



POWERING A NEW WAVE OF IMMUNE THERAPEUTICS

Corporate Presentation

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**.

Powering a New Wave of Immune Therapeutics

LEADERSHIP

Highly experienced executive team with a deep knowledge of biopharmaceutical drug discovery and development

CORPORATE FOCUS

Prioritize development of assets with partnering interest
Cost-cutting initiative to reduce operating expenses by approximately 30%

Existing collaborations with J&J and Roche offer licensing expansion opportunities

FORTHCOMING MILESTONES

SON-1010: Data from dose escalation portion of Phase 1 monotherapy study, 1H24

SON-1010: Safety data from Phase 1b/2a PROC study in combination with atezolizumab, 1H24

SON-080: Phase 1b/2a initial safety data in CIPN, 1Q23

SON-080: Potentially initiate Phase 2 study in DPN, after reviewing CIPN data

SON-1210: Initiate regulatory authorization process in 2023/2024, pending the outcome of any partnering activity

PLATFORM TECHNOLOGY

Proprietary, patented **Fully Human Albumin Binding (F_HAB[®])** platform provides considerable payload flexibility with asset generation capabilities across major biologic drug classes

- Targeted delivery with increased *in vivo* efficacy
- Single or bispecific mechanism of action
- Extended pharmacokinetics (PK)



Sonnet's 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

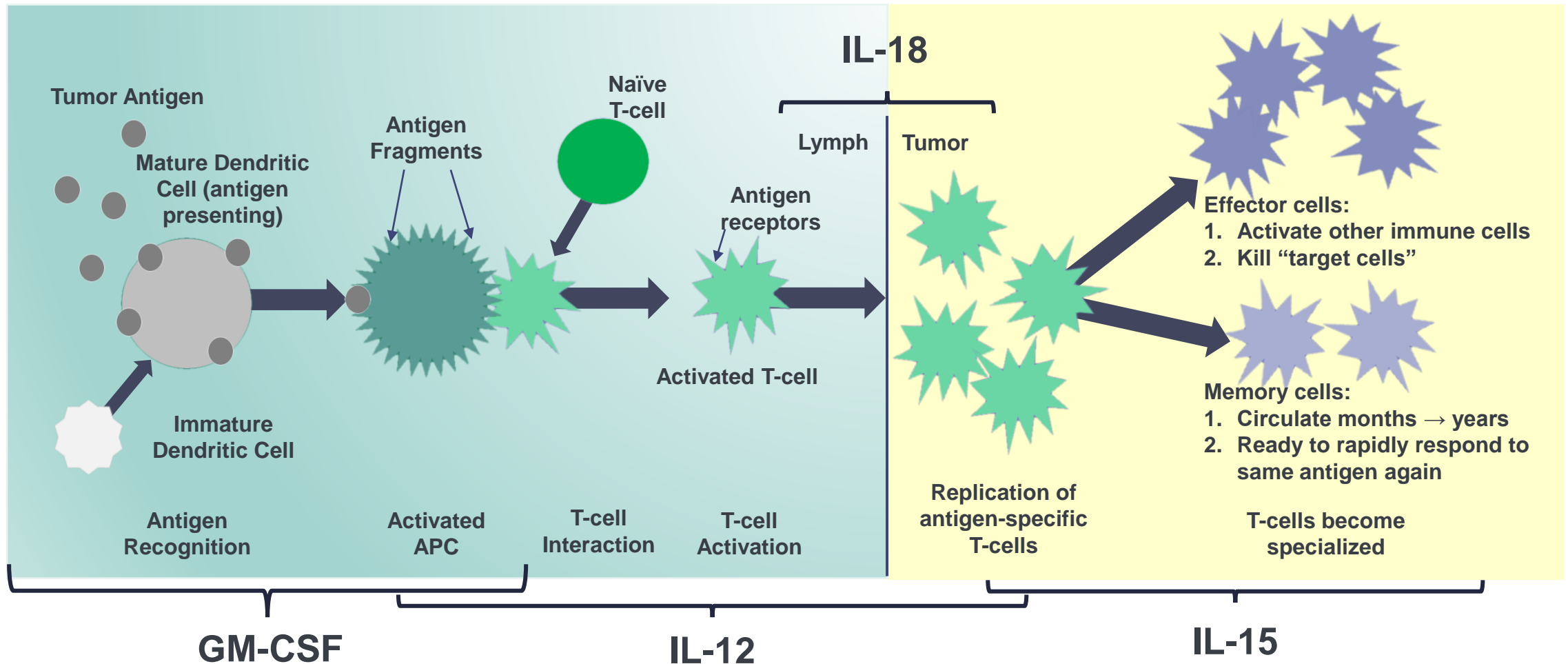
Following administration, Sonnet's F_HAB derived candidates bind to and "hitch-hike" on endogenous Human Serum Albumin (HSA) for transport to lymphoid tissues

- 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

Pipeline Overview

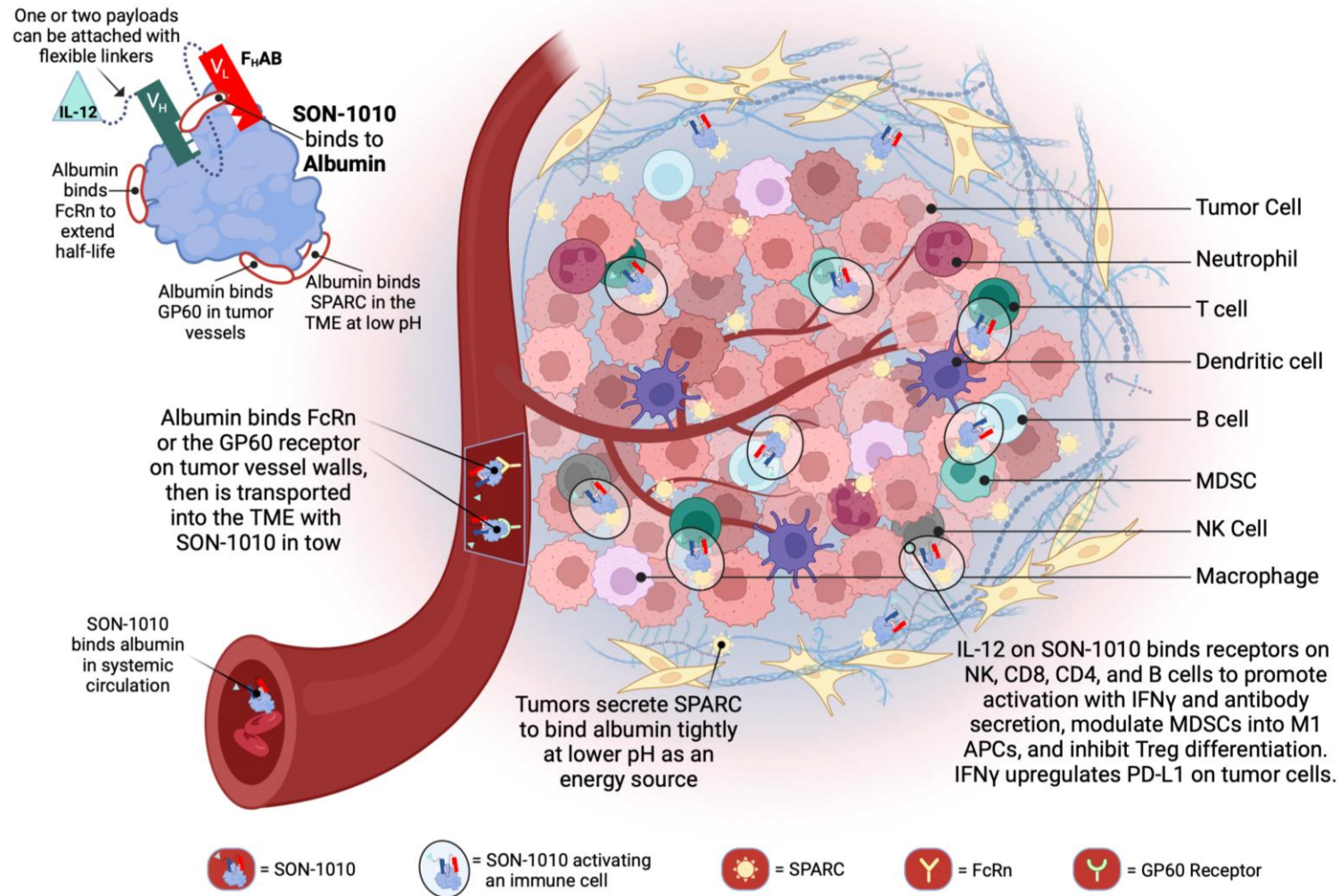
	PROGRAM	INDICATIONS	DISCOVERY	PRECLINICAL	PHASE I	PHASE II	PHASE III	PARTNER
I F _H AB Platform	SON-1010 (IL12-F _H AB)	Solid Tumors	▶					
	SON-1010 (IL12-F _H AB)	Platinum-Resistant Ovarian Cancer (PROC)	▶					
	SON-1210 (IL12-F _H AB-IL15)	Solid Tumors	▶					
	SON-1410 (IL18-F _H AB-IL12)	Melanoma, Renal Cancers	▶					
	SON-3015 (Anti-IL6-F _H AB-Anti-TGFβ)	Tumor and Bone Metastases	▶					
	SON-080 (Low-dose IL-6)	Chemotherapy Induced Peripheral Neuropathy (CIPN)	▶					
Diabetic Peripheral Neuropathy (DPN)		▶						

Multiple Points of Intervention



F_HAB PLATFORM TECHNOLOGY

Sonnet's Technology Advantage



Asset Profile: SON-1010 (IL12-F_HAB)

Stage: Phase 1b/2a combination study with atezolizumab initiated in PROC

Indications: Solid Tumors

Product Description: Asset delivery and targeting by albumin binding mechanism via the F_HAB domain, which results in accumulation of SON-1010 in the microenvironment of solid tumors (TME) through binding to FcRn, GP60, and SPARC, thereby enhancing penetration and retention with increased efficacy. SON-1010 has demonstrated improved pK via binding to FcRn, similar to full MAbs, and improved tumor delivery, all available in a single patented construct.

