Making Tumors Visible
So Immunotherapy Can Work

Developing targeted RNA therapeutics that unlock immune recognition in solid tumors by inducing neoantigen expression

August, 2025

Sebastian BioPharma

Making immunotherapy work for more patients, more tumors, more lives

Snapshot

· Focus: Immuno-Oncology & RNA therapeutics
· Unmet need: >70% of patients fail immunotherapy due to neoantigen deficiency
· Scientific solution: TAP modulation to induce shared tumor neoantigens
· Team: Pioneers in neoantigen biology; led 2 drugs to clinic
· IP & Validation: Licensed IP (University of Miami); strong preclinical efficacy

Opportunity & Readiness

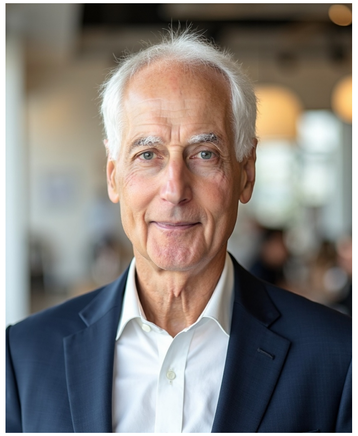
· Platform: Antibody-oligonucleotide conjugate modular and multivalent, tumor-agnostic RNA delivery via antibody targeting
· Lead asset: iTAP – microsatellite stable CRC lead; multi-indication potential
· Stage: Lead discovery
· Funding: $0.5M (dilutive or non-dilutive) to supplement early funding and complete lead-to-hit; $3–5M to support IND readiness and regulatory submission
· Market: Addresses 3/4 of cancer patients, currently ineligible for PD-1 inhibitors

Built to advance: Scientific vision, experimental precision, and development expertise

Greta Garrido, PhD

CEO & Co-Founder

Scientist leader in TAP modulation at Dr. Gilboa's lab. Seasoned biotech executive driving Immuno-Oncology innovation. Led 2 FDA approvals and secured over $50M in successful fundraising.



Eli Gilboa, PhD

CSO & Founder

Scientific leader in tumor neoantigen biology and RNA therapeutics. Secured multiple grants supporting Sebastian BioPharma's innovative pipeline.

gritstone bio · nurix · BlueSphere BIO · University of Miami · CIM Centro de Inmunología Molecular

University of Miami · Duke University · Memorial Sloan Kettering Cancer Center · Princeton University · Massachusetts Institute of Technology

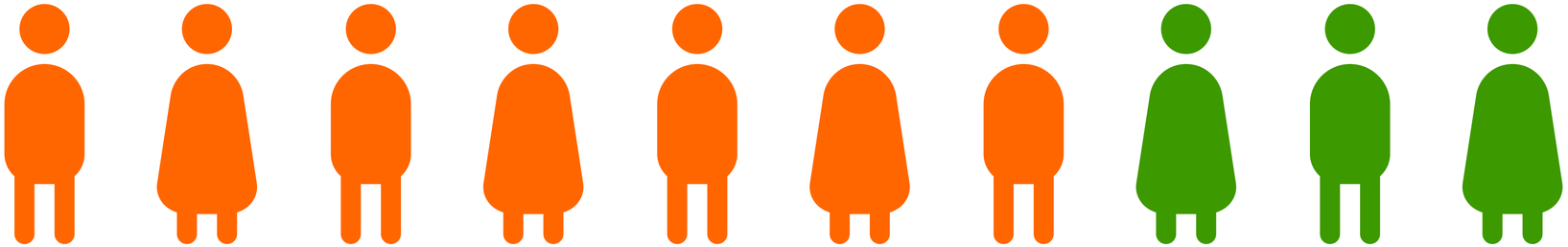
Advisors

Jane Lebkowski, PhD
President, Regenerative Patch Technologies
From Discovery to Commercialization

