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): September 16, 2021

Silverback Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-39756**	**81-1489190**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

500 Fairview Ave N, Suite 600 **Seattle, Washington**	**98109**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (206) 456-2900

N/A
(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	**SBTX**	**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 (§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 Disclosure.

On September 16, 2021, Silverback Therapeutics, Inc. (the "Company") updated its corporate slide presentation for use in meetings with investors, analysts and others. The presentation is available through the Company's website and a copy is attached as Exhibit 99.1 to this Current Report on Form 8-K.

The information in this Item 7.01 of this Current Report on 8-K (including Exhibit 99.1) is furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or subject to the liabilities of that section or Sections 11 and 12(a)(2) of the Securities Act of 1933, as amended. The information shall not be deemed incorporated by reference into any other filing with the Securities and Exchange Commission made by the Company, whether made before or after today's date, regardless of any general incorporation language in such filing, except as shall be expressly set forth by specific references in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Corporate Slide Presentation, dated September 16, 2021.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

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.

SILVERBACK THERAPEUTICS, INC.

By: /s/ Laura Shawver, Ph.D.
Laura Shawver, Ph.D.
Chief Executive Officer

Dated: September 16, 2021

Exhibit 99.1

SILVERBACK® THERAPEUTICS

Corporate Presentation

September 2021

Forward-looking statements and disclaimers

Any reproduction or distribution of this presentation, in whole or in part, or the disclosure of any of its contents is prohibited. This presentation includes certain forward-looking statements that involve risks and uncertainties that could cause actual results to be materially different from historical results or from any future results expressed or implied by such forward-looking statements regarding Silverback Therapeutics, Inc. (the "Company"). These forward-looking statement include, but are not limited to, those regarding the Company's plans and ability to bring new treatments to patients in need, including potential combination efforts, the progress and expected timing of the Company's drug development programs and clinical trials, clinical development plans and timelines, regulatory matters, market size and opportunity, the Company's future financial position, the Company's strategy and intellectual property matters, and Company estimates regarding expenses, capital requirements, and needs for additional financing. These forward-looking statements are based on the beliefs of the Company's management as well as assumptions made and information currently available to the Company. Such statements reflect the current views of the Company with respect to future events and are subject to business, regulatory, economic and competitive risks, uncertainties, contingencies and assumptions about the Company, including, among other things, the development of its business, trends in the industry, the legal and regulatory framework for the industry, and future expenditures. Factors that may cause actual results to differ materially include the risk that compounds that appeared promising in early research or clinical trials do not demonstrate safety and/or efficacy in later preclinical studies or clinical trials, the risk that the Company may not obtain approval to market its product candidates, uncertainties associated with performing clinical trials, regulatory filings and applications, risks associated with reliance on third parties to successfully conduct clinical trials, the risks associated with reliance on outside financing to meet capital requirements, and other risks associated with the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such drugs. In light of these risks, uncertainties, contingencies and assumptions, the events or circumstances referred to in the forward-looking statements may not occur. None of the future projections, expectations, estimates or prospects in this presentation should be taken as forecasts or promises nor should they be taken as implying any indication, assurance or guarantee that the assumptions on which such future projections, expectations, estimates or prospects have been prepared are correct or exhaustive or, in the case of the assumptions, fully stated in the presentation. The actual results may vary from the anticipated results and the variations may be material. You are urged to consider statements that include the words "may," "will," "would," "could," "should," "believes," "estimates," "projects," "promise," "potential," "expects," "plans," "anticipates," "intends," "continues," "designed," "goal," or the negative of those words or other comparable words to be uncertain and forward-looking. For a further list and description of the risks and uncertainties that the Company faces, please refer to the Company's periodic and other filings with the Securities and Exchange Commission, which are available at www.sec.gov. Such forward-looking statements are current only as of the date they are made, and the Company assumes no obligation to update any forward-looking statements, whether as a result of new information, future events, or otherwise.

This presentation discusses product candidates that are under clinical study and which have not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of these product candidates for the use for which such product candidates are being studied.

The trademarks included herein are the property of the owners thereof and are used for reference purposes only. Such use should not be construed as an endorsement of such products.

Corporate highlights

SILVERBACK THERAPEUTICS

1. ImmunoTAC conjugates are designed to **unlock a new class of targeted immuno-oncology agents** that direct a myeloid cell agonist to the tumor microenvironment for localized activation
2. Emerging clinical data supports **proof-of-mechanism for localized TLR8 agonism and the ImmunoTAC platform**, evidenced by the robust activation of innate and adaptive immune response seen in patients
3. SBT6050 has demonstrated **early signals of anti-tumor activity** as a monotherapy and in combination with a PD-1 inhibitor, with a **manageable safety profile** consistent with an active IO agent
4. Clinical development plan to evaluate SBT6050 in combinations designed to have long-term benefit in early lines of treatment, including **combo with anti-PD1, with Enhertu and with Herceptin/Tukysa**
5. Positive readthrough to Silverback's TLR8 pipeline with **value-generating milestones expected in the next 6-18 months**, including anticipated initiation of SBT6290 (Nectin4) Ph1 study and SBT8230 (HBV) Ph1-enabling studies

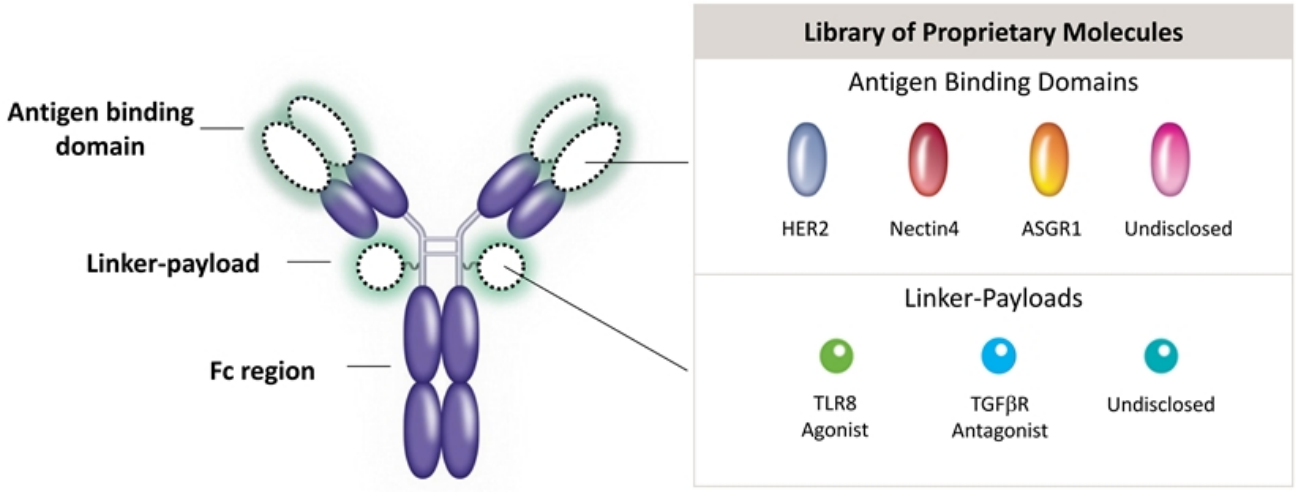
Advancing a pipeline of systemically delivered, tissue-targeted programs with value-generating milestones expected over the next 6-18 months

SILVERBACK THERAPEUTICS

Asset / Payload	Targeting Antigen	Indication(s)	Preclinical Studies	Phase 1	Phase 2	Anticipated Milestones
SBT6050 TLR8 Agonist	HER2	Breast Cancer, GEA, and NSCLC	**101**: Monotherapy and Combo with PD-1 Inhibitor			• 4Q 2021 – Initiate Libtayo tumor-specific expansion cohorts • 1Q 2022 – Initiate additional Phase 1b tumor-specific expansion cohorts • 1H 2022 – Additional interim Phase 1 dose-escalation data • 2H 2022 – First Phase 1b data and additional Phase 1 data
			201: Combo with Enhertu / Herceptin+Tukysa			• 1Q 2022 – Initiate dosing in combination with Enhertu and with Herceptin+Tukysa • 1H 2023 – Interim combo data
SBT6290 TLR8 Agonist	Nectin4	Bladder Cancer, TNBC, H&N Cancer, and NSCLC				• 4Q 2021 – Submit IND • 1Q 2022 – Initiate Phase 1 dose-escalation
SBT8230 TLR8 Agonist	ASGR1	Chronic Hepatitis B Virus				• 1Q 2022 – Initiate Phase 1-enabling tox studies • 4Q 2022 – Phase 1 regulatory submission