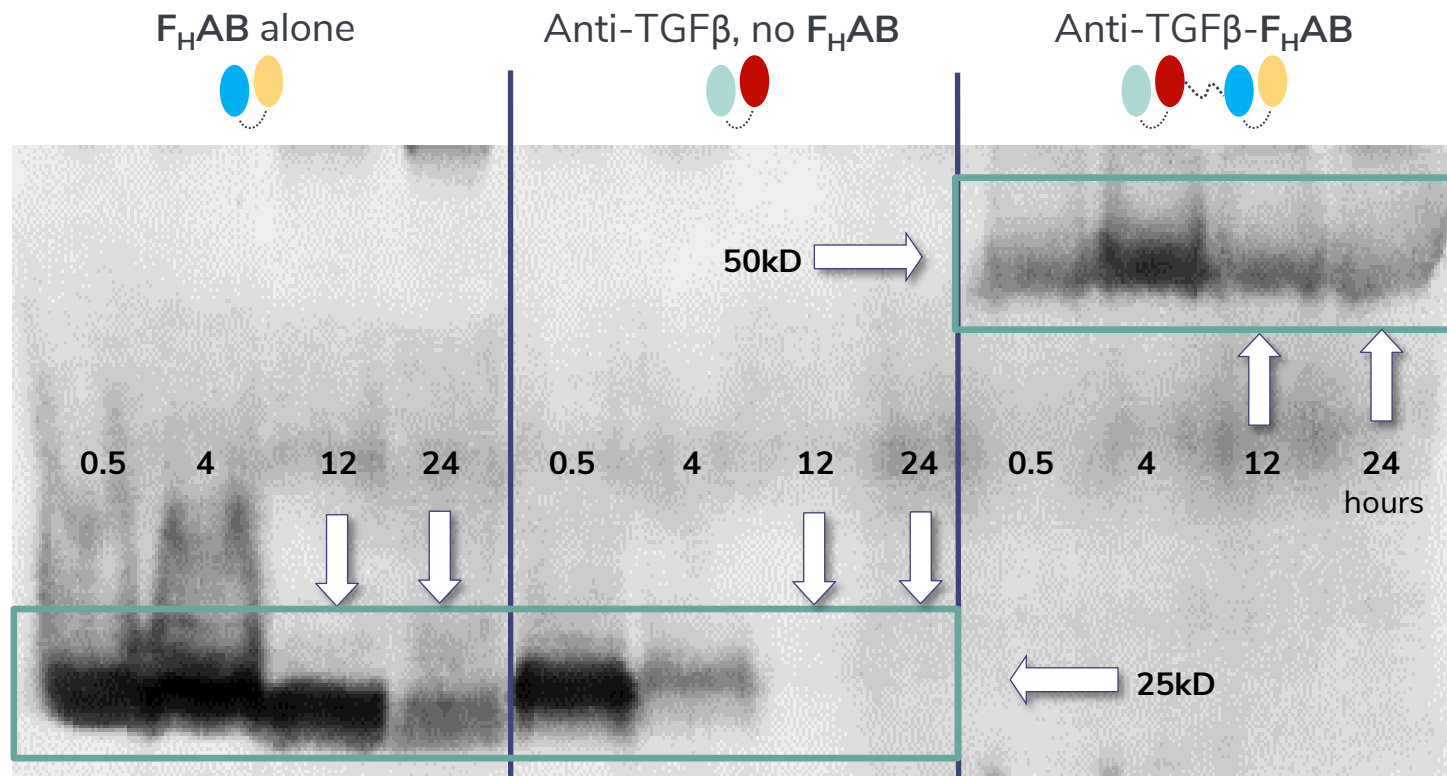
Platform Attributes:

- Fully human construct – Low/No Immunogenicity
- Mammalian cell production (CHO) – Glycosylated
- Small size with linear flexibility – Optimized tumor penetration
- Enhanced PK – FcRn binding
- Targeted – GP60 and SPARC
- Asset Optionality: Single or Bispecific payload capacity
- Modular – Rapid asset development

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

F_HAB: Superior Uptake and Retention in Tumor Tissue

An *in vivo* demonstration of SPARC-mediated binding with optimized retention using albumin



Results show F_HAB enhanced EPR = Efficacy

Western blot of Mouse 4T1 (TGFβ positive tumor@150mm³) extracts from mice 0.5-24 hours post IV injection with 100 μg/mouse of F_HAB, anti-TGFβ or anti-TGFβ-F_HAB

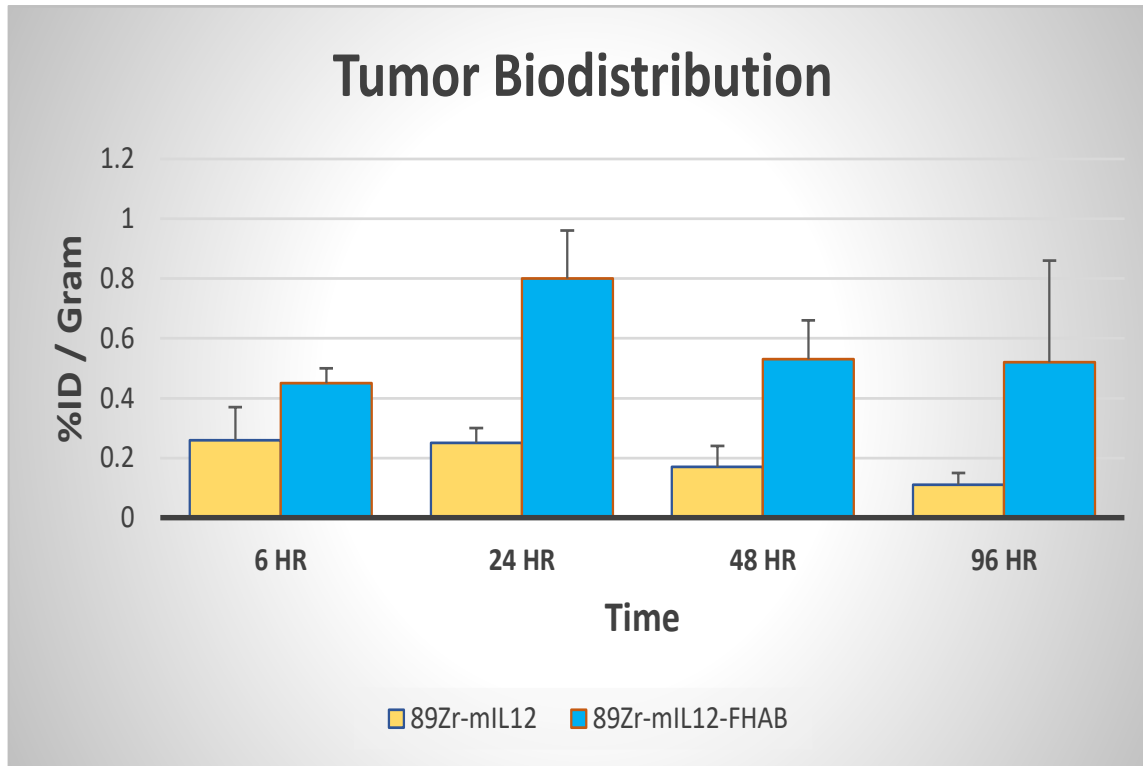
F_HAB present at 0.5 hours, peaks at 4 hours and detectable through 24 hours

Anti-TGFβ present at 0.5 hours, declines at 4 hours and undetectable at 12 and 24 hours