John Goldberg, MD
CMO, Rafael Holdings, Inc.
Clinical & Business Development

The unmet clinical need for Immuno-Oncology

**2M+ new cancer cases in the US (2025),
yet most won't benefit from PD-1 inhibitors.**



70-80% of cancer patients do not respond to immunotherapy

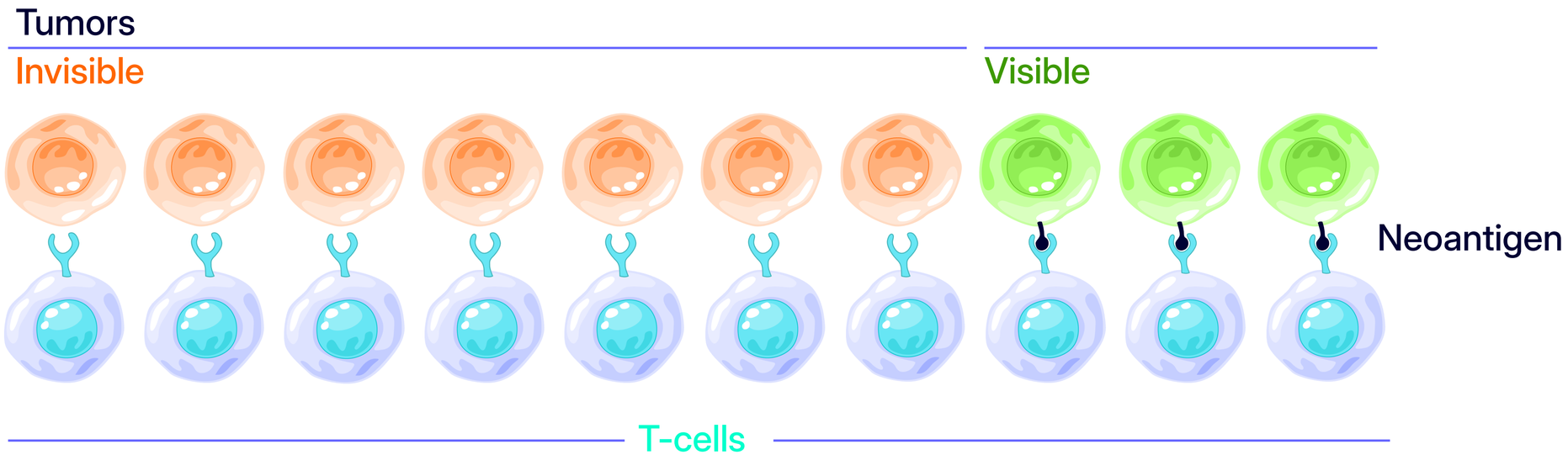
20-30% responders to PD-1 inhibitors

A primary reason for unresponsiveness is the paucity of neoantigens, making tumors effectively invisible to the immune system. An effective T-cell response requires recognizable neoantigens, yet many tumors fail to present them, blocking immune activation at its source.

Neoantigen deficiency is an unresolved challenge

60–80% of solid tumors lack sufficient neoantigens to be recognized by T-cells.[1]

FDA recognizes neoantigen deficiency as a major cause of resistance to PD-1 inhibitors.[2]



Most immunotherapies activate T-cells but fail when tumors lack neoantigens.
No approved drug addresses this upstream barrier.

Sebastian BioPharma's therapeutic strategy induces tumor neoantigens, enabling immune recognition where others fail.

1. https://pubmed.ncbi.nlm.nih.gov/34083238/

2. https://www.mskcc.org/news/clearing-fog-around-tumor-mutational-burden

The genesis of Sebastian BioPharma

Pioneering neoantigen induction to unlock immune response

Our team was first to demonstrate that tumor visibility can be restored by inducing neoantigens-**published in Nature (2010).**[1]

· Induced neoantigens via targeted inhibition of RNA fidelity

· Delivered RNA interference payloads using tumor-specific aptamer

· Achieved potent antitumor efficacy

Limitation of early approach: Neoantigen induction was stochastic-each tumor cell presented unique antigens, limiting clinical translatability.

Strategic evolution: Sebastian BioPharma (SBP) now targets TAP inducing uniformly expressed (shared) neoantigens-a key predictor of response to PD-1 inhibitors.[2]

1. Induction of tumour immunity by targeted inhibition of nonsense-mediated mRNA decay | Nature

2. Mismatch repair deficiency is not sufficient to elicit tumor immunogenicity - PMC

TAP modulation restores tumor visibility through shared neoantigen induction

Reduction of **TAP (Transporter associated with Antigen Processing)** expression reveals **non-canonical peptides: shared, immunogenic, and consistently recognized by T-cells.** This bypasses reliance on random, patient-specific mutations.