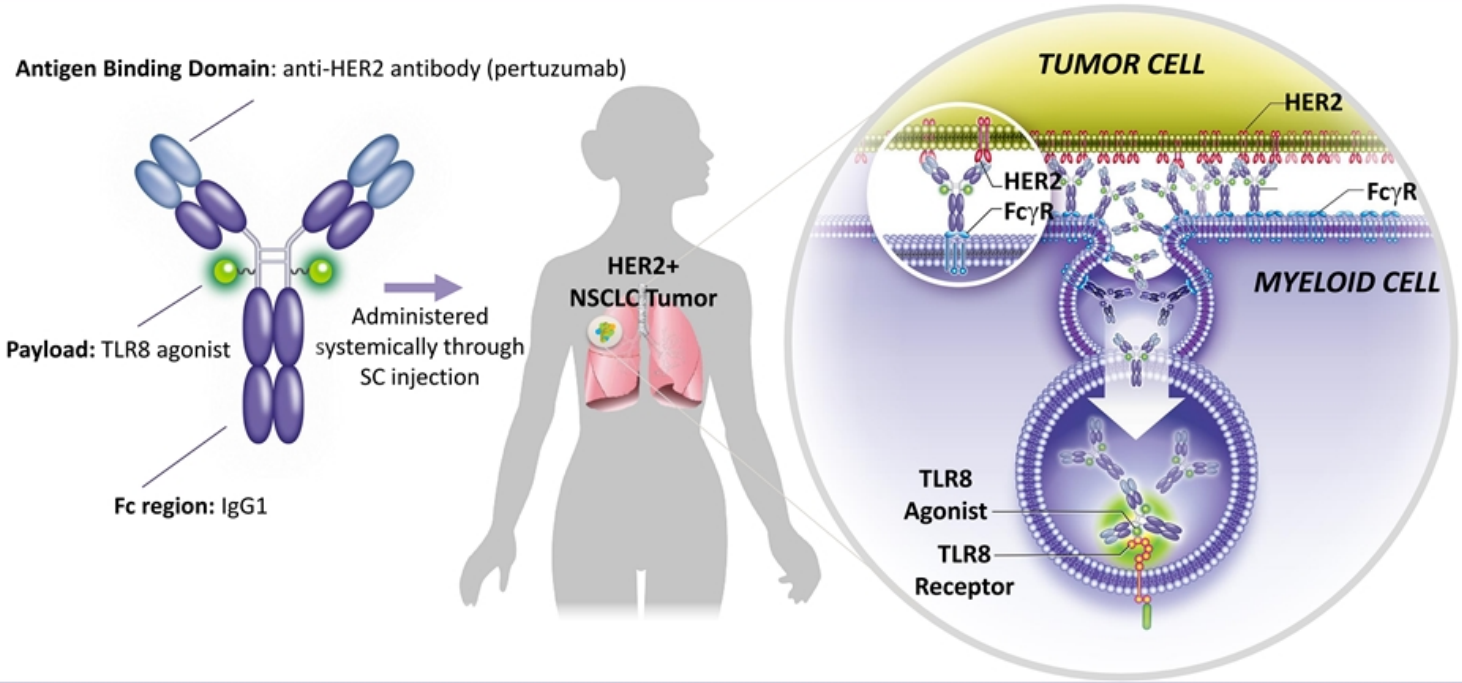
ASGR1 = Asialoglycoprotein Receptor 1 (Liver Localized Protein)
GEA = Gastroesophageal Adenocarcinoma
HER2 = Human Epidermal Growth Factor Receptor 2
H&N = Head and Neck
Nectin4 = Nectin Cell Adhesion Molecule 4
NSCLC = Non-Small Cell Lung Cancer
TLR8 = Toll Like Receptor 8
TNBC = Triple Negative Breast Cancer

ImmunoTAC platform strategically pairs antigen binding domains with linker-payloads to modulate pathways underlying serious diseases



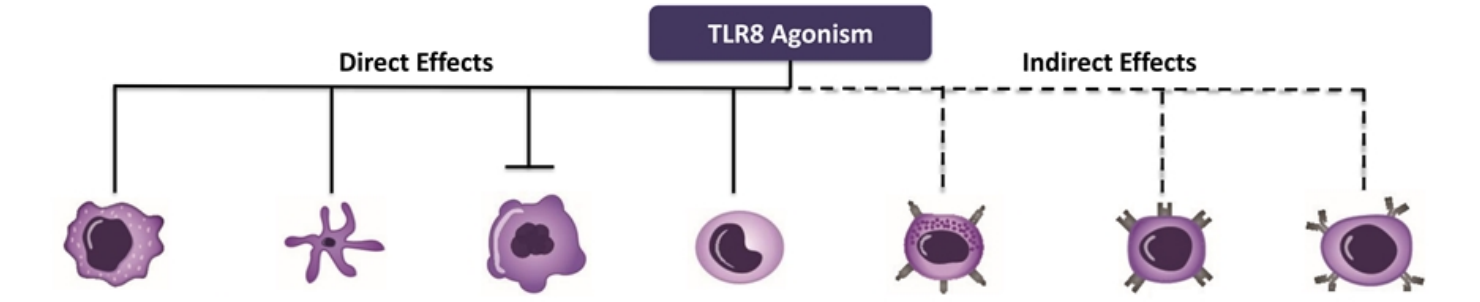
Robust IP portfolio with **4 issued patents and over 100 patent applications** pending worldwide directed to payloads, conjugates, and antibodies, for use in cancer, virology and fibrosis

SBT6050 is designed to localize TLR8 activation of myeloid cells in tumors via a HER2 antibody



TLR8 is highly expressed in human myeloid cell types that elicit anti-tumor responses when activated

SILVERBACK THERAPEUTICS



Macrophages	Dendritic Cells	Myeloid Derived Suppressor Cells	Monocytes	NK Cells	T Cells	B Cells
Direct tumor killing Pro-inflammatory environment Immune cell recruitment	Promote anti-tumor T cell responses and infiltration	Reprogramming to a pro-inflammatory state	Immune cell recruitment Tumor killing and stimulation	Direct tumor killing Creation of a pro-inflammatory environment	Direct tumor killing	Antigen presentation Activate T cells Produce antibodies

Myeloid cells *can comprise between 5-10% of the tumor, at least twice the prevalence of T cells**

**Zhang et al, Journal of Cancer 2019*

SBT6050

Tumor-localizing antigen: HER2 moderate and high expression (pertuzumab epitope targeted)

Target cell: myeloid cells

Payload: proprietary TLR8 agonist

Next readout: 1H 2022 – additional interim Phase 1 dose-escalation data

Proof-of-mechanism established in 40 patient dose escalation study*

- Pharmacodynamic (PD) markers indicative of myeloid and T/NK cell activation generally increase with dose, plateauing at 0.6 mg/kg
- PD activity is maintained with repeat dosing
- SBT6050 payload detected in intratumoral macrophages and on tumor cells

SBT6050 monotherapy or in combo with pembro has a manageable safety profile

- Common adverse events consistent with immune activation
- Safety profile of SBT6050 in combination with pembrolizumab was similar to SBT6050 monotherapy
- Non-overlapping adverse events with other HER2-directed agents support combination with Enhertu and Herceptin+Tukysa

Early signals of anti-tumor activity in a heavily pre-treated heterogenous population

- Among 18 evaluable patients for tumor types of interest, one Partial Response (PR) (-55%, NSCLC) maintained at the most recent available scan obtained at 36 weeks post-enrollment, and 8 weeks after discontinuing study treatment
- Stable Disease (SD) reported in seven patients