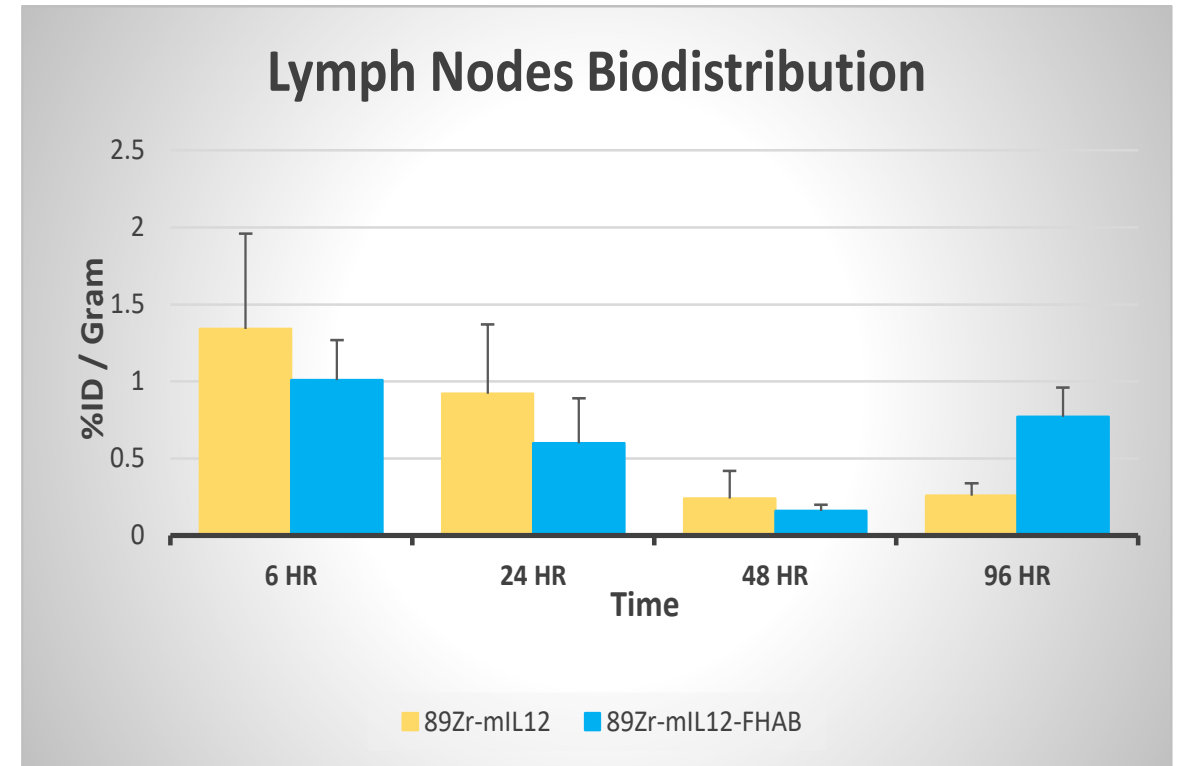
Anti-TGFβ-F_HAB present at 0.5 hours and detectable through 24 hours

Biodistribution Profile Using Radiolabeled mIL12-FHAB and mIL12

mIL12-FHAB Accumulates in Tumor and Draining Lymph Nodes



Comparative time course accumulation in B16F10 melanoma tumors of ⁸⁹Zr-mIL12 versus ⁸⁹Zr-mIL12-FHAB at 6, 24, 48 and 96 hours

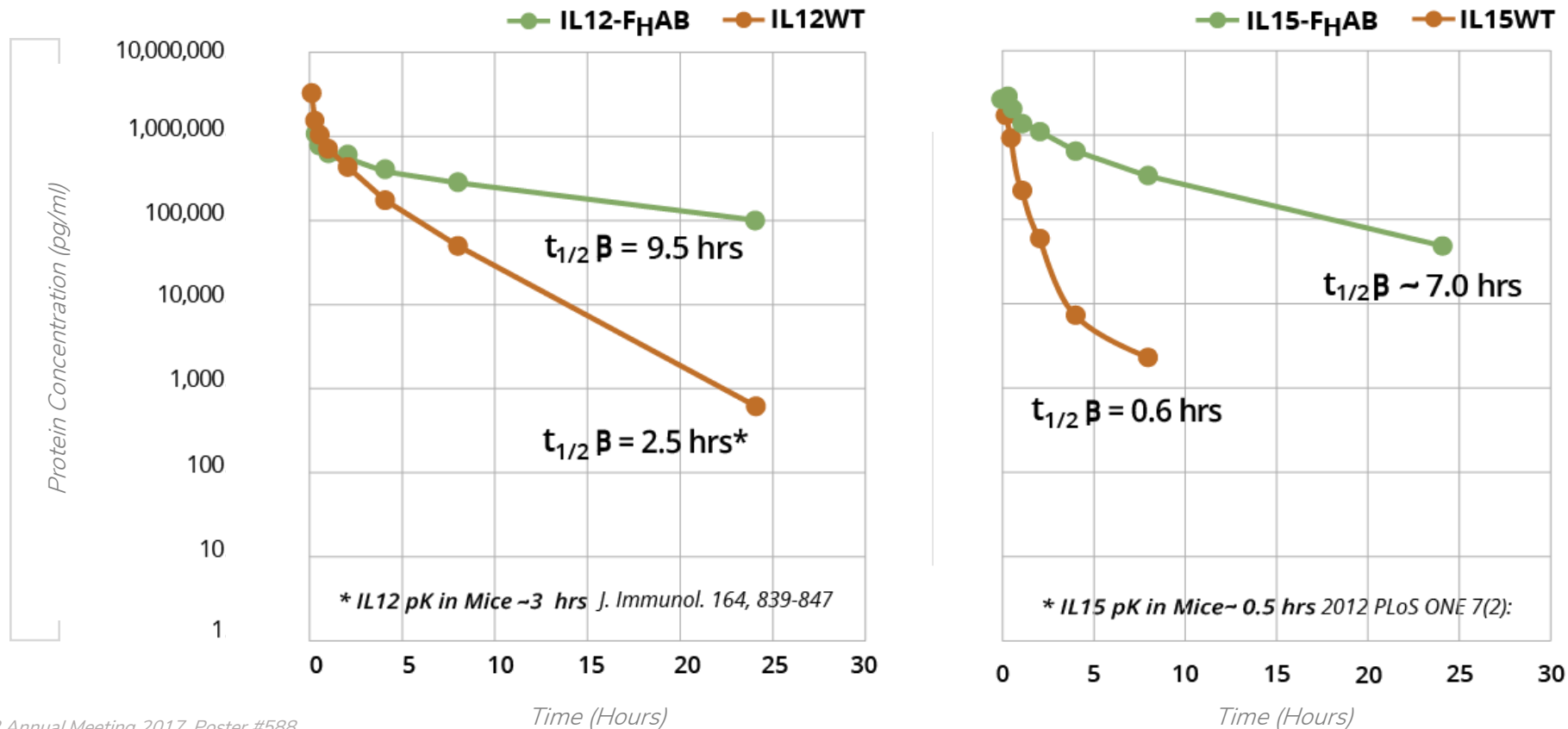


Comparative time course accumulation in lymph nodes of ⁸⁹Zr-mIL12 versus ⁸⁹Zr-mIL12-FHAB at 6, 24, 48 and 96 hours

F_HAB: Enhanced Pharmacokinetic Characteristics

Comparing the pharmacokinetic characteristics of naked IL-12 and IL-15 versus the same interleukins linked to Sonnet's F_HAB

Method: 8 mice C57B/ TP, age 9.5 weeks, dose IV, sacrificed @ 5, 15, 30 mins, 1, 2, 4, 8, 24 & 48 hrs. Serum tested by ELISA.



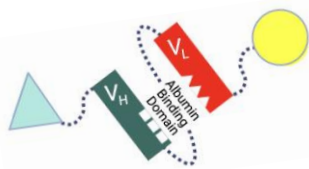
Fusion to F_HAB increased the plasma half-life of IL-12 > 4x and IL-15 > 10X

IL-12 MW = 70 Kd vs IL-15 MW = 13Kd

F_HAB: Defining A Better Platform Technology

Sonnet F_HAB Constructs

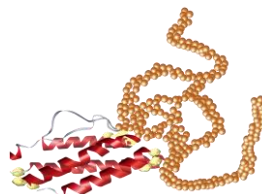
Albumin Binding



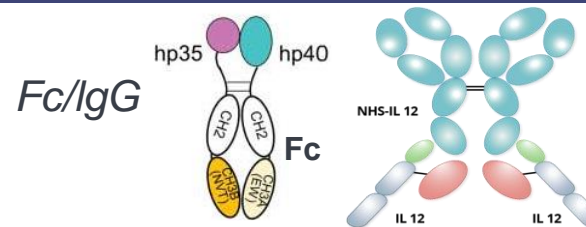
ATTRIBUTES	QUALIFIER
Mode	Mono or Bi-Specific
pK; Alb binding to FcRn	+++ Dosing 3-4 weeks
Glycosylated CHO expressed	+
Tumor Targeting and Retention	++++ Albumin binds gp60 and SPARC
Tumor Penetration, Size and Linear Flexibility	+++ 85-104 kD
Controllable Quantity Dosing	+++

PEG

1-PEG-IL-2(active)



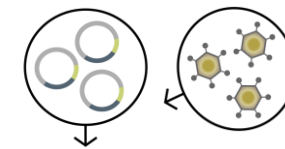
ATTRIBUTES	QUALIFIER
Mode	Mono
pK; Size only	++ Dosing 1-2 weeks
Glycosylated Non mammalian	-
Tumor Targeting and Retention	-
Tumor Penetration Globular	+ ~100+ kD
Controllable Quantity Dosing	++



ATTRIBUTES	QUALIFIER
Mode	Mono or Bi-Specific
pK; FC Binding to FcRn	+++ Dosing 3-4 weeks
Glycosylated CHO expressed	+
Tumor Targeting and Retention	++
Tumor Penetration Globular	++ 100-300 kD
Controllable Quantity Dosing	+++

