

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

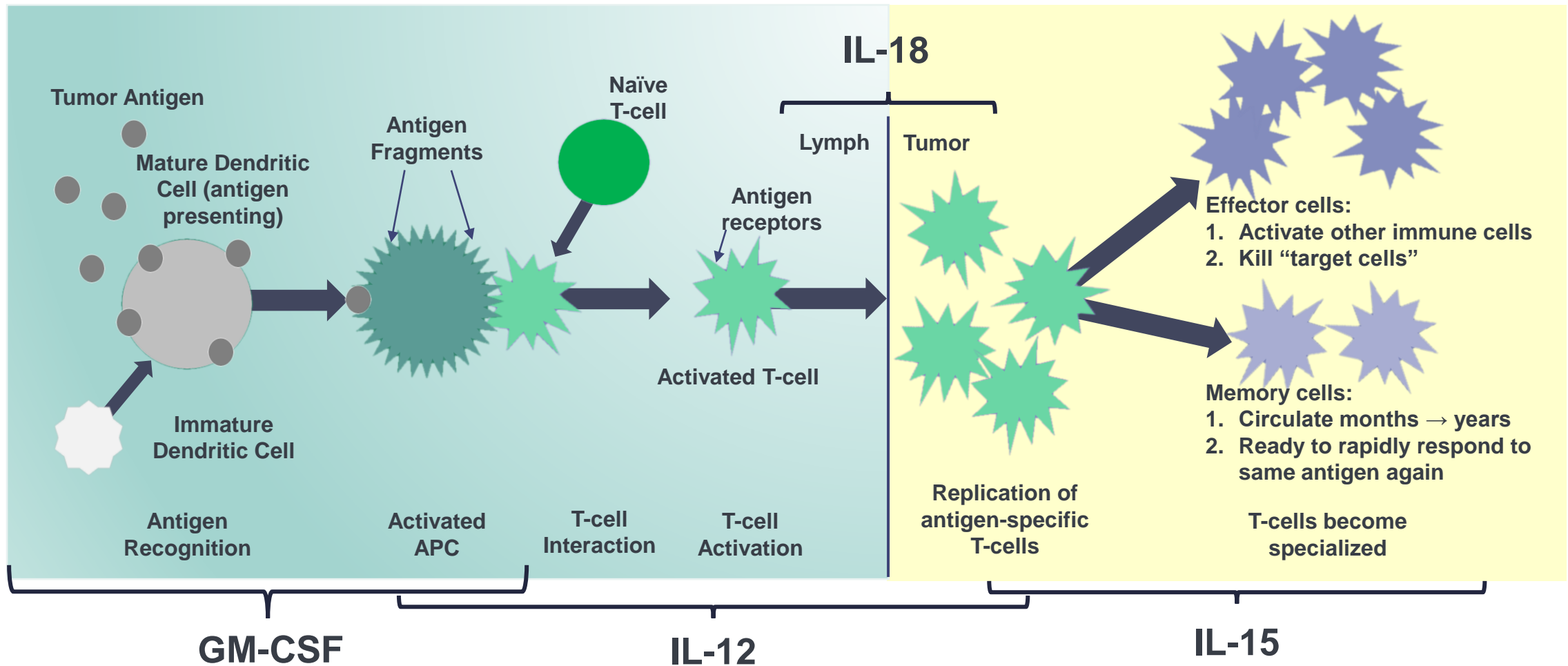
This presentation contains forward-looking statements about **Sonnet BioTherapeutics** based on management's current expectations which are subject to known and unknown uncertainties and risks. Words such as "anticipated," "initiate," "expect," "intend," "plan," "believe," "seek," "estimate," "may," 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_HAB)**
 - ❑ 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_HAB platform**
- ▶ **Encouraging preclinical data in a cancer model**
 - ❑ Tumor growth inhibition, associated with the induction of IFN γ (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_HAB**
 - ❑ 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
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Multiple Points of Intervention