* August 1, 2021 data cut-off date

Phase 1/1b dose escalation study; projected RP2D determined for expansion cohorts

SILVERBACK THERAPEUTICS

Part 1: monotherapy dose escalation

SBT6050 SC injection Q2W

HER2-expressing (IHC 2+ or 3+) or HER2-amplified advanced cancers

0.3 mg/kg | **0.6 mg/kg** | **0.9 mg/kg** | **1.2 mg/kg**

Part 2: monotherapy tumor specific cohorts

SBT6050 SC injection Q2W

$HER2^{expressing}$ BC, gastric/GEJ, and NSCLC

Part 3: pembrolizumab combination dose escalation

HER2-expressing (IHC 2+ or 3+) or HER2-amplified advanced cancers

SBT6050 SC injection Q2W; pembrolizumab 400 mg IV Q6W

0.15 mg/kg | **0.3 mg/kg** | **0.6 mg/kg***

Part 4: pembrolizumab combination expansion cohort

SBT6050 SC injection Q2W; pembrolizumab 400 mg IV Q6W

$HER2^{expressing}$ solid tumors

Part 5: cemiplimab combination expansion cohort

SBT6050 SC injection Q3W; cemiplimab 350 mg/kg IV Q3W

$HER2^{positive}$ gastric/GEJ cancer, $HER2^{expressing}$ NSCLC

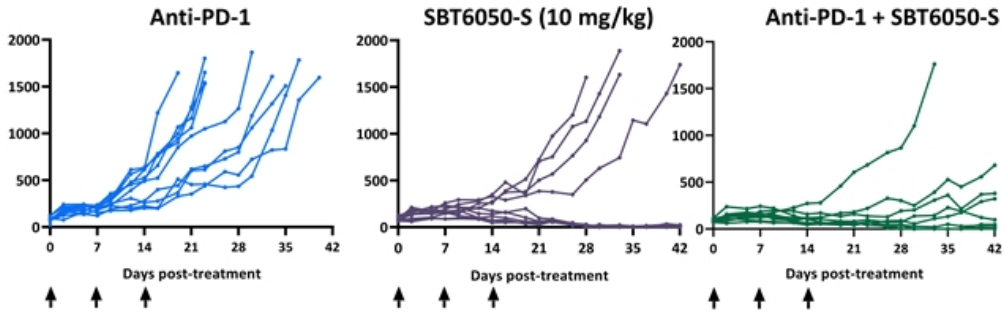
HER2 status:
$HER2^{positive}$ = HER2 IHC 3+ or IHC 2+/amplified
$HER2^{expressing}$ = HER2 IHC 2+, or IHC3+, or amplified
$HER2^{low}$ = HER2 IHC 2+/ not amplified

*Currently enrolling | Data presented are interim data with a data cut-off date of August 1, 2021

SBT6050 activation of innate and adaptive immune response may enhance and expand the effectiveness of Libtayo

SILVERBACK THERAPEUTICS

1. SBT6050 activates myeloid cells, including dendritic cells, which then recruit and activate anti-tumor T cells
2. Induction of myeloid cell activation along with increases in immune cell infiltrate/activation in tumors can result in PD-L1 upregulation
3. Libtayo approved in first-line NSCLC, a prioritized tumor type for Silverback
4. In preclinical mouse tumor model studies, the combination of SBT6050-S and CPI shows increased anti-tumor activity over either agent alone



Anti-PD-1 Combination

EMT6 tumor model with low T cell infiltrate, moderate and heterogeneous HER2 expression, and refractory to CPI

Combination with Enhertu and with Tukysa + Herceptin +/- capecitabine are supported by a strong scientific and clinical rationale

SILVERBACK THERAPEUTICS

Enhertu | Herceptin+Tukysa +/- capecitabine	Combination with SBT6050
1 Drive immunogenic tumor cell death and release of tumor neoantigens	» Activates DCs, potentially enhancing presentation of neoantigens and T cell activation
2 Comprised of trastuzumab, capable of ADCC and ADCP	» Induces cytokines that amplify ADCC by NK cells » Downmodulates SIRPα on myeloid cells, increasing ADCP through attenuation of CD47-SIRPα interaction » Pertuzumab backbone is designed to combine with trastuzumab-based regimens
3 Approved for 2L therapy in tumor types of interest	» Designed to overcome common resistance mechanisms to 1L PD-(L)1 refractory patients » Addition of IO could deepen or prolong responses

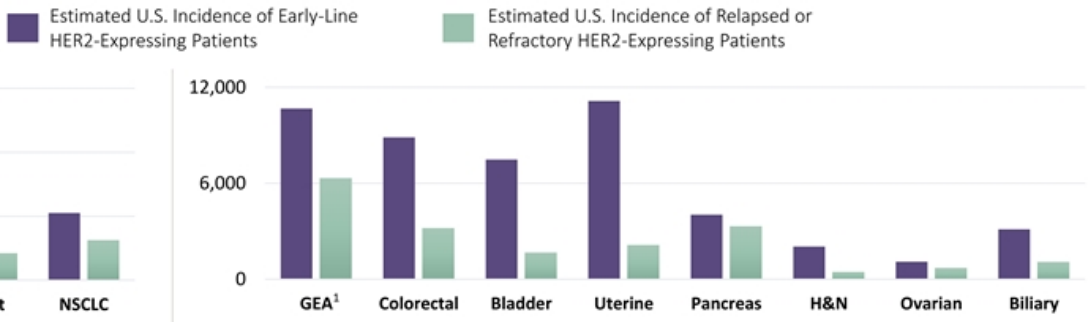
Clinical development plans beyond monotherapy

SILVERBACK THERAPEUTICS

Combination regimen *(estimated start)*		Strategic Initiative
Libtayo *(4Q21)*	2L+ NSCLC 3L+ GEA	Combine with foundational IO therapy to lay groundwork in early lines of treatment
Enhertu *(1Q22)*	2L+ NSCLC 2L+ GEA	Novel combination with HER2-based cytotoxic ADC to seek breakthroughs in 2L+ settings
Herceptin + Tukysa[1] *(1Q22)*	2L+ mBC 2L+ CRC	Novel combination with HER2-targeted therapies and chemo to seek breakthroughs in 2L+ settings

1. +/- capecitabine

SBT6050 is designed to be used in combo with SOC agents such as CPIs and/or trastuzumab-based agents, potentially unlocking large market opportunities



	Breast	NSCLC	GEA[1]	Colorectal	Bladder	Uterine	Pancreas	H&N	Ovarian	Biliary
Estimated HER2 Expression (IHC 2+/3+) & Amplifications	30%	16-32%	23%	6-13%	9%	17-33%	7-33%	3-50%	5-19%	26%
FDA Approved HER2 Pathway Inhibitors	✓		✓							
FDA Approved HER2 Antibody Drug Conjugates	✓	Phase 2	✓	Phase 2						
FDA Approved Checkpoint Inhibitor	Phase 3	✓	✓	✓	✓	✓		✓		✓

Estimated early-line U.S. cases per year > 160k | Estimated relapsed or refractory U.S. cases per year > 48k

1. Gastroesophageal adenocarcinoma. Includes esophageal, gastric, gastroesophageal junction cancers

SBT6050 administered alone or in combination with pembrolizumab has a manageable safety profile

SILVERBACK THERAPEUTICS

Most frequent* treatment-related treatment emergent adverse events (TEAEs), by maximum severity

	Part 1: SBT6050 Monotherapy (n=32)			Part 3: SBT6050 + Pembrolizumab (n=8)		
	Grade 1	**Grade 2**	**Grade 3**	**Grade 1**	**Grade 2**	**Grade 3**
Injection site reaction**	15 (46.9%)	11 (34.4%)	1 (3.1%)	5 (62.5%)	2 (25%)	0
Pyrexia	11 (34.4%)	9 (28.1%)	3 (9.4%)	3 (37.5%)	4 (50%)	0
Chills	14 (43.8%)	9 (28.1%)	0	3 (37.5%)	2 (25%)	0
Hypotension	5 (15.6%)	4 (12.5%)	6 (18.8%)	2 (25%)	4 (50%)	0
Nausea	6 (18.8%)	8 (25%)	1 (3.1%)	1 (12%)	4 (50%)	0
Vomiting	5 (15.6%)	9 (28.1%)	0	3 (37.5%)	0	0
Fatigue	0	7 (21.9%)	0	1 (12.5%)	1 (12.5%)	0