DNA / Viral

Gene Therapy
Viral Gene Therapy



ATTRIBUTES	QUALIFIER
Mode	Mono
pK	++ Dosing 2-4 weeks
GMP - BSL-2 classified facility	+
Tumor Targeting DNA	Intratumoral Injection *
Tumor Targeting Viral	Viral tumor cell lysis
Controllable Quantity Dosing	Issues of variable spread, penetration, resistance and anti-viral immunity

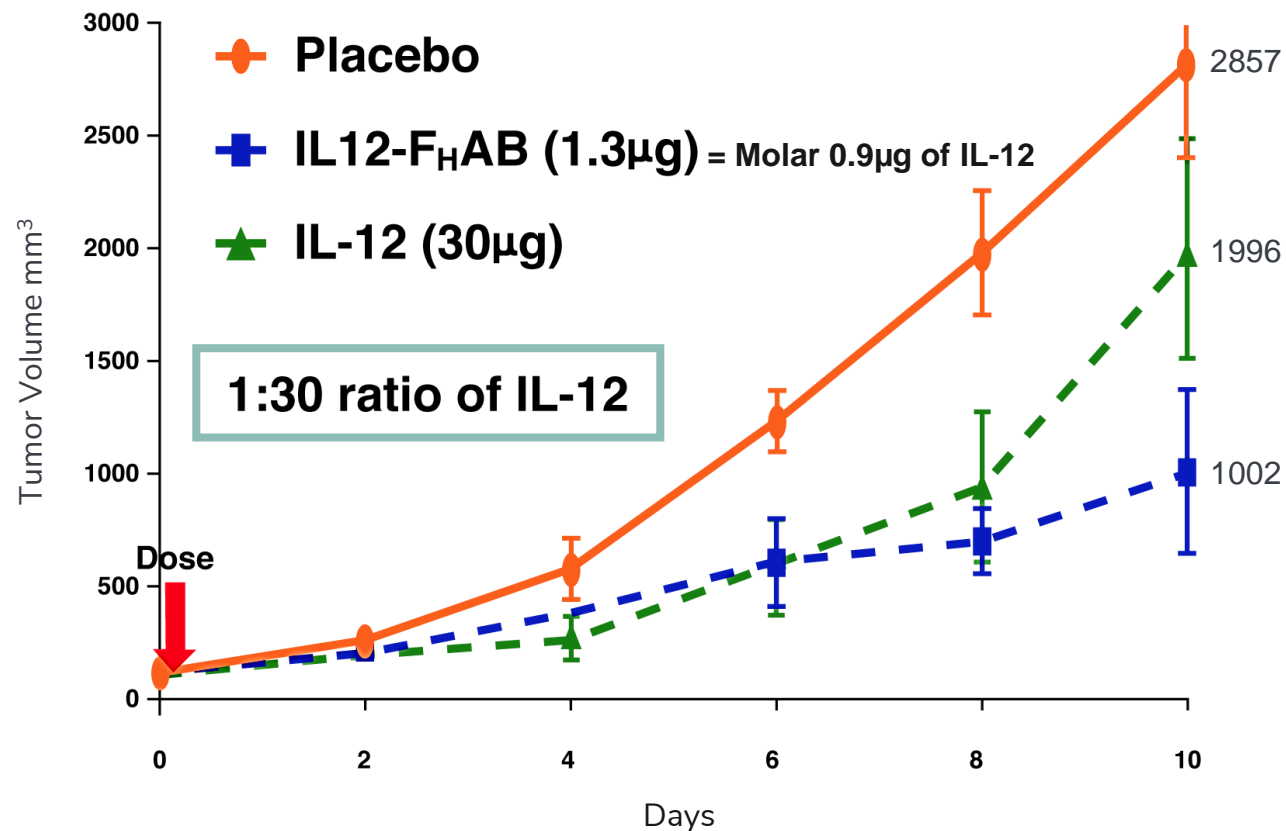
* No ADCC / CDC Activity

Jung, Oncolmm 2018, 7:e1438800
Greiner, Imm Targ & Ther 2021, 10:155-69
Algazi, Clin Canc Res 2020, 26:2827-37
Martinez, JCI, 2019; 129:1407-18

F_HAB: PRECLINICAL PROOF- OF-CONCEPT

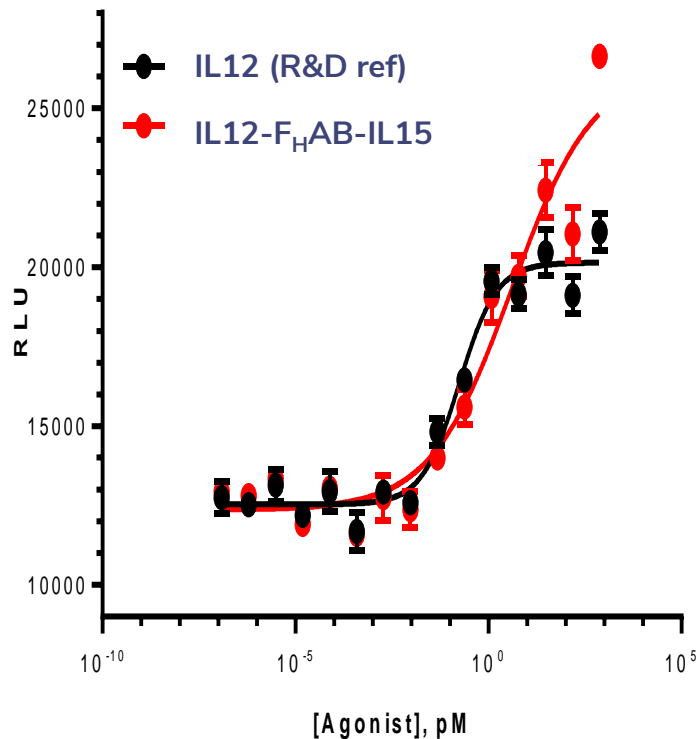
SON-1010: Reduces Tumor Growth in Mice

IL12-F_HAB (1.3μg) vs IL-12 (30μg) in B16F10 Melanoma

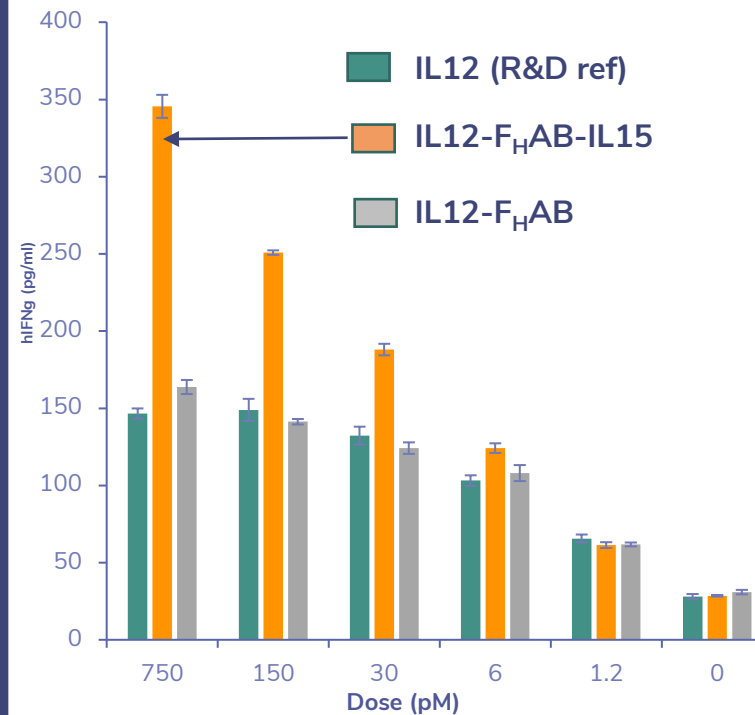


IL-12 (1μg) and IL12-F_HAB (1.3μg) are molar equivalent and have similar bioactivity, *in vitro*; however, *in vivo*, F_HAB is approximately 30-fold more potent than IL-12 (at day 10, 1.3μg IL12-F_HAB > IL-12 30μg)