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

STRUCTURE/FUNCTION

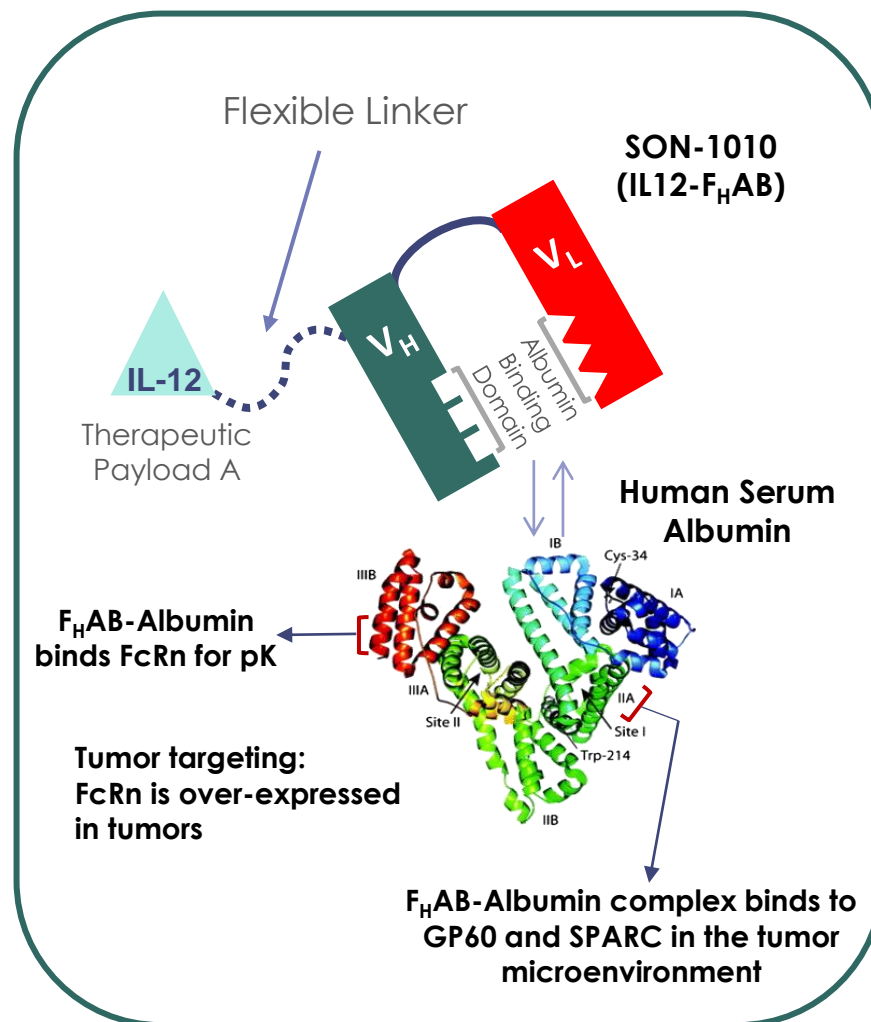
Sonnet's Fully Human Albumin Binding (F_HAB) technology utilizes a single chain antibody fragment (scFv) capable of delivering one or two active drug compounds

- Therapeutic payloads attached via **flexible linker peptides**

Following administration, Sonnet's F_HAB -derived candidates **bind to and “hitch-hike” on endogenous human serum albumin (HSA)** for transport to target tissues

- F_HAB 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

For a video displaying the F_HAB mechanism, please click [here](#)



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)

