 30µg)

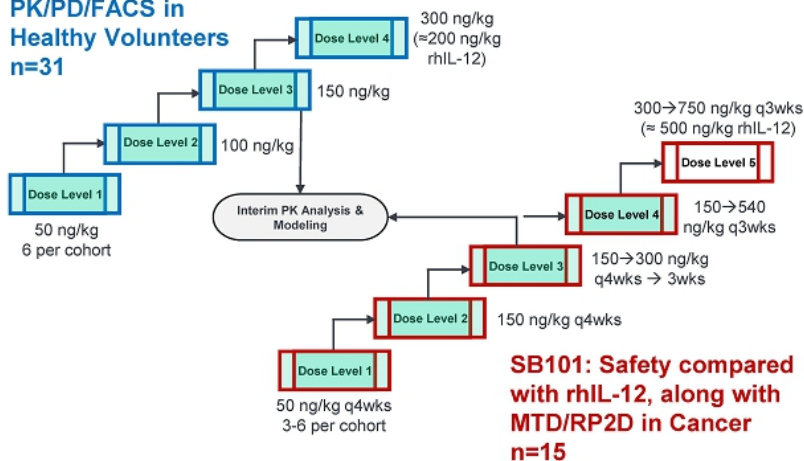
AACR Annual Meeting 2017, Poster #588

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## Clinical Program: SB101 & SB102 Study Designs



**SB102: SAD for PK/PD/FACS in Healthy Volunteers n=31**



- ▶ Rapid enrollment of healthy volunteers in the SAD provides clean PK data without interpretation challenges from prior cancer treatment effects
- ▶ Simulation using continual reassessment model allows prediction of safe doses in the MAD that have more potential for effect on the tumor micro-environment, encouraging enrollment
- ▶ Clinical pharmacology support and HV SAD allows for much lower cost and faster completion
- ▶ MTD/RP2D in solid tumor patients provides path to combination studies

Shen, Clin Transl Sci (2019) 12:6  
Karakunnel, (2018) J Transl Med 16:336

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# Safety Data from SB101 (unaudited, as of 28Feb23)