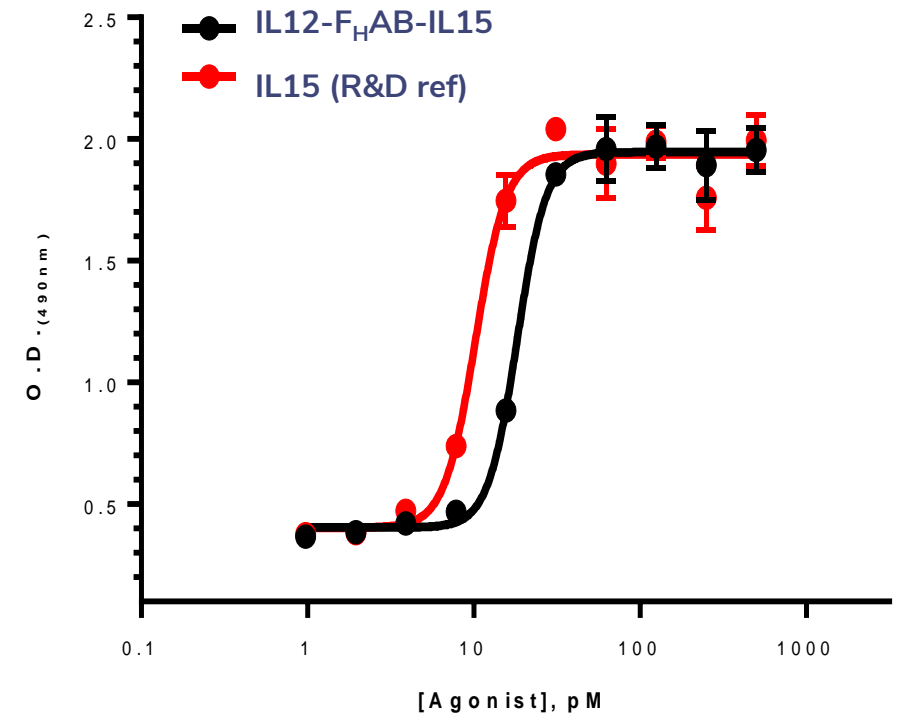
Lymphoblast proliferation assay (IL-12)



IFN- γ release assay (IL-12)



CTLL-2 proliferation assay (IL-15)



- Cell-based assays showed no loss of biological activity for either IL-12 or IL-15, suggesting no steric hindrance of the bispecific construct
- Synergistic effect of IFN- γ production was observed with the IL-12, IL-15 bispecific F_HAB

Comparison of Efficacy Tumor & Spleen Immune Cell Type Day 5, TV ~400mm ³	IL12-F _H AB (1μg)		IL12-F _H AB-IL15 (5μg)		IL18-F _H AB-IL12 (5μg)	
	Inhibition 37%		Inhibition 78%		Inhibition 65%	
	Tumor	Spleen	Tumor	Spleen	Tumor	Spleen
Cell Population						
T cells	0.8	1.0	0.5	0.9	1.2	0.9
CD4+ T Cells	0.8	0.6	1.2	0.5	1.2	0.7
Th1 Cells	1.6	1.0	1.7	0.8	3.4	1.8
CD8+ T Cells	1.2	0.8	1.4	0.7	6.5	0.9
Cytotoxic CD8+, IFN _γ	1.8	1.5	3.6	1.7	1.8	1.5
NK Cells	1.5	1.1	3.3	1.3	2.5	1.3
NK Cells, IFN _γ	1.7	0.6	6.0	0.7	12.0	2.7
M1 Macrophages	1.4	2.9	1.4	3.0	1.8	3.2
M2 Macrophages	0.2	1.2	0.3	4.0	0.1	3.5
Regulatory (T Reg) Cells	0.9	1.2	0.6	0.8	1.7	1.6

Flow cytometry analysis of interleukin constructs: At Day 5 post single dose, an increase in immune-stimulating cells was observed within tumors, corresponding to a decrease in tumor volume. Also, there was a transition of M2 to M1 in the tumor. IL18-F_HAB-IL12 showed the strongest infiltration of immune cells into the tumor, likely due to the biology of IL-18.

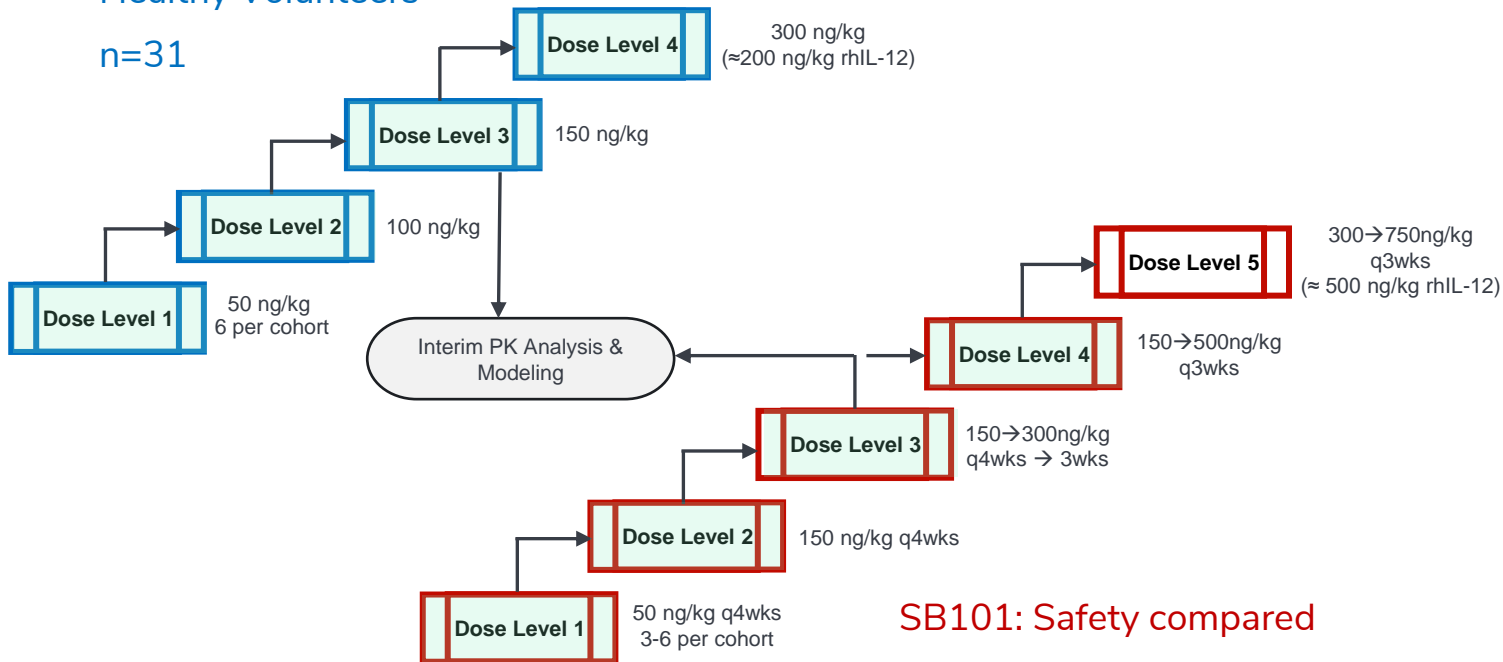
IL18-F_HAB-IL12 showed statistically significant tumor size reduction versus placebo in a mouse melanoma study, as well as a dose response.

Test Article	Day 0, Single Dose Tumor @ 100 mm ³	Day 8 Tumor Volume (mm ³ ± SEM), N=8	Day 8 Percentage Tumor Shrinkage
Placebo	NA	1747 ± 301	-
IL18-F _H AB-IL12	1 µg	918 ± 130	47%
IL18-F _H AB-IL12	5 µg	619 ± 141	65%

- Synergy between these interleukins, as IL-18 upregulates the IL-12 receptor and IL-12 upregulates the IL-18 receptor
- IL-18 also increase chemokines CXCL9 and CXCL10 for immune cell migration into the tumor
- FACS analysis showed SON-1410 has the potential to make a nonresponsive tumor immunologically responsive
- Data indicated significantly greater reduction in tumor volume, higher IFN-γ levels and immune cell responses (NK, NKT, Th1, and cytotoxic CD8 T cells), and enhanced infiltration into tumor