These induced neoantigens are the equivalent of **clonal neoantigens, considered best-in-class for anti-tumor response.** Enables broad, tumor-agnostic immune recognition.

No approved therapies exploit TAP downregulation to induce neoantigens. SBP is first to unlock this therapeutic axis.

Foundational papers describing the mechanism:

TAP-independent self-peptides enhance T cell recognition of immune-escaped tumors - PMC.
Identification of non-mutated neoantigens presented by TAP-deficient tumors | Journal of Experimental Medicine | Rockefeller University Press.
Selective cytotoxic T-lymphocyte targeting of tumor immune escape variants | Nature Medicine.

Preclinical validation: TAP modulation reverses immunotherapy resistance

Using a tumor-specific aptamer to deliver TAP siRNAs, SBP achieves:

MoA #1: Downregulation of TAP - Induction of shared neoantigens
MoA #2: Recruitment of innate and adaptive immune cells to the tumor microenvironment
MoA #3: Epitope spreading - Activation of T-cells targeting TAP-sufficient epitopes

Potent antitumor activity across 5 tumor models

· Potent antitumor activity as monotherapy
· Robust synergy with PD-1 inhibitors
· No observed toxicity - Broad therapeutic window
· See experimental data here

Strong translational potential

· 18/906, 621: Filed Oct 4, 2024 (Composition & method of treating tumors by inducing neoantigens modulating multiple targets including TAP).
· 2 Papers published in high-impact peer-reviewed journals*

* Tumor-targeted silencing of the peptide transporter TAP induces potent antitumor immunity | Nature Communications
Vaccination against Nonmutated Neoantigens Induced in Recurrent and Future Tumors | Cancer Immunology Research | American Association for Cancer Research

Strategic shift: From aptamers to antibodies - streamlining regulatory pathways and expanding tumor reach

Antibody-oligonucleotide platform for targeted, modular RNA delivery

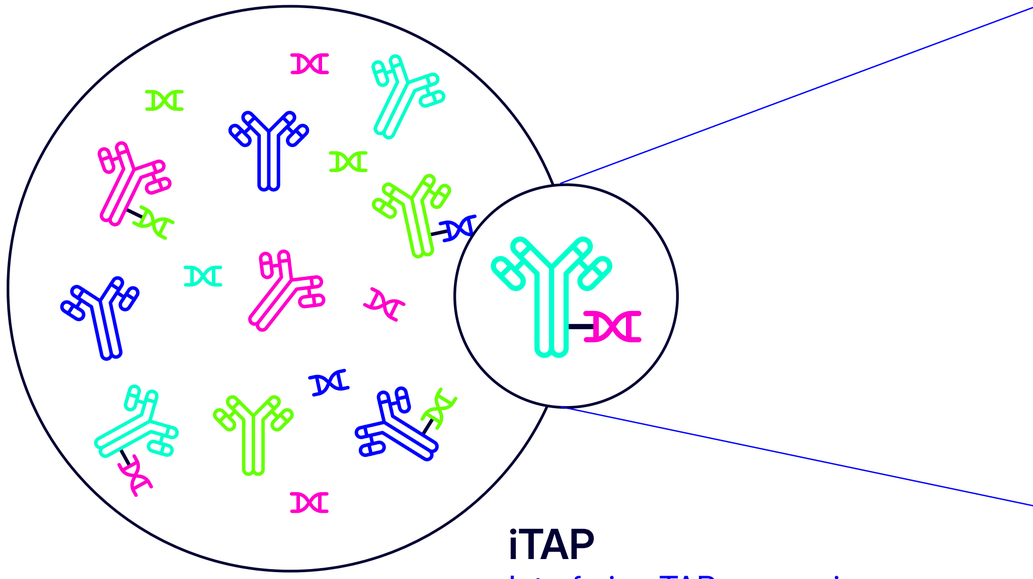
Features

· **Targeted delivery:** Utilizes clinically validated antibodies for precise tissue targeting-minimizing systemic exposure and enhancing safety.

· **Potent RNA activity:** Delivers robust gene modulation at low nanomolar concentrations-enabling therapeutic efficacy with minimal dosing.

· **Multivalent delivery:** Engineered for proven intracellular uptake of multiple payloads per construct, enabling synergistic modulation of complex tumor pathways.

· **Modular architecture:** Inspired by proven platforms (e.g., Avidity, Dyne), supporting rapid payload interchangeability and indication-specific adaptation.