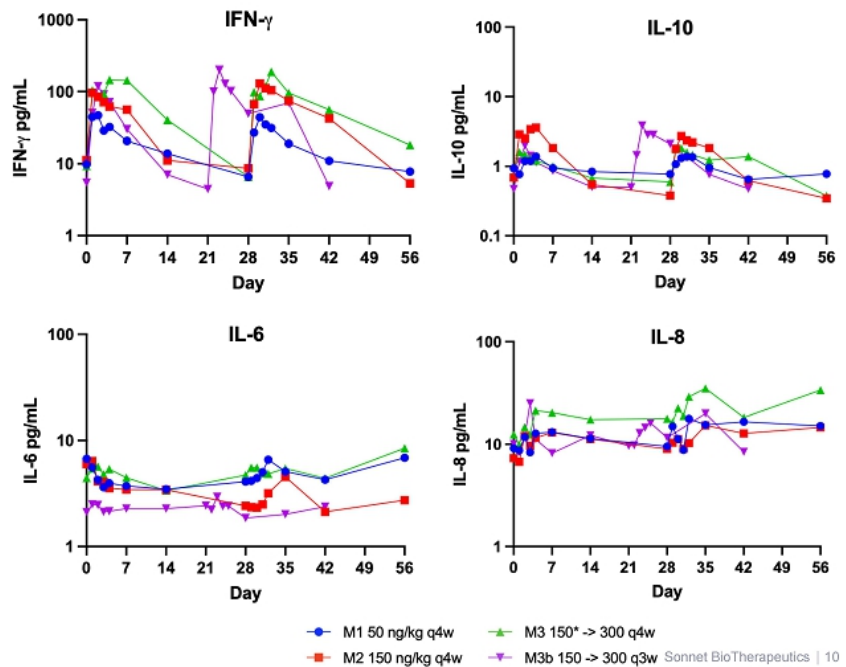
Related TEAEs by Grade	50 ng/kg q4w (N=3)	150 ng/kg q4w (N=3)	150 → 300 ng/kg q4w (N=3)	150 → 300 ng/kg q3w (N=3)	150 → 540 ng/kg q3w (N=3)
Tachycardia (Grade 1)		1 (33.3)			
Nausea (Grade 1)	1 (33.3)				
Chills (Grade 1)		1 (33.3)		1 (33.3)	
Fatigue (Grade 1)		1 (33.3)		1 (33.3)	
Injection site pain (Grade 1)	1 (33.3)	3 (100.0)			
Pain (Grade 1)	1 (33.3)				
Pyrexia (Grade 1)		1 (33.3)	1 (33.3)		1 (33.3)
Decreased appetite (Grade 1)	1 (33.3)				
Oedema peripheral (Grade 1)	1 (33.3)	1 (33.3)			
Arthralgia (Grade 1)	1 (33.3)				
Limb discomfort (Grade 1)	1 (33.3)				
Muscular weakness			1 (33.3)		
Myalgia (Grade 1)	2 (66.7)			1 (33.3)	1 (33.3)
Pain in extremity (Grade 1)	1 (33.3)	1 (33.3)			
Headache (Grade 1)		1 (33.3)		1 (33.3)	
Night sweats (Grade 1)		1 (33.3)			
Rash pruritic (Grade 1)	1 (33.3)			1 (33.3)	
Hot flush (Grade 1)	1 (33.3)				
Abdominal Pain (Grade 1)				1 (33.3)	
Eyelid swelling (Grade 1)				1 (33.3)	
Dysphonia (Grade 1)				1 (33.3)	
Oropharyngeal pain (Grade 1)					1 (33.3)
Lymphadenitis (Grade 1)				1 (33.3)	
Fatigue (Grade 2)	3 (100.0)		1 (33.3)		
Pruritis (Grade 2)				1 (33.3)	
ALT increased (Grade 2)		1 (33.3)			
AST increased (Grade 2)		1 (33.3)			
Lipase Increased (Grade 3)			1 (33.3)*		



## SB101 Cytokine Assay Results

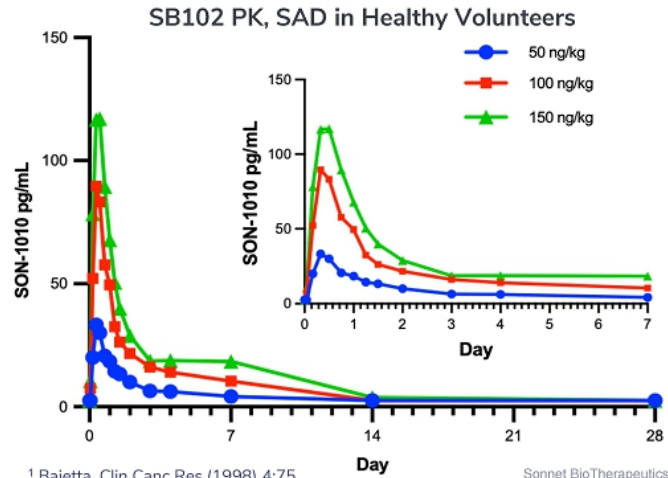
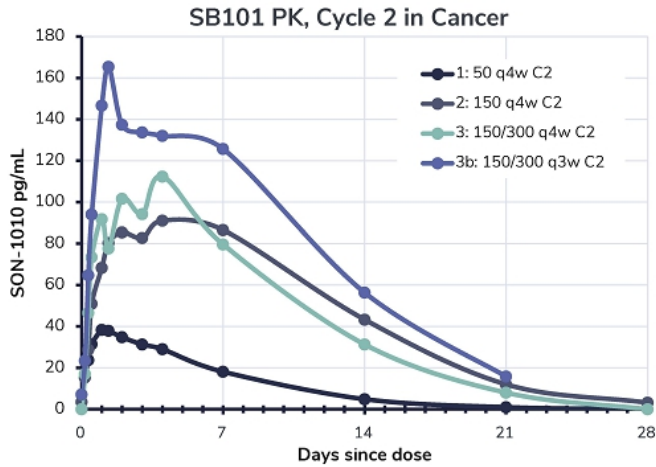