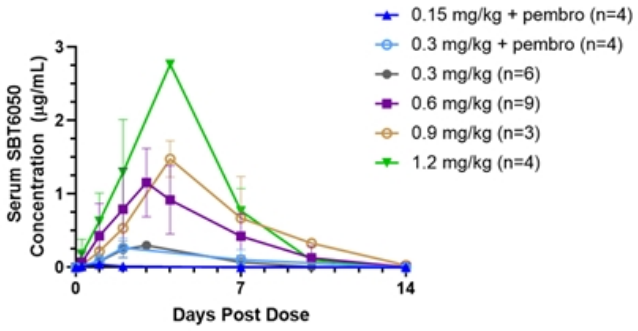
* ≥ 20% patients overall in Parts 1 and 3 ** Includes Injection Site Rash

- No ≥ Grade 4 treatment-related TEAEs reported
- No treatment-related TEAEs led to discontinuation
- Grade 3 DLTs observed in Part 1 only and resolved with supportive care. These included hypotension, hypoxia, ISR and fever
- 7 of the 8 patients who reported DLTs continued treatment at a reduced dose
- Transient decreases in hemoglobin are similar across all dose levels

PK studies reflect saturation of HER2-mediated clearance at dose levels ≥ 0.6 mg/kg and conjugate stability

SILVERBACK THERAPEUTICS

Serum PK Profiles



Dose-proportional increases in AUC at doses ≥ 0.6 mg/kg

SBT6050 dose (mg/kg)	AUC (µg*d/mL)	*Fold increase*
0.15 + pembro	0.10 ± 0.17	*~15.7x*
0.3 + pembro	1.57 ± 1.19	
0.3	1.16 ± 0.76	*~5.0x*
0.6	5.84 ± 2.57	*~1.4x*
0.9	8.14 ± 3.55	*~1.5x*
1.2	12.6 ± 2.6	

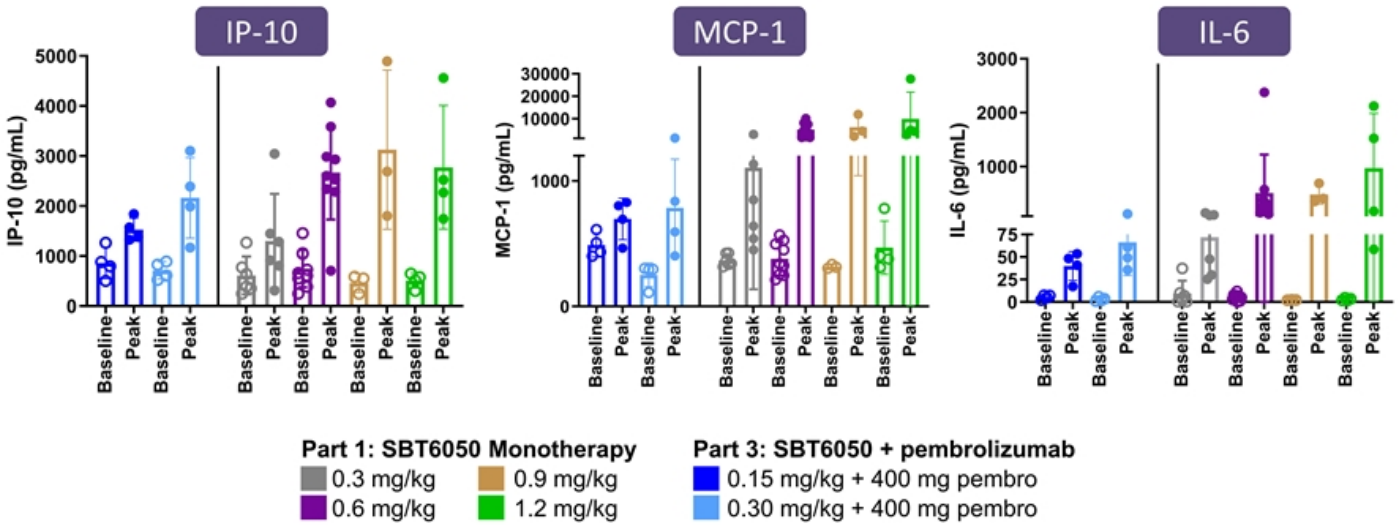
Mean values increased greater than dose proportionally up to 0.6 mg/kg (~5-fold from 0.3 to 0.6 mg/kg), but proportionally at dose levels ≥ 0.6 mg/kg

Free payload is not detected in ~98% of serum samples

Dose Range (mg/kg)	Frequency of Free Payload Detection (n=136 blood samples)		Free Payload Concentrations (nM)	Reference Payload Potency (nM)
0.15 to 1.2	**Not quantifiable**	**133**	**Below LLOQ[1]**	EC_{50} ~100
	quantifiable	3	0.05-0.09	LAC[2] ~50

1. LLOQ = Lower Limit of Quantitation (0.04 nM)
2. LAC = Lowest Active Concentration

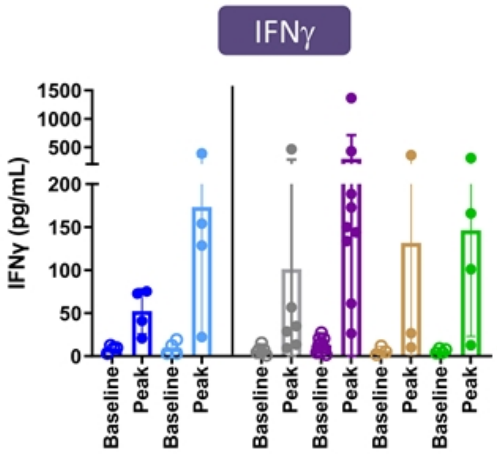
Induction of PD biomarkers of myeloid cell activation observed across all dose levels and generally plateau at 0.6 mg/kg

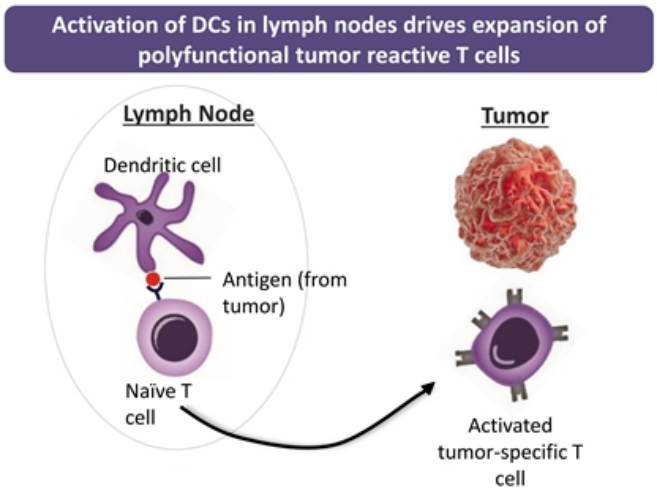


For MCP-1 and IP-10, peak levels were significantly higher (unpaired t-test, $p \leq 0.05$) at 0.6 mg/kg vs. lower dose levels, while no significant differences in peak levels were observed across the 0.6 to 1.2 mg/kg dose levels for any analyte

Induction of IFNγ, a biomarker of T and NK cell activation, observed across all dose levels and generally plateaus at 0.6 mg/kg