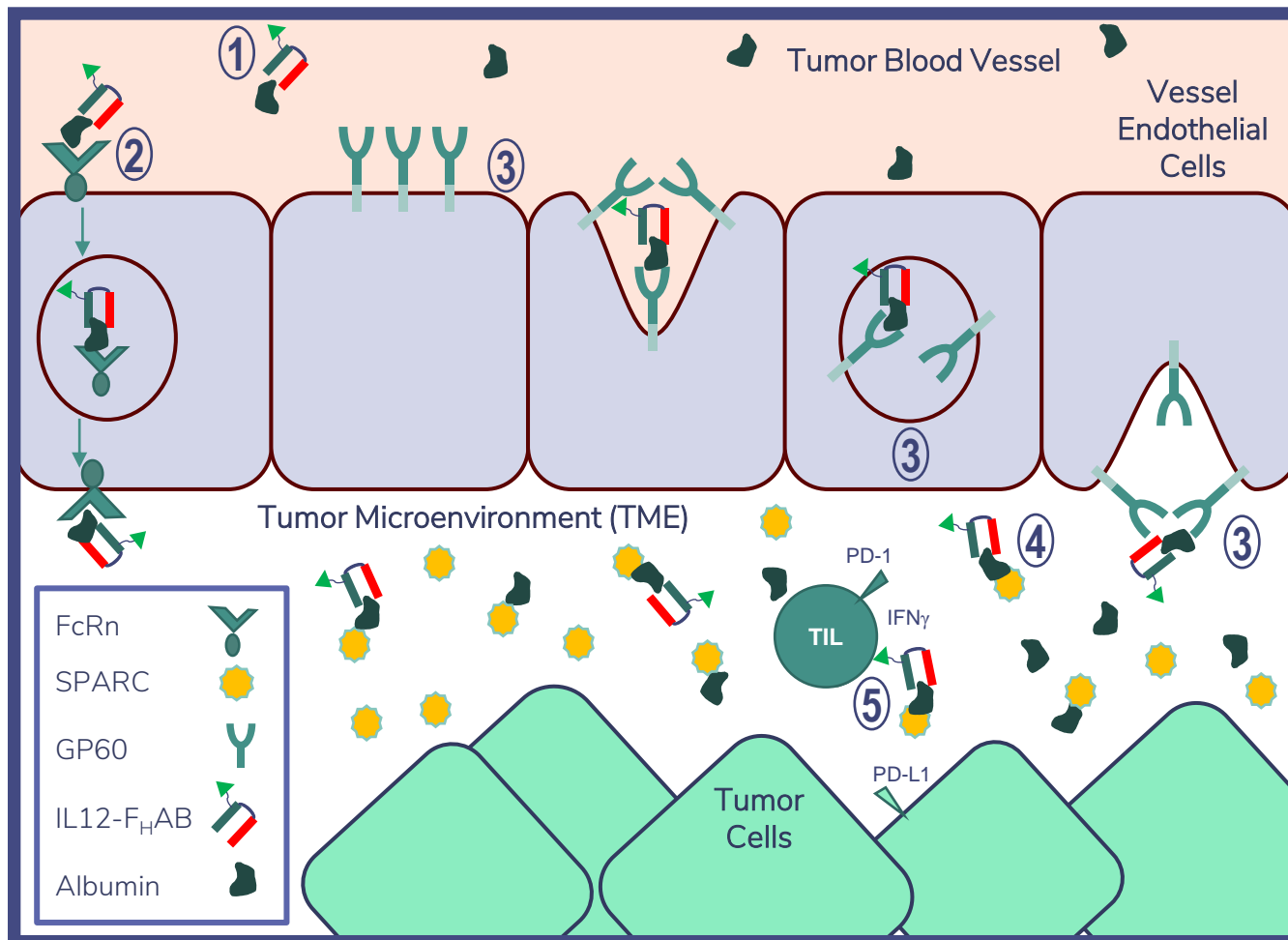
- Continuous intensive perfusion

Modular

- Off-the-shelf system
- Rapid asset development


SON-1010 F_HAB: 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

1. IL-F_HAB binds Albumin in the blood

2. IL-F_HAB – Albumin binds to FcRn resulting in transport from blood to TME

3. IL-F_HAB – Albumin binds to GP60, resulting in transport from blood to TME