SON-1010: CLINICAL PROGRAM

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

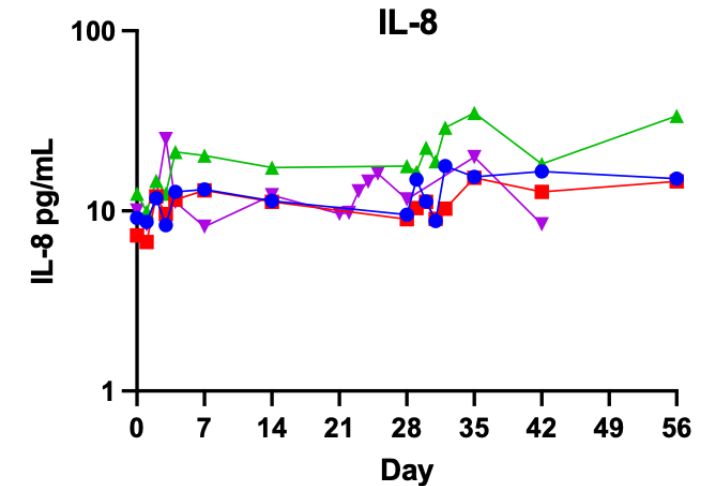
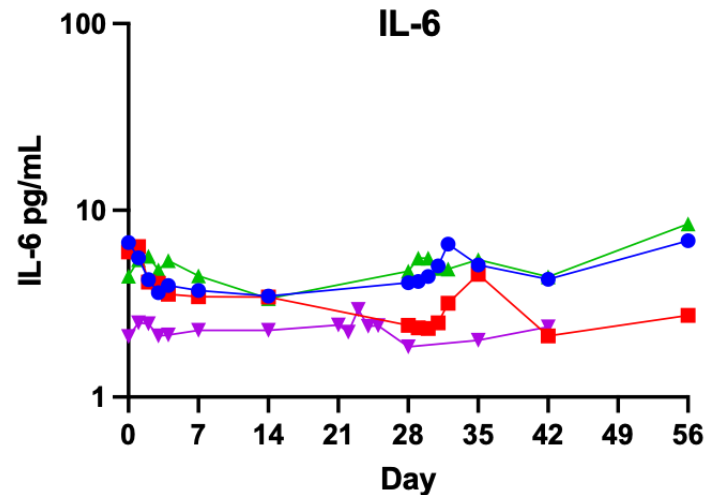
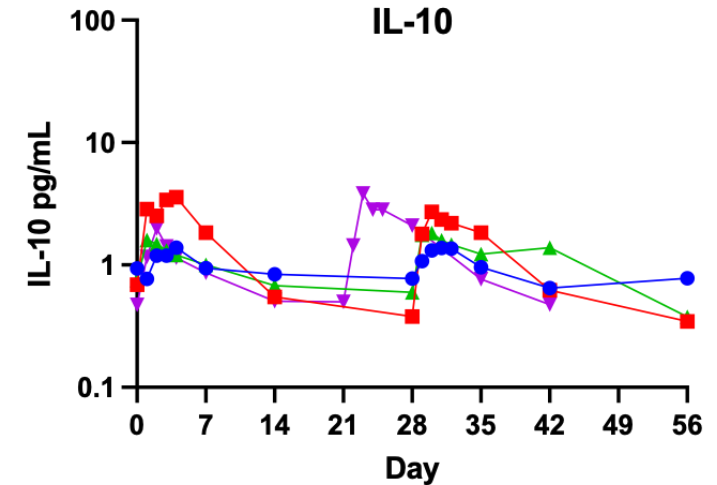
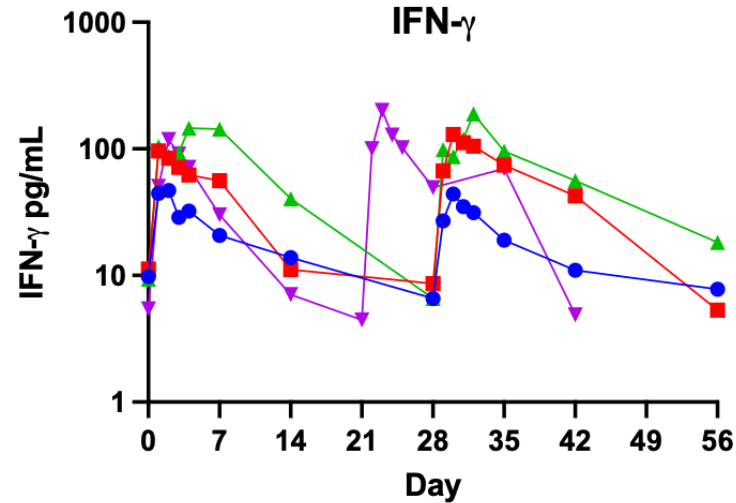
Shen, *Clin Transl Sci* (2019) 12:6
Karakunnel, *J Transl Med* (2018) 16:336

SB101: Safety Data

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

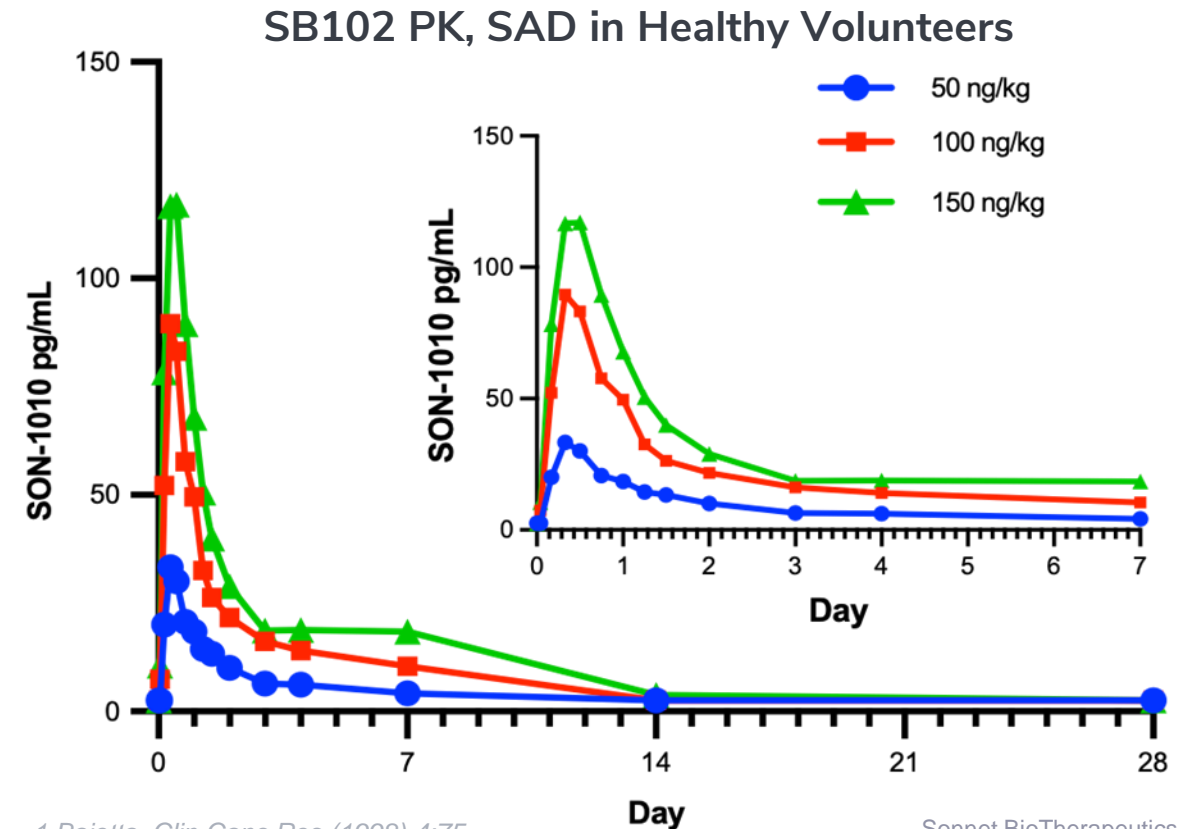
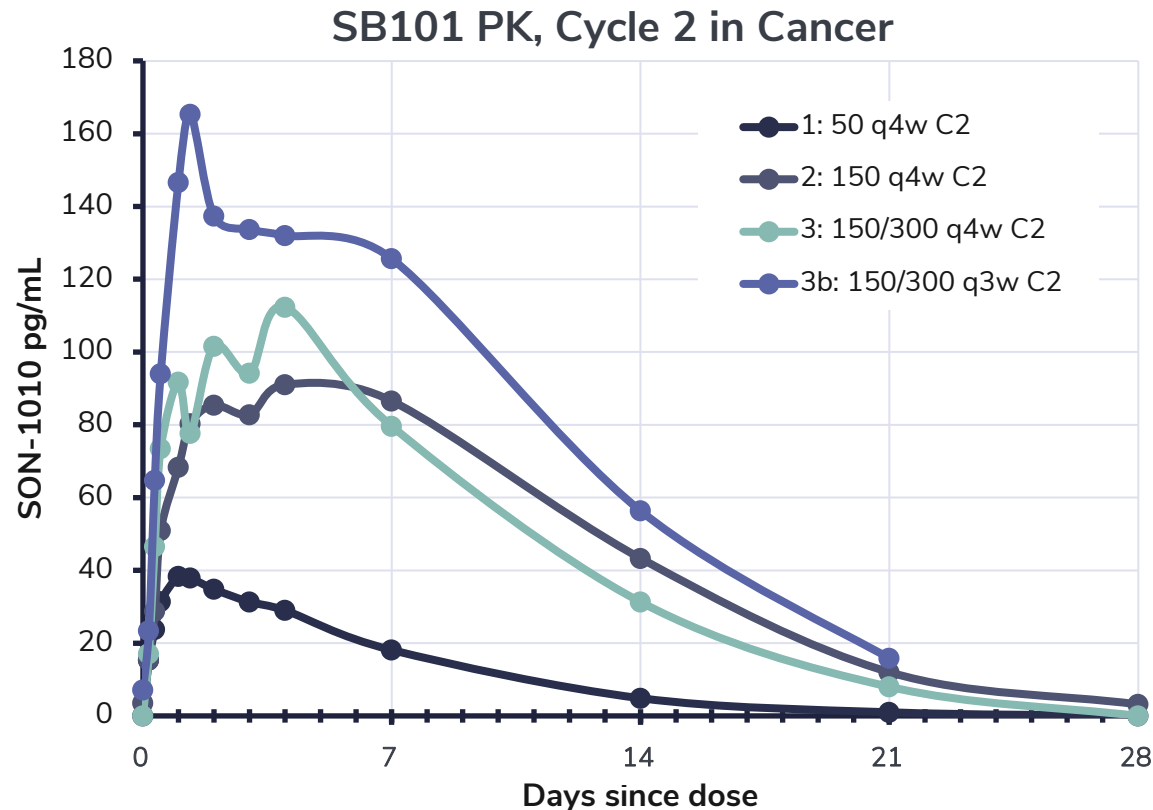
- Primary PD parameters included IFN γ , IL-1 β , IL-2, IL-4, IL-6, IL-8, IL-10, and TNF α , assayed using the MSD platform.
- Increases in IFN γ (showing an IL-12 effect and potential for tumor control) were dose-related, controlled, and prolonged.
- SON-1010 induced IFN γ with both the first and second 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.