SILVERBACK THERAPEUTICS

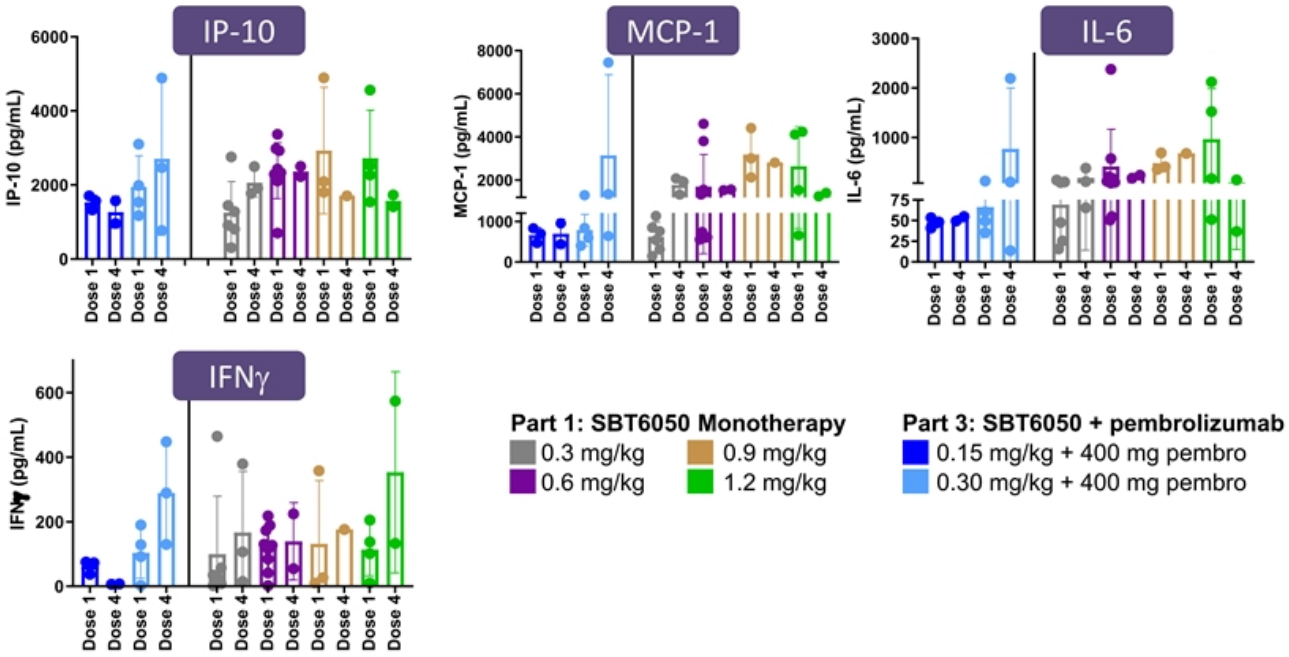




Part 1: SBT6050 Monotherapy
- 0.3 mg/kg
- 0.6 mg/kg
- 0.9 mg/kg
- 1.2 mg/kg

Part 3: SBT6050 + pembrolizumab
- 0.15 mg/kg + 400 mg pembro
- 0.30 mg/kg + 400 mg pembro

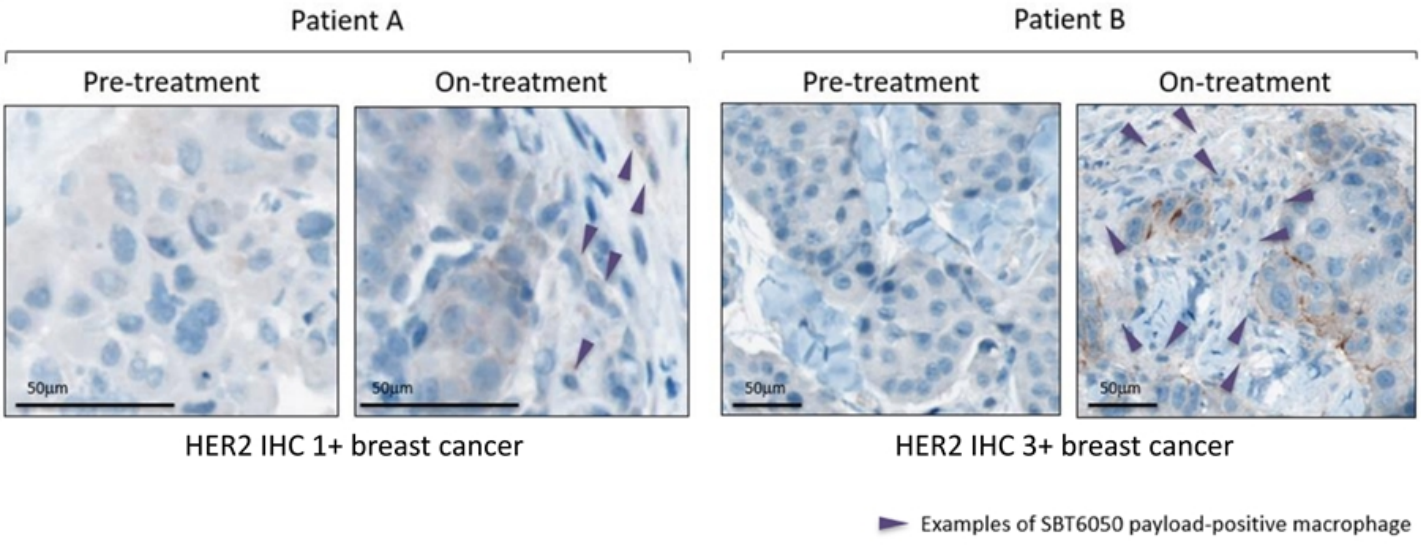
PD activity is maintained with repeat dosing



SBT6050 payload is detected on tumor cells and in intratumoral macrophages, supporting the proposed mechanism of action in the TME

SILVERBACK THERAPEUTICS

SBT6050 payload is detected on tumor cells and in intratumoral macrophages of patients dosed at 0.6 mg/kg



SBT6050 demonstrated early signals of anti-tumor activity in tumor types prioritized for expansion cohorts

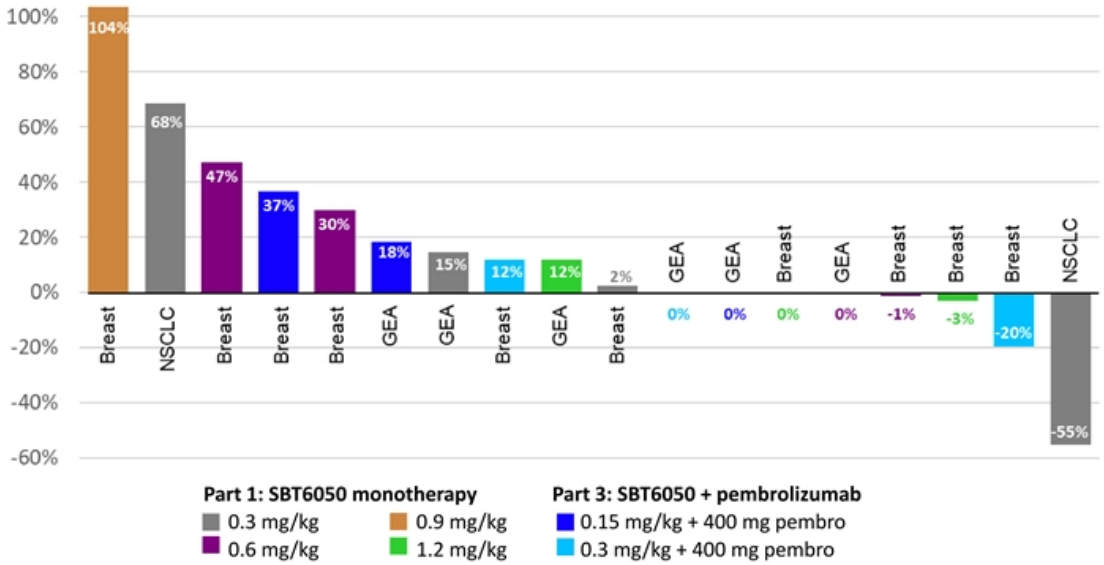
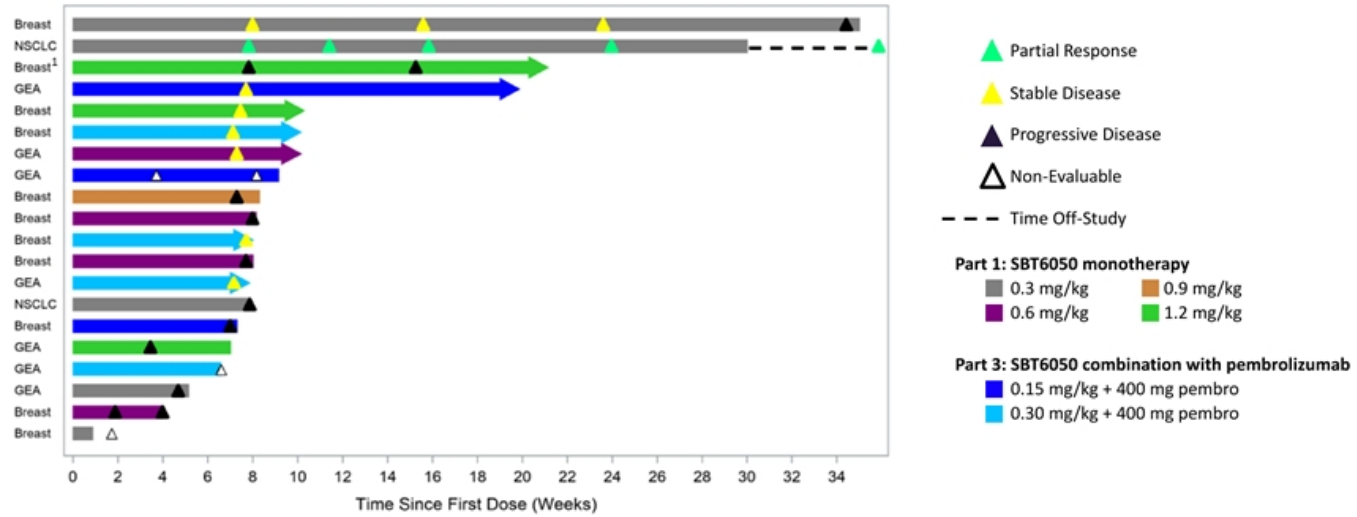