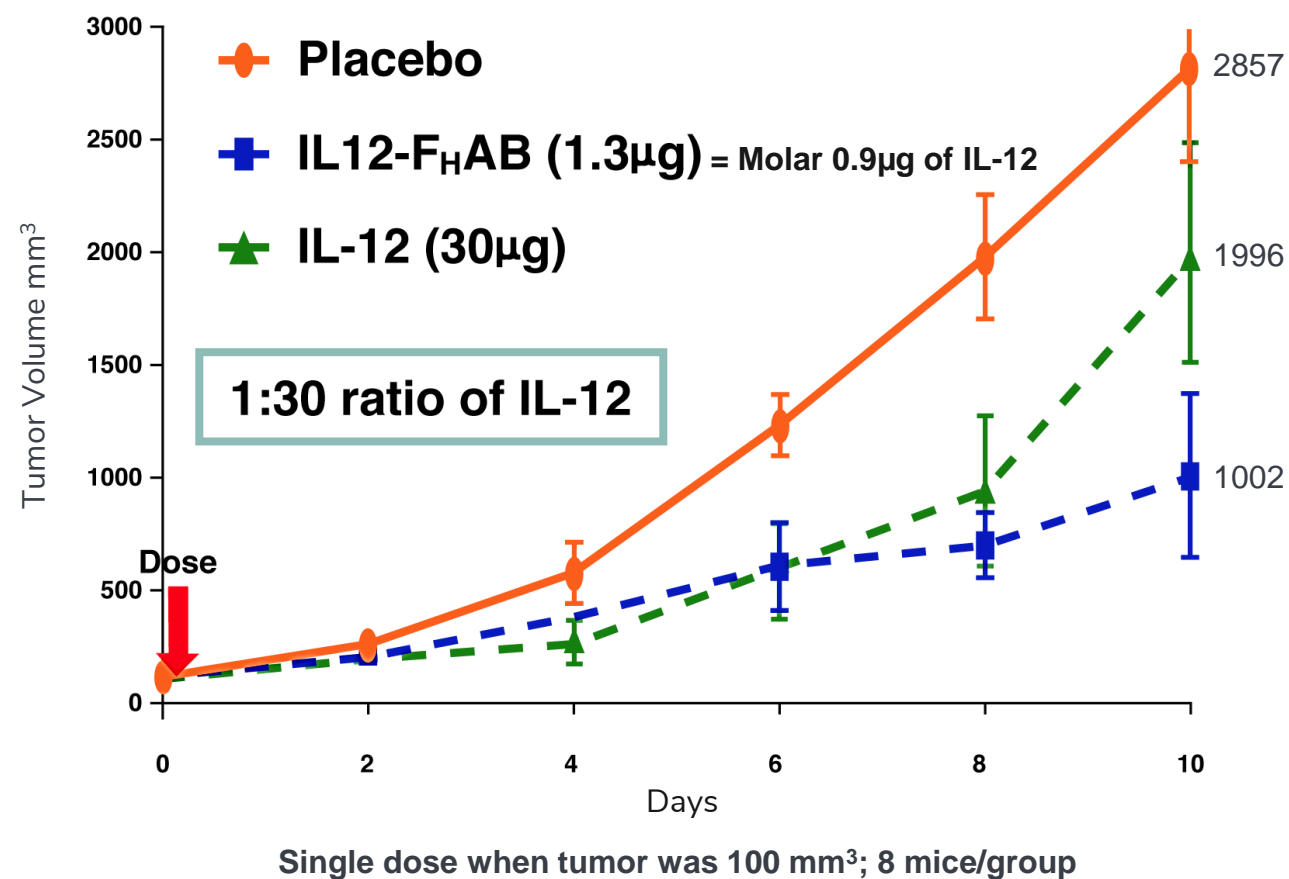
4. IL-F_HAB – Albumin binds to SPARC

5. Cytokine activates local immune cells

This mechanism of action results in SPARC retaining IL-F_HAB in the TME

SON-1010: Reduces Tumor Growth in Mice

IL12-F_HAB vs IL-12 in B16F10 Melanoma

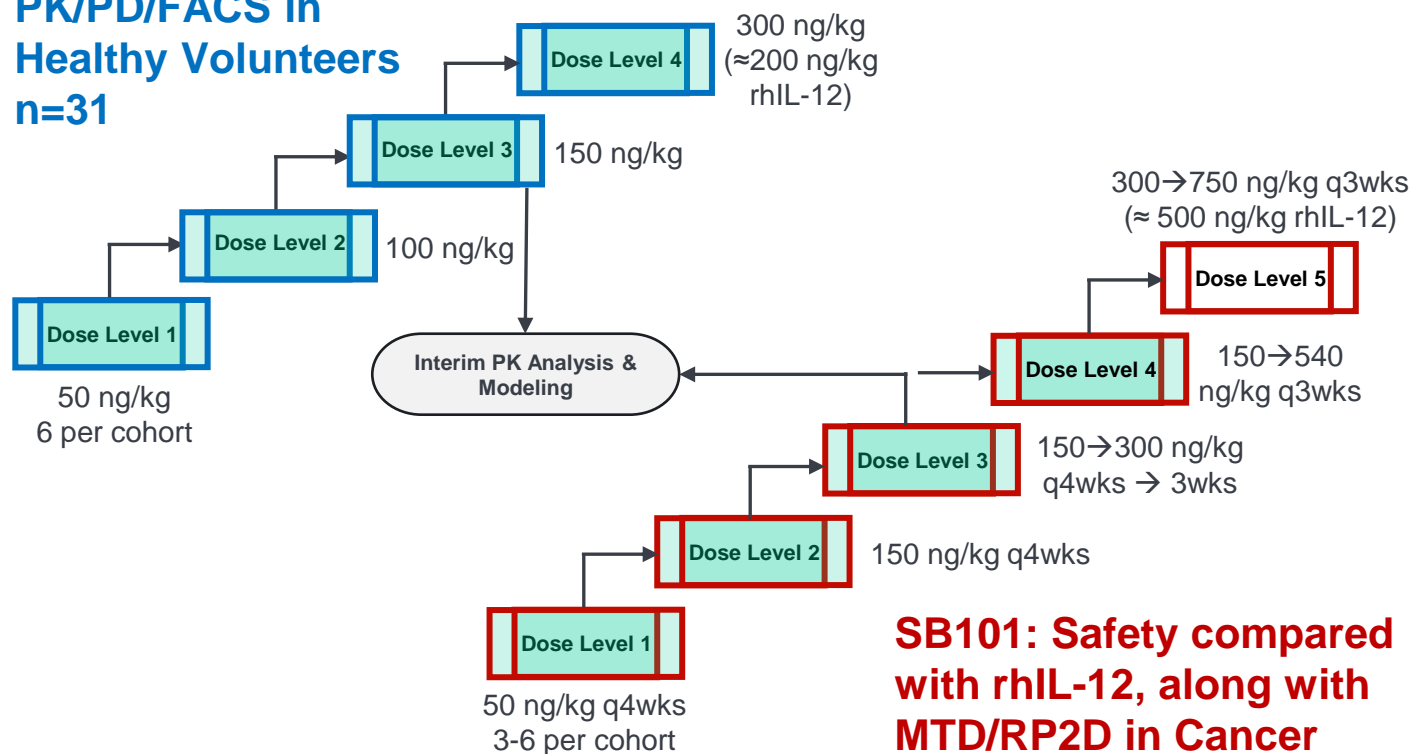


IL-12 (1µg) and IL12-F_HAB (1.3µg) are molar equivalent and have similar bioactivity, *in vitro*; however, *in