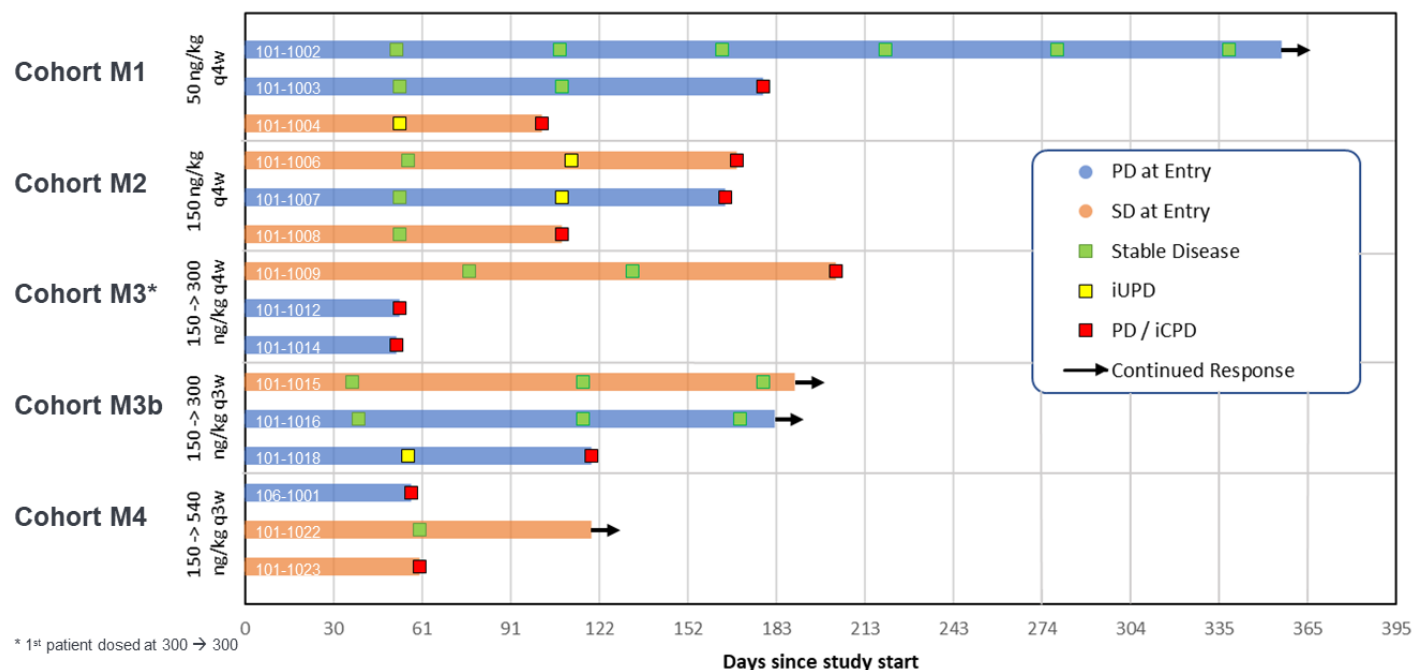
● M1 50 ng/kg q4w ▲ M3 150* -> 300 q4w
■ M2 150 ng/kg q4w ▼ M3b 150 -> 300 q3w

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 hours 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



SB101: 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

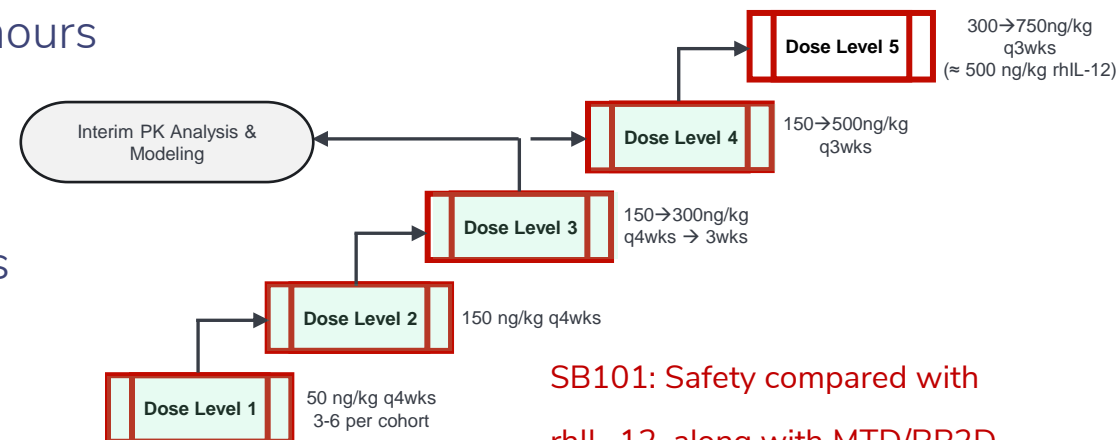
- ▶ Mostly mild with very few more significant adverse events

- ❑ 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 INF γ response was dose-related, controlled and prolonged

- ▶ 5 of the first 14 patients (36%) have evidence of clinical benefit (SD at 4 months)

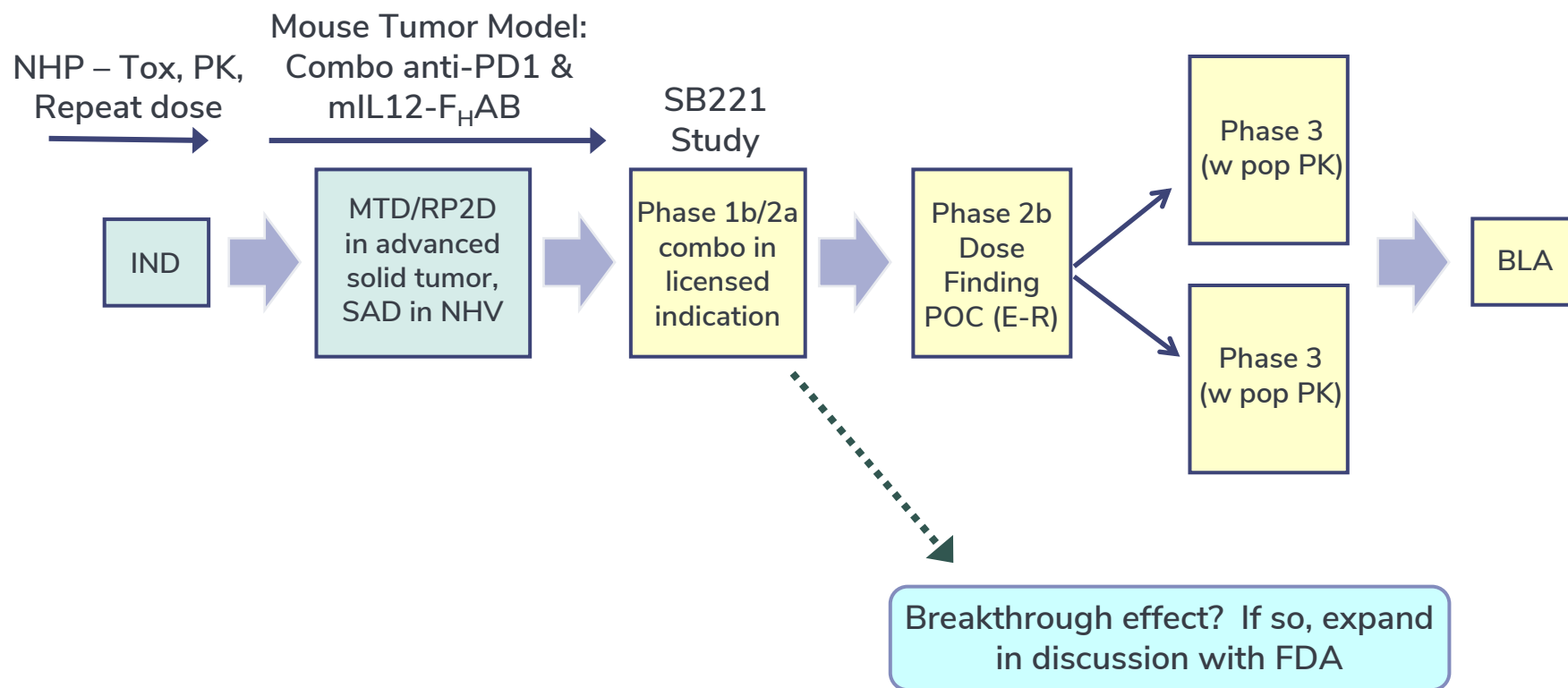
- ▶ Cytokine results suggest SON-1010 has extended PK, targeting of tumor tissue, and induction of an IL-12 effect, without Cytokine Release Syndrome



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

SON-1010: Proposed Development Pathway

Core Safety and Efficacy Studies



Next Steps

SON-1010 in Combination with atezolizumab (Tecentriq®)