- Primary PD parameters included IFN $\gamma$ , IL-1 $\beta$ , IL-2, IL-4, IL-6, IL-8, IL-10, and TNF $\alpha$ , assayed using the MSD platform.
- Increases in IFN $\gamma$  (showing an IL-12 effect and potential for tumor control) were dose-related, controlled, and prolonged.
- SON-1010 induced IFN $\gamma$  with both the first and second doses in all patients. The levels peaked at 24 to 48 hours and returned to baseline after 2 to 4 weeks.
- The C<sub>max</sub> was about 50 pg/mL after 50 ng/kg SON-1010, 125 pg/mL after 150 ng/kg, and 200 pg/mL after 300 ng/kg.
- Low amounts of IL-10 were induced with each dose in a dose-dependent manner, which could also be a result of the increase in IFN $\gamma$ .
- No consistent pattern of response was seen with IL-1 $\beta$ , IL-6, IL-8, or TNF $\alpha$  and there was no evidence of cytokine release syndrome (CRS) at these doses.



# SON-1010 Interim PK Analysis after Cohort 3

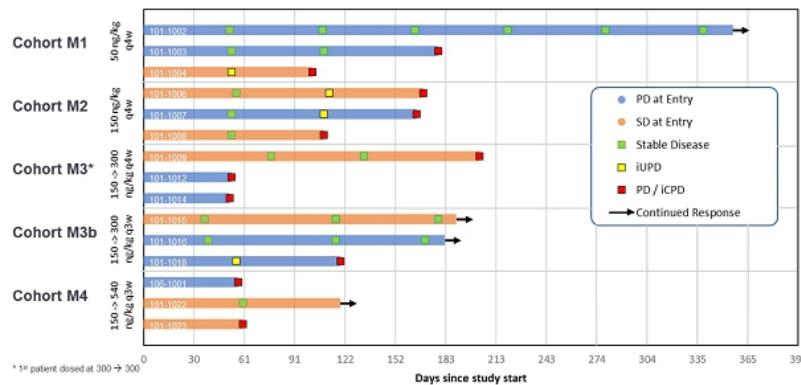
- ◆ Typical dose-related increases were seen with SON-1010, with single compartment kinetics in cancer and the potential for two compartments in healthy volunteers
- ◆ The preliminary geometric mean elimination half-life ( $t_{1/2}$ ) was 113 hours in SB101, compared to 12 hrs with rhIL-12<sup>1</sup>
- ◆  $C_{max}$  was 39 to 197 pg/mL, and the geometric exposure ( $AUC_{0-inf}$ ) was 8,620 to 43,600 h\*pg/mL
- ◆ The accumulation estimates are not likely to be physiologically significant with dosing of SON-1010 every 3 weeks



<sup>1</sup> Bajetta, Clin Canc Res (1998) 4:75

Sonnet BioTherapeutics | 11

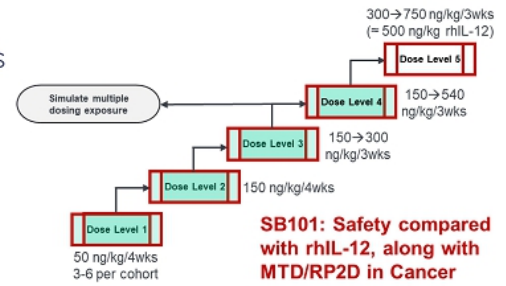
# SB101: SON-1010 Influence on Tumor Size



\* 1<sup>st</sup> patient dosed at 300 → 300

- The swimmers plot shows the status for each patient and whether they had PD or SD at study entry. If patients are clinically stable and have tumor growth that might represent either tumor inflammation (a positive effect of SON-1010) or 'unconfirmed progression' (iUPD by iRECIST), they can continue on study until progression is confirmed (iCPD).
- Nine of 15 (60%) patients had SD at the first follow-up CT, 4 of whom were progressing at study entry. 5 of 14 (36%) patients remained stable at 4 months, suggesting clinical benefit. The mean PFS is 141 days (4.5 months).
- One patient (#1002) with endometrial sarcoma who was progressing at study entry has SD after 11 months on SON-1010 with smaller tumors and complete resolution of her ascites for a time, but her ascites has partially returned. Two patients (in M3b) at higher doses are stable at 6 months.