vivo*, F_HAB is approximately 30-fold more potent than IL-12 (at day 10, 1.3µg IL12-F_HAB > IL-12 30µg)

PROOF-OF-CONCEPT

Clinical Program: SB101 & SB102 Study Designs

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



SB101: Safety compared with rhIL-12, along with MTD/RP2D in Cancer n=15

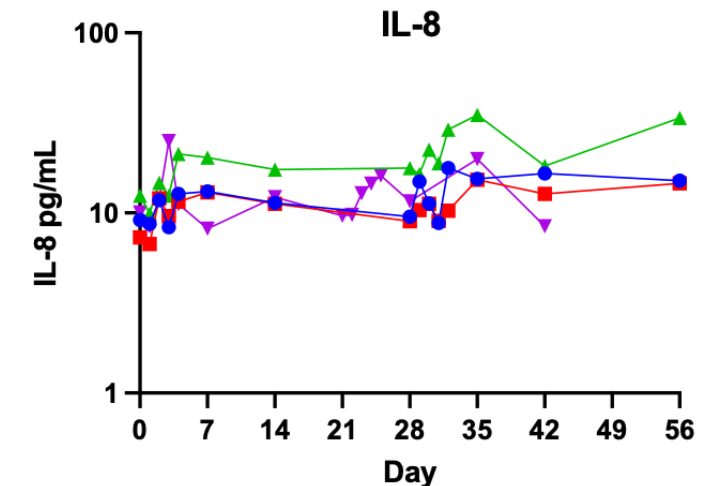
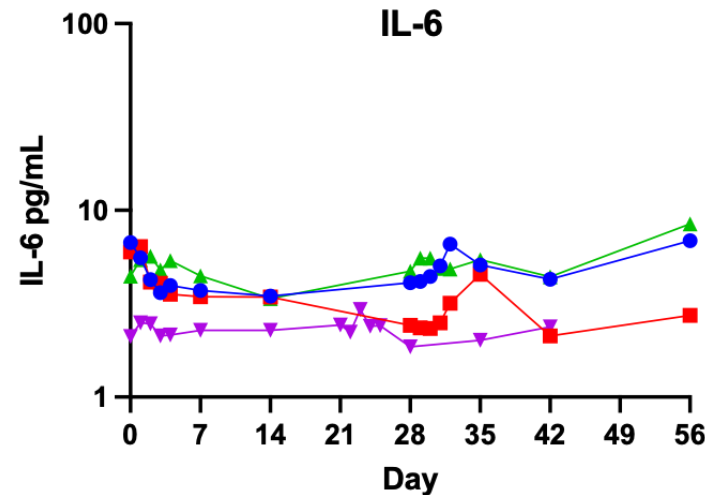
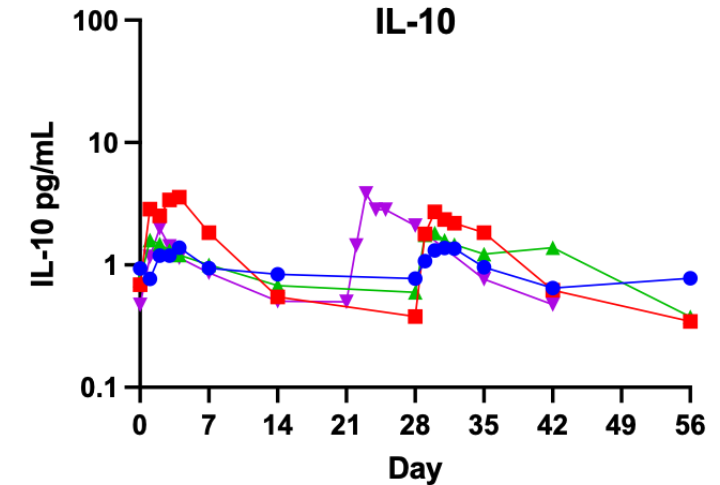