Figure includes patients with tumor types prioritized for expansion cohorts (breast, gastroesophageal, NSCLC), who have restaging CT scans evaluable per RECIST

Adverse events do not change with repeat dosing; PR maintained while off study



- Overall response in patients with RECIST-evaluable CT scans (n=24) was PR: n=1, SD: n=8, PD: n=15. Figure includes patients with tumor types prioritized for expansion cohorts (breast, gastroesophageal, NSCLC), who have restaging CT scans evaluable per RECIST
- Interim data as of August 1, 2021

1. Patient classified as progressive disease based on a new 5mm CNS lesion, but remains on study and demonstrated a 3% reduction in target lesions

SBT6050 conferred clinical benefit to patients with heavily pre-treated, advanced solid tumors

SILVERBACK THERAPEUTICS

	NSCLC HER2 IHC 2+ Not amplified	Breast Cancer HER2 IHC 3+	Bladder Cancer HER2 IHC 2+ Amplification unknown	Breast Cancer HER2 IHC 3+	Breast Cancer HER2 IHC 3+	Gastric Cancer HER2 IHC 3+
Age	67F	73F	60M	48F	40F	49M
Dose	0.3 mg/kg monotherapy	0.3 mg/kg monotherapy	0.6 mg/kg monotherapy	1.2 mg/kg monotherapy (decreased to 0.6 mg/kg at dose 3)	0.3 mg/kg plus pembro	0.3 mg/kg plus pembro
Treatment Duration	**26 weeks** (11 doses)	**33 weeks** (17 doses)	**>8 weeks** and remains on treatment	**>21 weeks** and remains on treatment, per investigator decision	**>8 weeks** and remains on treatment	**>8 weeks** and remains on treatment
Prior Lines of Therapy	**3 prior lines** with progression on prior PD-1 treatment	**7+ prior lines** including HER2-ADC and HER2 targeted therapy	**2 prior lines** including anti-PD-L1 and cisplatin-gemcitabine	**4 prior lines** including HER2-ADC, anti-PD-L1, and HER2 targeted therapy	**3+ prior lines** including HER2-based cytotoxic ADC and HER2 targeted therapy	**1 prior line** including HER2 targeted therapy
Best Response	**Confirmed Partial Response** (-55%) Response ongoing at 36 weeks from first dose	**Stable Disease** (+2%) Maintained stable disease through 24-week scan	**Stable Disease** (-2.7%)	**Progressive Disease** (-3% in target lesions) PD based on new 5mm CNS lesion	**Stable Disease** (-20%)	**Stable Disease** (0%) Decreasing tumor marker (CA19-9 decrease from 135 to 64 U/mL)

Safety profile, PK, and PD data support a projected RP2D of 0.6 mg/kg

SILVERBACK THERAPEUTICS

At the 0.6 mg/kg dose level:

- ✓ Safety and tolerability profile consistent with an immune activator and manageable
- ✓ Serum PK suggests HER2 target saturation
- ✓ Pharmacodynamic markers indicative of myeloid, T/NK cell activation reach a plateau
- ✓ Payload is detected in intratumoral macrophages and on tumor cells
- ✓ Signals of anti-tumor activity, as single agent or in combo, observed at doses at or above 0.15 mg/kg

SBT6290

Tumor-targeting antigen: Nectin4

Target cell: myeloid cells

Payload: proprietary TLR8 agonist

Next milestones:
- 4Q 2021 - submit IND
- 1Q 2022 - initiate Phase 1 dose-escalation

SBT6290 comprises the same TLR8 agonist linker-payload used in SBT6050, conjugated to a proprietary Nectin4-directed monoclonal antibody

- Nectin4 is a clinically validated target by Seagen through the 2019 accelerated approval of ADC enfortumab vedotin (Padcev) in bladder cancer
- SBT6290 is tuned for activity in settings of Nectin4 moderate to high expression
- Preclinical studies demonstrate a similar functional profile to SBT6050, with robust anti-tumor activity and upregulation of key cytokines and chemokines in tumor that are indicative of myeloid and T/NK cell activation
- Non-GLP toxicology studies with SC administration in NHP indicate a favorable therapeutic window
- Pre-IND alignment with FDA on preclinical, CMC, and clinical plan was achieved in February 2021
- GLP toxicology study completed, with IND filing on track for the fourth quarter of 2021

SBT6290 is selective for Nectin4 and blocks TIGIT:Nectin4 interaction

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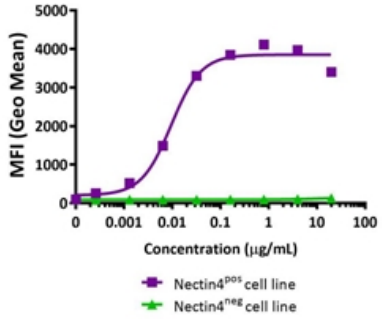
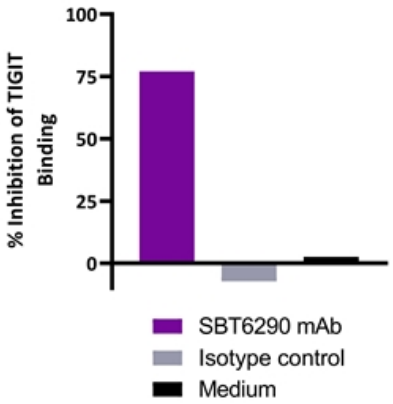
SBT6290 is Selective for Nectin4

Nectin Family Members	Binding Affinity
Nectin4	<1 pM
Nectin1	No binding detected; affinity is >1μM
Nectin2	
Nectin3	