- ▶ Preliminary PK modeling suggests  $t_{1/2}$  in humans is >120 hours
  - ❑ Compares favorably with rhIL-12  $t_{1/2}$  of 5-12 hours
- ▶ No Dose Limiting Toxicities to date in 15 patients
- ▶ Mostly mild with very few more significant AEs
  - ❑ AEs consistent with published literature for IL-12
  - ❑ All have been transient in nature
  - ❑ AEs are less numerous and less intense after the first dose
- ▶ The IFN $\gamma$  response was dose-related, controlled, and prolonged
- ▶ 5 of the first 14 patients (36%) have evidence of clinical benefit (SD at 4 months)
- ▶ Cytokine results suggest SON-1010 has extended PK, with induction of an IL-12 effect without CRS



## Next Steps

### SON-1010 in Combination with Atezolizumab

- ▶ **SB221 Study:** Collaboration with Roche/Genentech<sup>1</sup>
- ▶ Phase 1b/2a adaptive design study to assess the safety, tolerability, PK/PD, and POC of SON-1010 alone or in combination with atezo in patients with platinum-resistant ovarian cancer (PROC)<sup>2</sup>
- ▶ **Part 1**
  - ❑ Dose escalation of SON-1010 with fixed dose atezolizumab
  - ❑ Expand at RP2D in PROC
  - ❑ Designed to show statistically significant clinical effect
  - ❑ Expansion of SB101 at RP2D in PROC allows:
- ▶ **Part 2**
  - ❑ Randomized comparison of SON-1010 as monotherapy vs. combination with atezo vs. SOC
  - ❑ Designed to show proof-of-concept in PROC

<sup>1</sup> Sonnet PR, 9 Jan 2023

<sup>2</sup> <https://clinicaltrials.gov/ct2/show/NCT05756907>

- ◆ **Next Generation Oncology Platform (F<sub>H</sub>AB)**
  - ❑ Confers both tumor targeting and enhanced pharmacokinetics (PK);
  - ❑ Fully human protein sequence, and thus, no predicted immunogenicity
- ◆ **First immune activator with tumor-targeting functions on a proprietary F<sub>H</sub>AB platform**
- ◆ **Encouraging preclinical data in a cancer model**
  - ❑ Tumor growth inhibition, associated with the induction of IFN $\gamma$  (i.e., potentially better efficacy with lower dosing), in the “immunologically cold” B16F10 melanoma model, with a 30-fold therapeutic index vs. wild-type IL-12
- ◆ **GLP toxicology data**
  - ❑ Up to 50x the human dose is safe in monkeys with NO cytokine release syndrome (CRS)
- ◆ **Clinical data experience for IL12-F<sub>H</sub>AB**
  - ❑ Normal healthy volunteer study – PK was significantly enhanced compared to historical rIL-12
  - ❑ Cancer patient study – demonstrates transient, mild-to-moderate toxicity with NO cytokine release syndrome;
    - ❑ Preliminary clinical benefit in 36% of patients with advanced solid tumors
- ◆ **Broad, global intellectual property, including composition of matter, indications and manufacturing.**
- ◆ **Pipeline includes first-in-class bifunctional oncology products: SON-1210 and SON-1410**
  - ❑ Agreement with Janssen for the evaluation of three Sonnet product candidates
  - ❑ Collaboration with Roche for clinical evaluation of SON-1010 with atezolizumab (Tecentriq®) in ovarian cancer