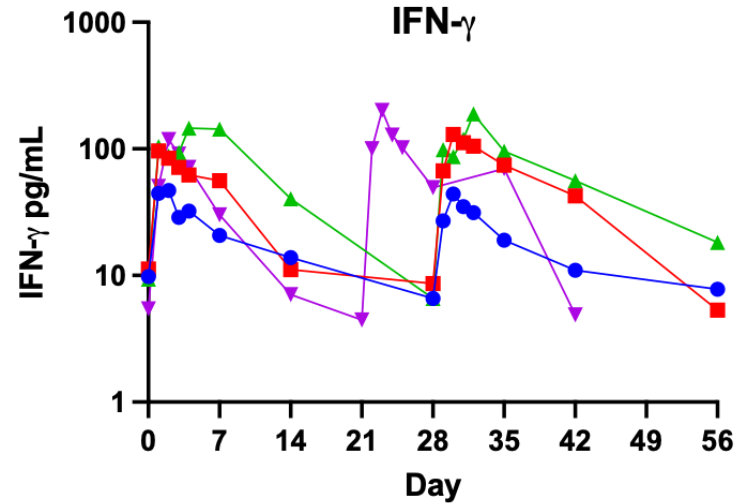
- Rapid enrollment of healthy volunteers in the SAD provides clean PK data without interpretation challenges from prior cancer treatment effects
- Simulation using continual reassessment model allows prediction of safe doses in the MAD that have more potential for effect on the tumor micro-environment, 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