SBT6290 Binds With High Affinity to Tumor Cells Expressing Nectin4



SBT6290 binding domain blocked TIGIT binding to Nectin4-expressing tumor cells



SBT6290 activates human myeloid cells in a Nectin4- and Fc-dependent manner

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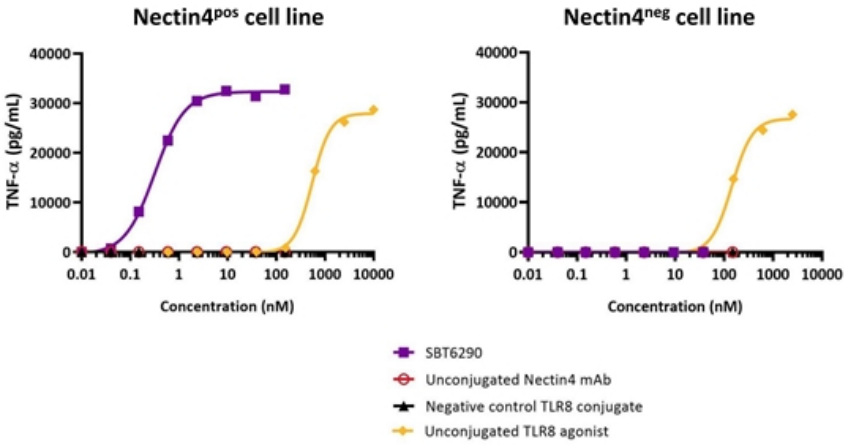
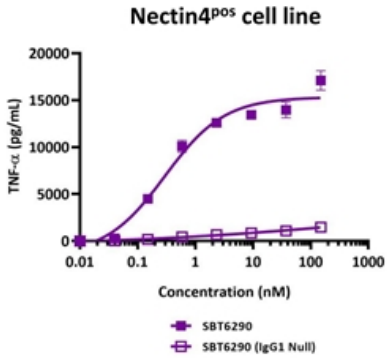
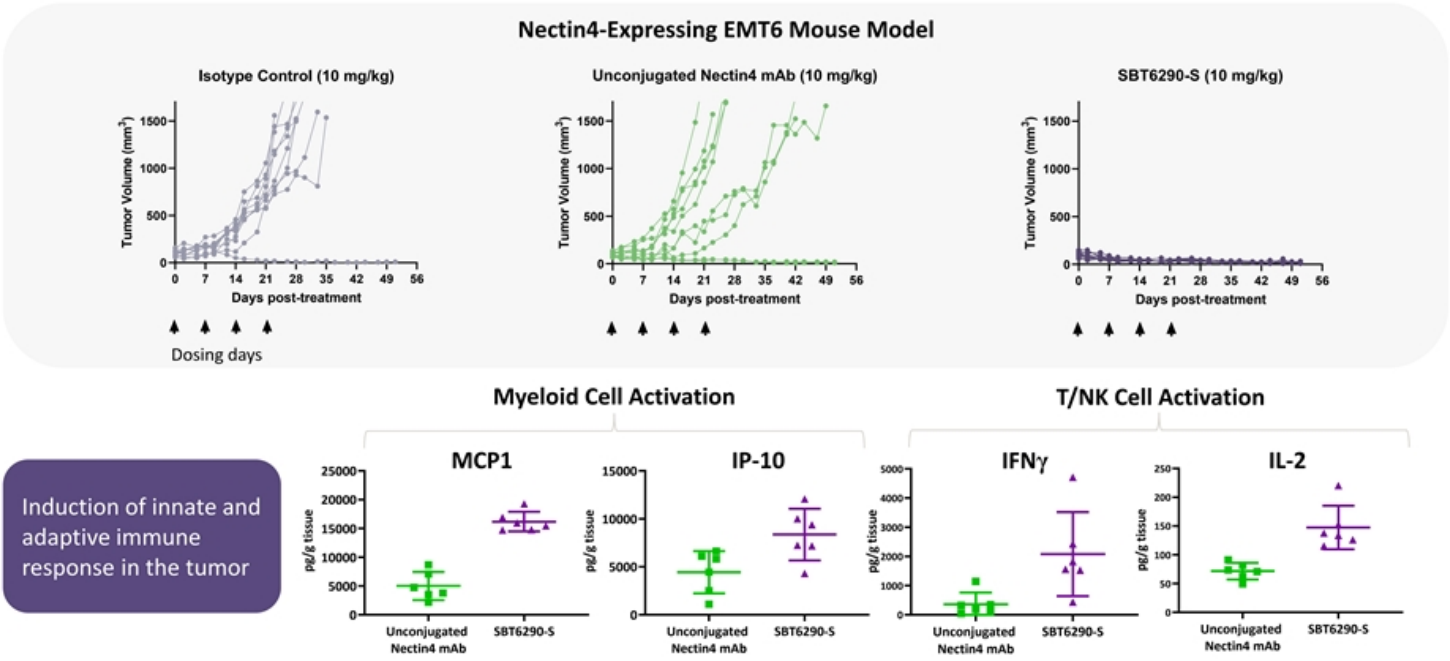
SBT6290 Activity is Nectin4-Dependent



SBT6290 Activity Requires Fc Engagement



SBT6290-S demonstrates robust single agent activity *in vivo*



Nectin4 is overexpressed in bladder, TNBC, H&N, and NSCLC, among other indications, unlocking a large opportunity in an untapped market

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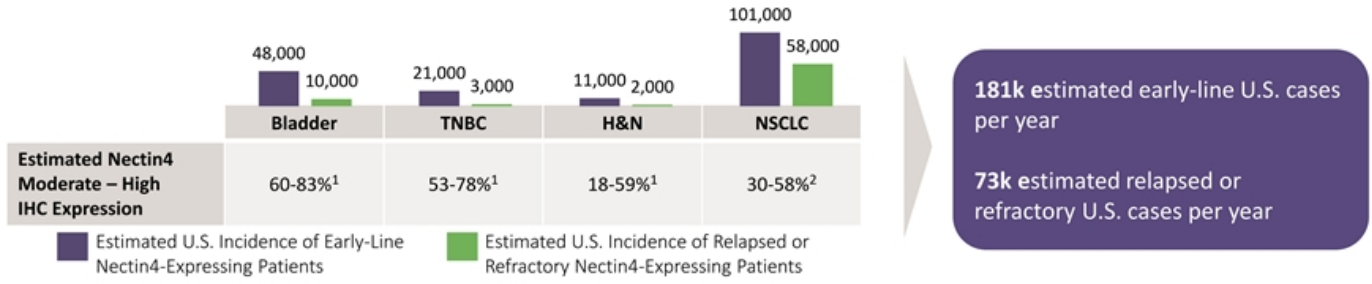
Nectin4 Overexpression Across Select Tumor Types



181k estimated early-line U.S. cases per year

73k estimated relapsed or refractory U.S. cases per year

Nectin4-Targeted Therapies in Development

	Bladder	Breast	Lung	H&N	GEC
Approved	Seagen [3]				
Ph 3	Seagen				
Ph 2 – Solid Tumor Basket Study		Seagen	Seagen	Seagen	Seagen
Ph 1 – Solid Tumor Basket Study	bicycle therapeutics	bicycle therapeutics	bicycle therapeutics	bicycle therapeutics	bicycle therapeutics

[1]Challita-Eid et al *Cancer Research* 2016, et al. | [2] Takano et al *Cancer Research* 2009 | [3] Padcev accelerated approval