- ▶ **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 atezolizumab 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 enables Part 2
- ▶ **Part 2**
 - ❑ Randomized comparison of SON-1010 as monotherapy vs. combination with atezolizumab vs. SOC
 - ❑ Designed to show proof-of-concept in PROC

¹ Sonnet PR, 9 Jan 2023

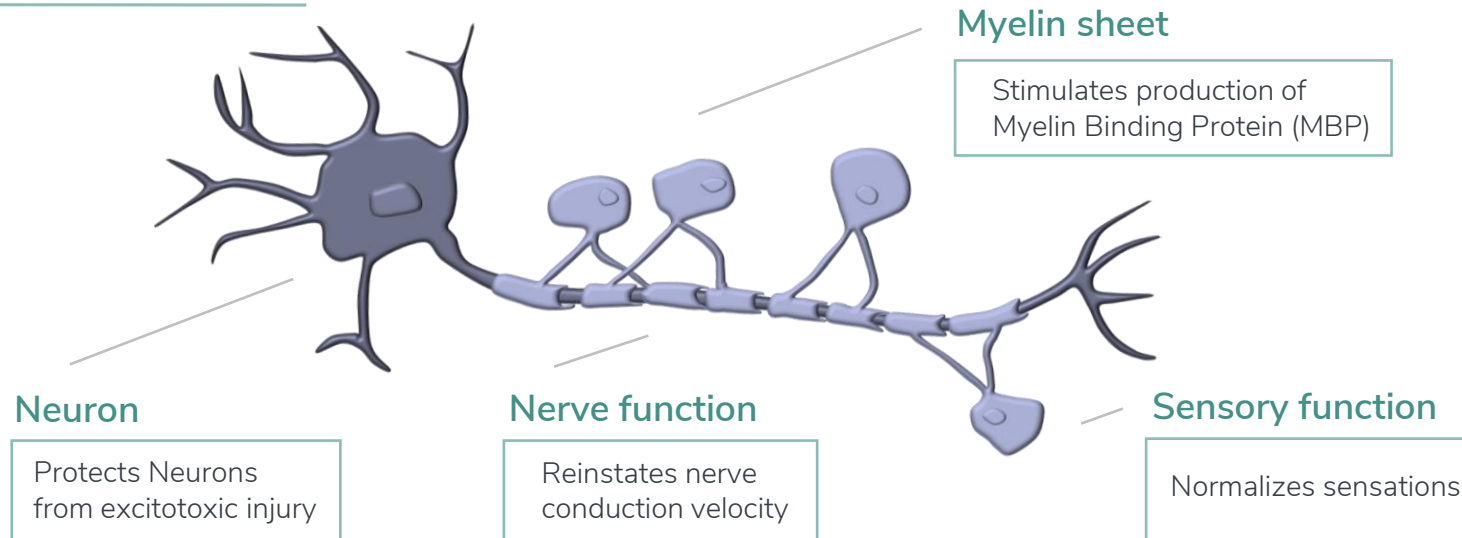
² <https://clinicaltrials.gov/ct2/show/NCT05756907>

- ▶ **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 increase in 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
- ▶ **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
 - ❑ PK profile suggests direct targeting of tumor tissue, consistent with F_HAB construct design
 - ❑ 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

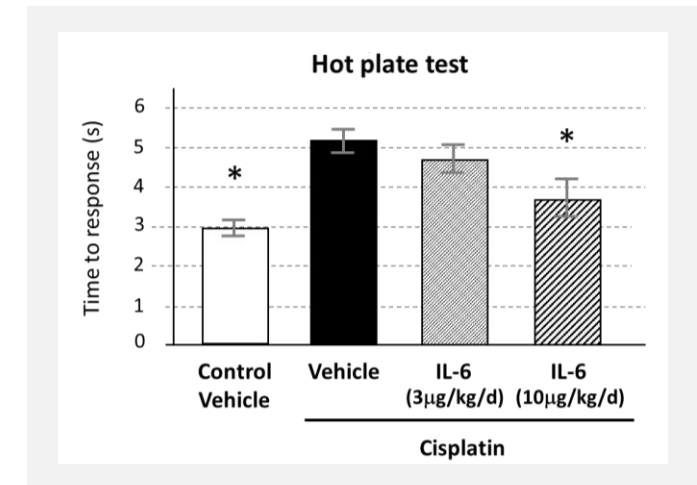
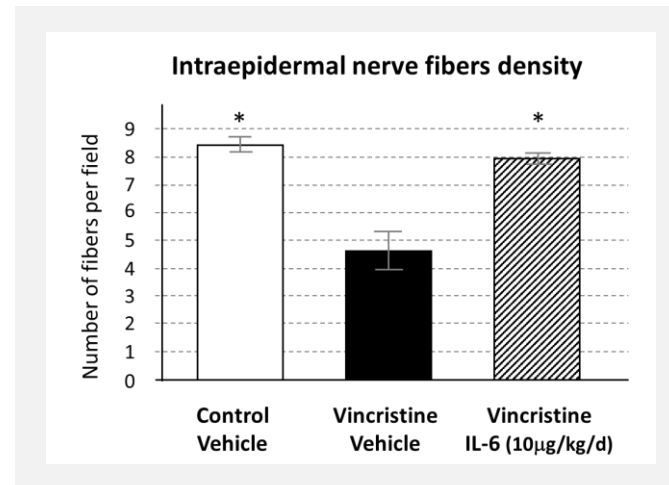
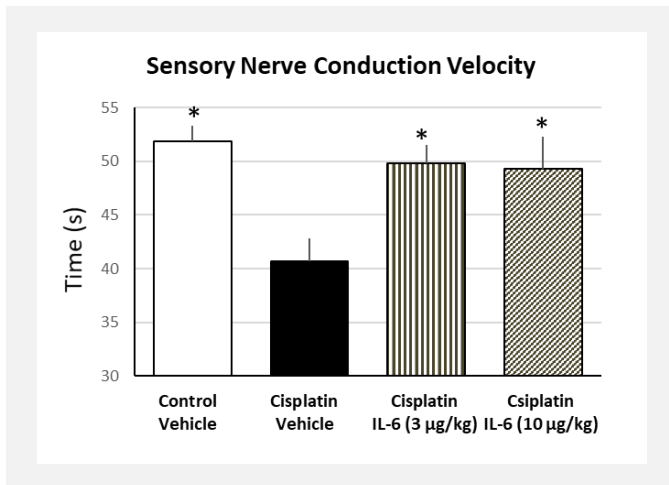
SON-080 (LOW-DOSE IL-6)

**CHEMOTHERAPY-INDUCED
PERIPHERAL NEUROPATHY AND
DIABETIC PERIPHERAL NEUROPATHY**

IL-6 Is Neurotrophic



Epidermal Innervation reinstates nerve fiber density



IL-6: Safe and Well Tolerated at the Target Dose

Phase I / II Clinical Data

CONDITION	Thrombocytopenia	SIDE EFFECT PROFILE	Similar AEs and SAEs to controls, e.g. fever and rigor, headache, vomiting (at target dose range)
PATIENT	n = 213; all types also including Grade III/IV cancer		No exacerbation of pain or neuropathy were observed after IL-6 administration
STUDIES	10 independent Phase I/II studies		
CO-TREATMENT	Diverse antineoplastic therapies	SAFETY WINDOW	MTD = 5µg/kg/day or 10µg/kg/TIW
DOSES	0.25-32 µg/kg/day, or 5-20 µg/kg/TIW SC		Doses below 2.5 µg/kg/day were well tolerated
DURATION	Up to 10 weeks		Sonnet target dose will be 0.2 – 0.8 µg/kg/TIW, 50 times below the estimated MTD

Corporate Summary

Immune Oncology

Immune stimulation using a proprietary Fully Human Albumin Binding (F_H AB) platform to target the tumor microenvironment

Safety

Single dose of SON-1010 shown to be safe and well tolerated in healthy volunteers.

Multiple doses of SON-1010 shown to be safe with early clinical benefit in patients with solid tumors.

Demonstrated Activity in Clinical Studies

- 10x enhanced PK compared to rIL-12
- Tumor targeting shown by comparing PK curves with healthy volunteers
- Superior efficacy of cytokines while attached to F_H AB compared to their naked counterparts in preclinical studies

Milestones:

SON-1010: Data from dose escalation portion of Phase 1 monotherapy study, 1H24

SON-1010: Safety data from Phase 1b/2a PROC study in combination with atezolizumab, 1H24

SON-080: Phase 1b/2a initial safety data in CIPN, 1Q23

SON-080: Potentially initiate Phase 2 study in DPN, after reviewing CIPN data

SON-1210: Initiate regulatory authorization process in 2023/2024, pending the outcome of any partnering activity

F_H AB Pipeline Expansion

Existing collaborations with J&J and Roche offer licensing expansion opportunities

Intellectual Property

PCT and US Patents in prosecution, as well as six provisional patents filed (*i.e.*, potential utility with ADCs, Checkpoint Inhibitors and CAR-Ts; Continuous Intensified Perfusion Manufacturing; Novel Formulations)

US Patent No. 11,028,166, "*Albumin Domain Fusion Proteins*", Issued June 2021