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 γ , IL-1 β , IL-2, IL-4, IL-6, IL-8, IL-10, and TNF α , assayed using the MSD platform.
- Increases in IFN γ (showing an IL-12 effect and potential for tumor control) were dose-related, controlled, and prolonged.
- SON-1010 induced IFN γ 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_{max} 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 γ .
- No consistent pattern of response was seen with IL-1 β , IL-6, IL-8, or TNF α and there was no evidence of cytokine release syndrome (CRS) at these doses.



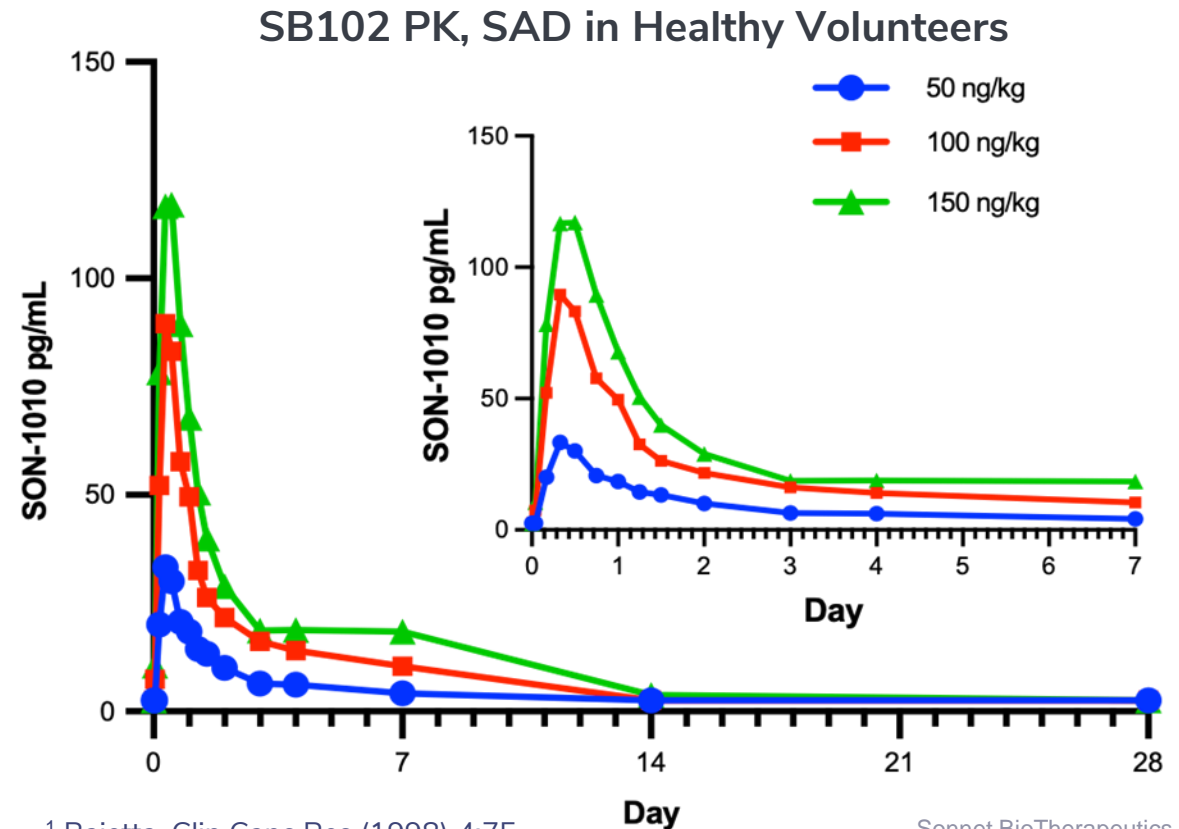
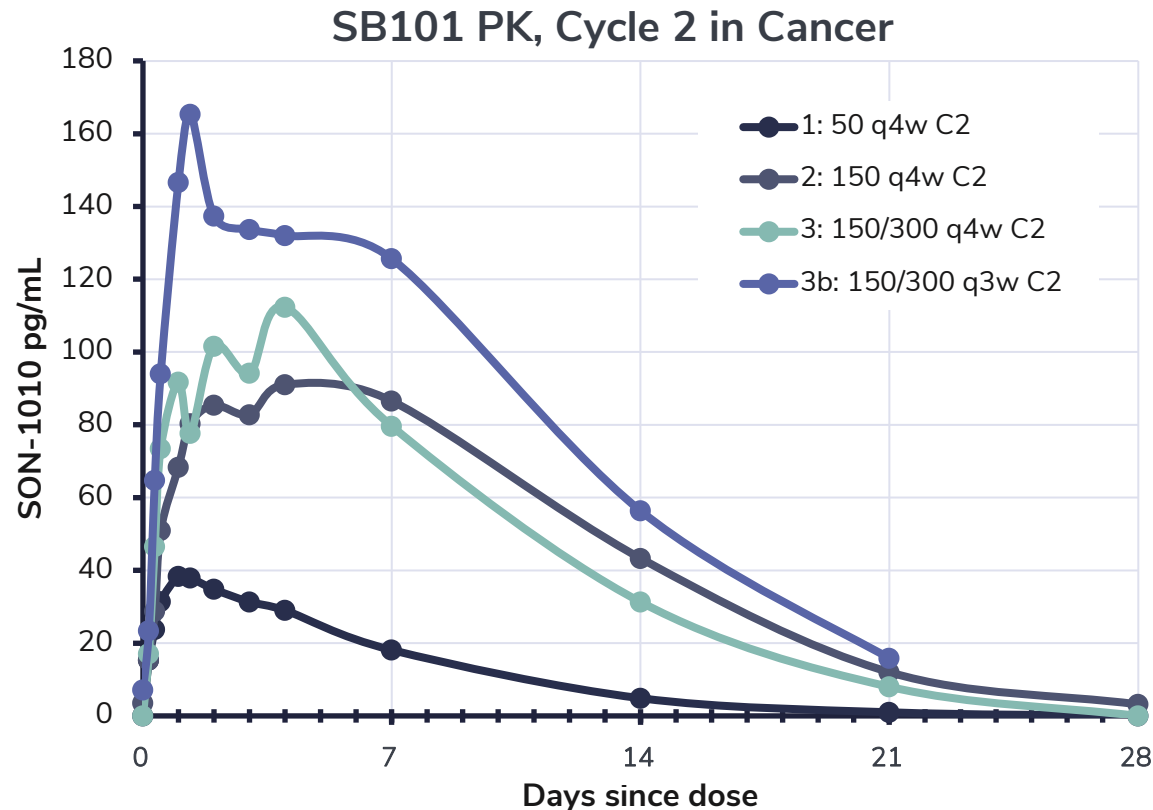
● M1 50 ng/kg q4w
■ M2 150 ng/kg q4w