SBT8230

Liver-targeting antigen: ASGR1

Target cell: myeloid cells

Payload: proprietary TLR8 agonist

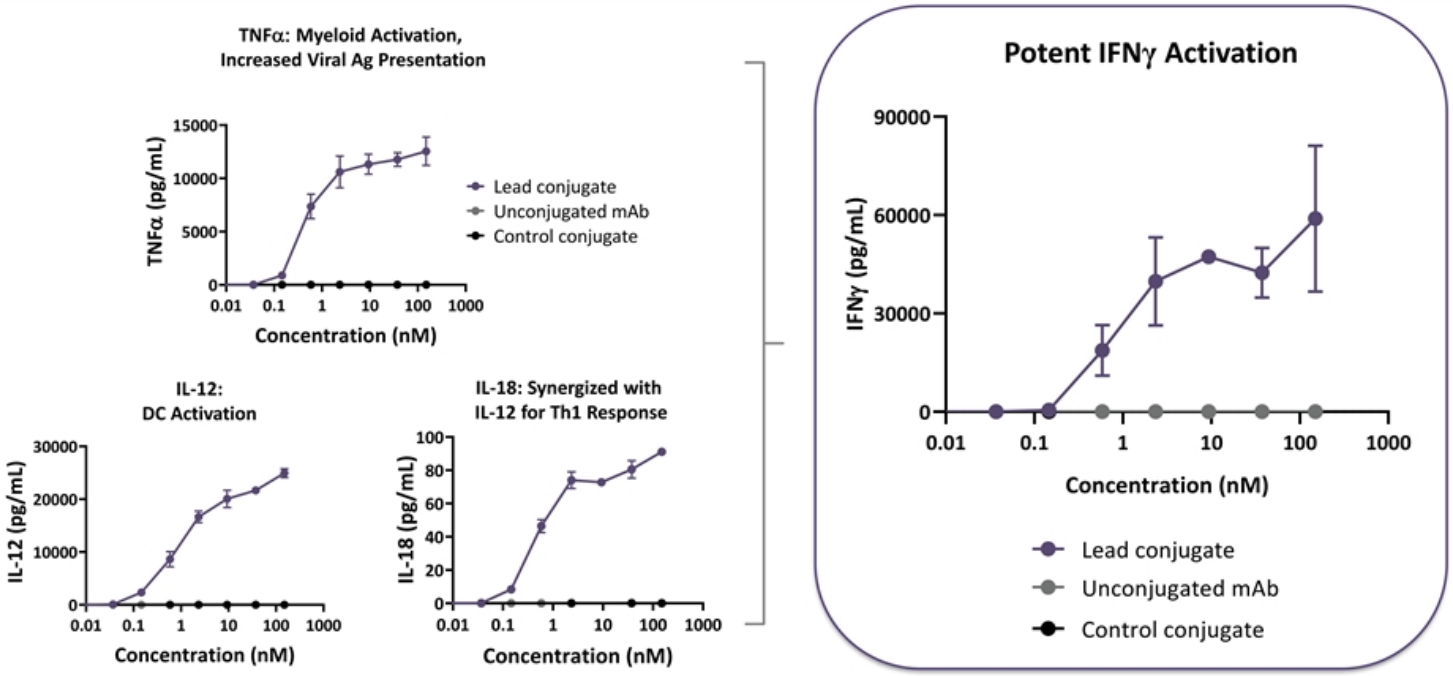
Indication: cHBV

Next milestone:
- 1Q 2022 - initiate IND-enabling tox studies

SBT8230 provides opportunity to further realize potential of TLR8 agonism with liver-localized activity, if approved

- Potent IFNγ-mediated immune response and seroconversion, which TLR8 agonism has been shown to drive, is key determinant of achieving a functional cure in cHBV
- Clinical validation provided by Gilead's untargeted, orally administered TLR8 agonist small molecule selgantolimod (GS-9688)
- SBT8230 binds to ASGR1 (GalNAc target) and is combinable with RNAi approaches and other cHBV therapies
- Designed to achieve exposure not possible with untargeted, systemically administered TLR8 agonists
- Exploratory NHP toxicology study demonstrates wide therapeutic window
- Early CMC activities initiated, including selection of the clone and creation of a master cell bank

ASGR1-TLR8 potently activated human myeloid cells, resulting in a robust IFNγ response



ASGR1-S reduces Hepatitis B surface antigen (HBsAg) and drives seroconversion in AAV-HBV mouse model

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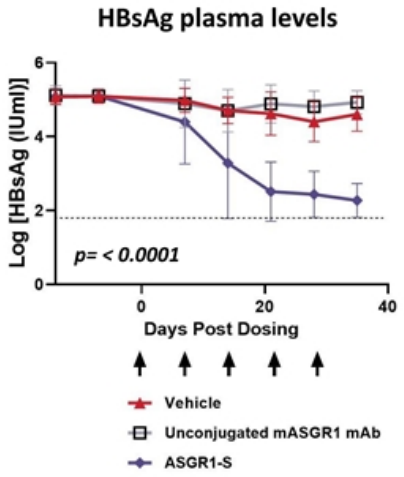

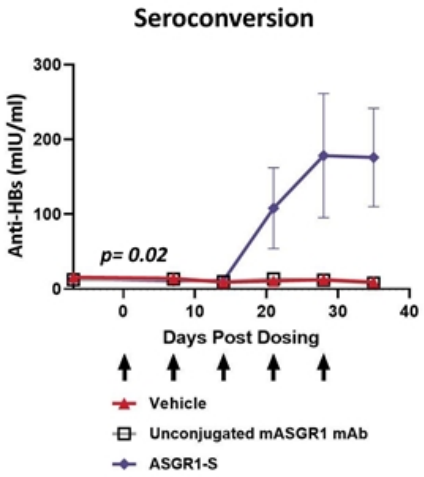

ASGR1-S lowered average plasma viral DNA titers 2.5 logs

Multiple preclinical programs to expand ImmunoTAC platform

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IO TLR8 Programs

- Two additional undisclosed IO targets may enable us to expand coverage of solid tumor indications
- Same TLR8 linker-payload utilized in SBT6050 and SBT6290 and similar in vitro functional profile

Liver-Directed TGFβRi ImmunoTAC for Liver Fibrosis

- Designed for liver-localized TGFβ signaling inhibition for anti-fibrotic effects
- Designed to inhibit the TGFβR directly for complete pathway inhibition
- Blockade of TGFβ/SMAD signaling in hepatocytes in mice (CCl4 model) prevents liver fibrosis

Additional Discovery Programs

- Additional ImmunoTAC conjugates comprised of novel payload classes in preclinical development and entering in vivo models

Led by a veteran team with a track record of advancing transformative therapies

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Leadership Team

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synthorx · CLEAVE BIOSCIENCES · SUGEN

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Corporate highlights

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1. ImmunoTAC conjugates are designed to **unlock a new class of targeted immuno-oncology agents** that direct a myeloid cell agonist to the tumor microenvironment for localized activation

2. Emerging clinical data supports **proof-of-mechanism for localized TLR8 agonism and the ImmunoTAC platform**, evidenced by the robust activation of innate and adaptive immune response seen in patients

3. SBT6050 has demonstrated **early signals of anti-tumor activity** as a monotherapy and in combination with a PD-1 inhibitor, with a **manageable safety profile** consistent with an active IO agent

4. Clinical development plan to evaluate SBT6050 in combinations designed to have long-term benefit in early lines of treatment, including **combo with anti-PD1, with Enhertu and with Herceptin/Tukysa**

5. Positive readthrough to Silverback's TLR8 pipeline with **value-generating milestones expected in the next 6-18 months**, including anticipated initiation of SBT6290 (Nectin4) Ph1 study and SBT8230 (HBV) Ph1-enabling studies

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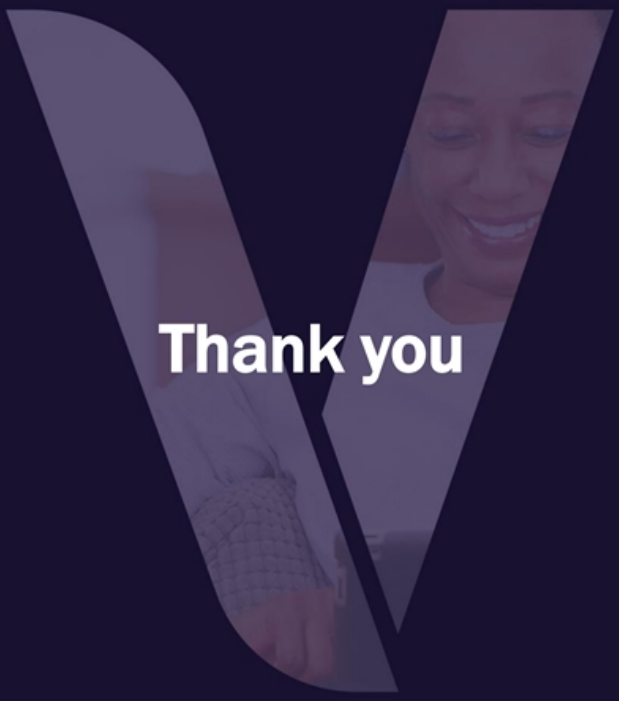

Thank you