▲ M3 150* -> 300 q4w

▼ M3b 150 -> 300 q3w

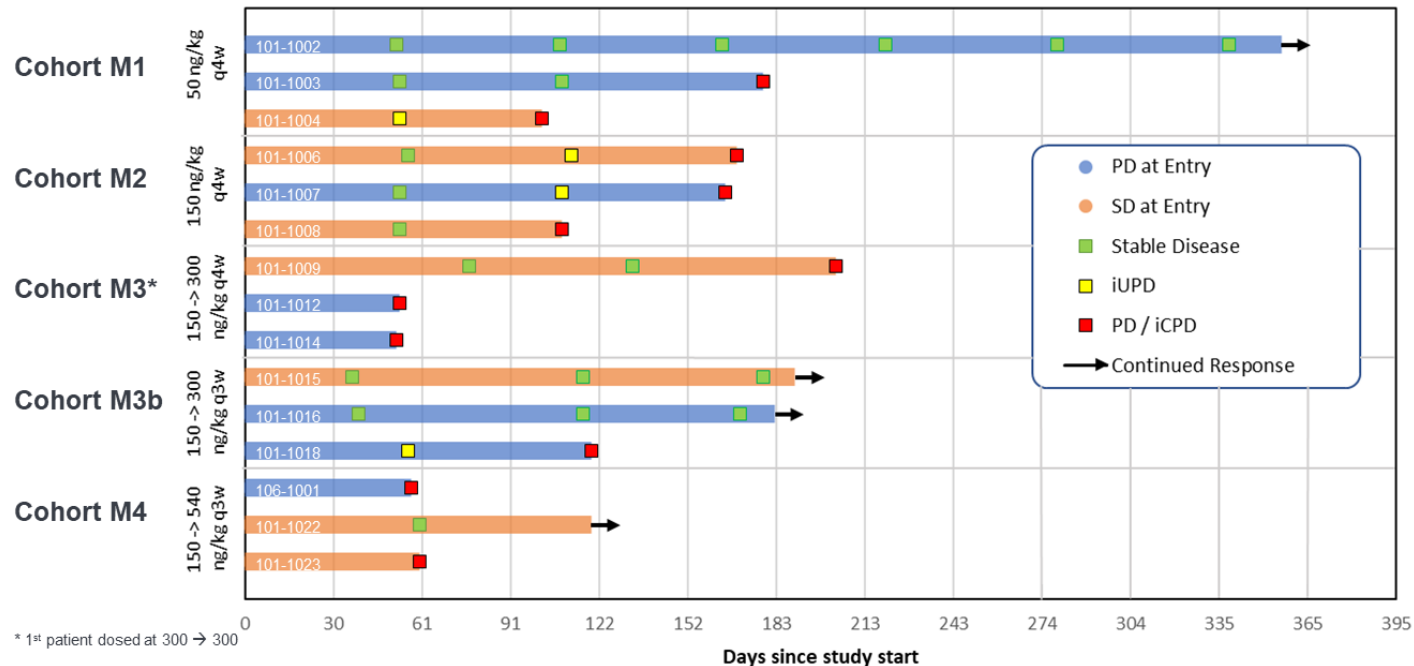
SON-1010 Interim PK Analysis after Cohort 3

- 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-12¹
- 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



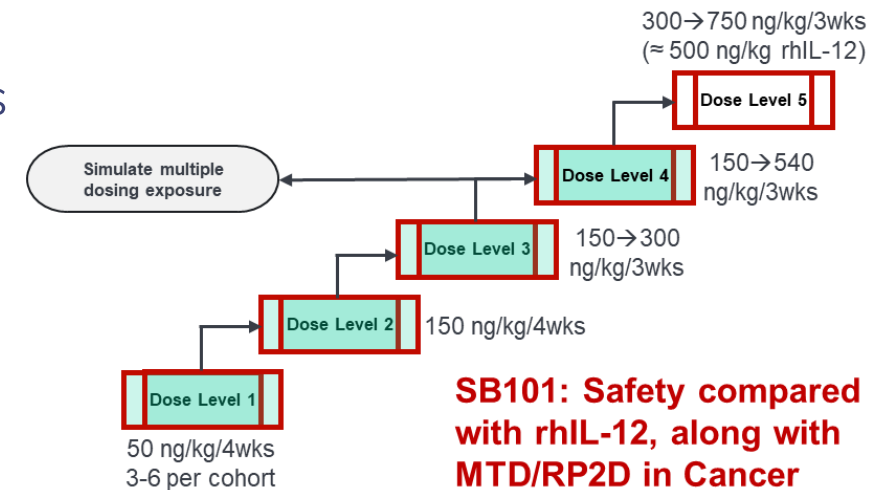
¹ Bajetta, Clin Canc Res (1998) 4:75

SB101: SON-1010 Influence on Tumor Size



- ❑ 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 γ 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/Genentech¹
- 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)²
- **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

¹ Sonnet PR, 9 Jan 2023

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

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