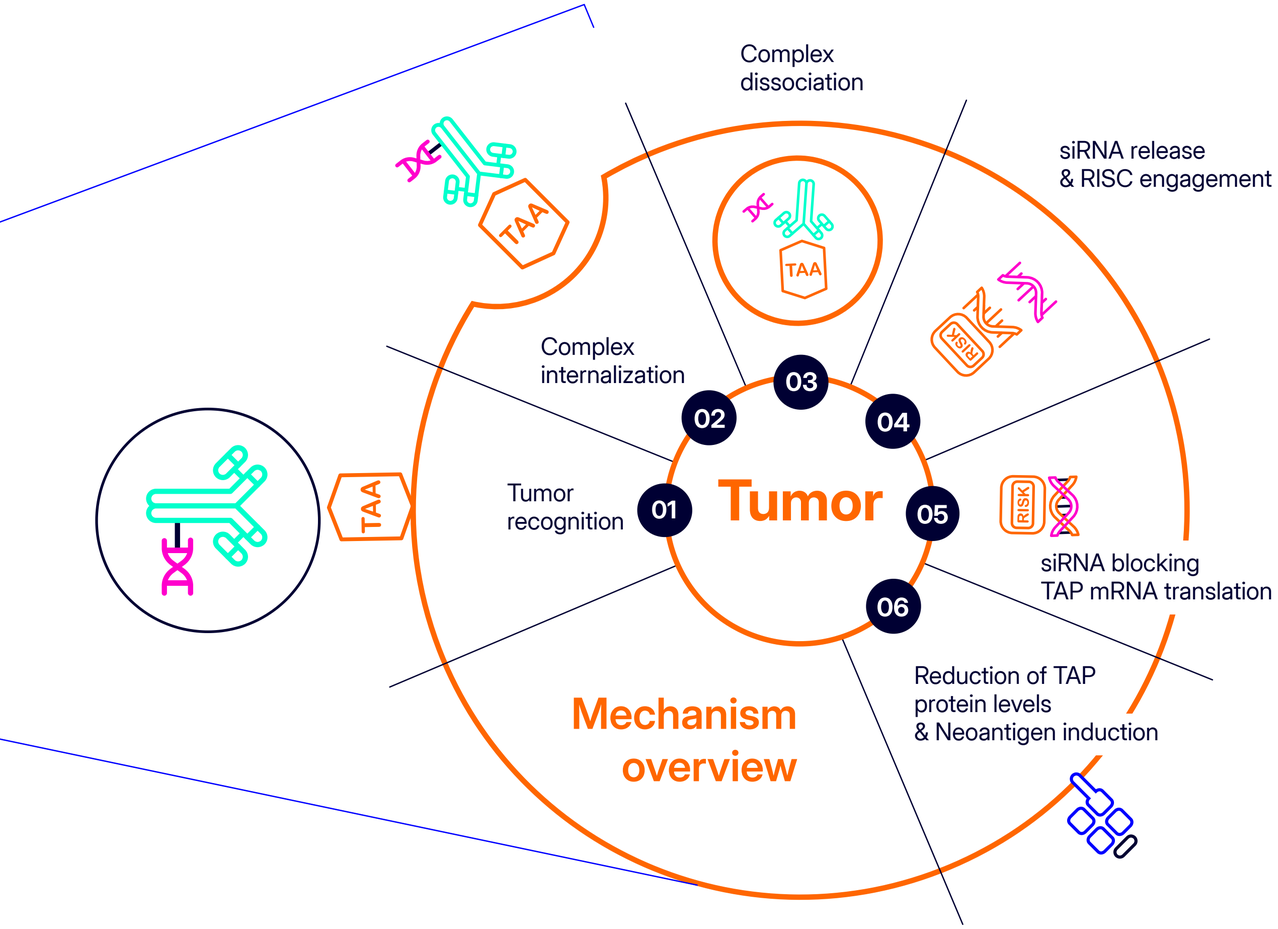


iTAP
Interfering TAP expression

Proof-of-concept publications:

Vaccination against neoantigens induced in cross-priming cDC1 in vivo | Cancer Immunology, Immunotherapy
KLF2 inhibition expands tumor-resident T cells and enhances tumor immunity - PMC

iTAP: Tumor-targeted TAP silencing to induce neoantigens via OligoBridgeX platform



De-risking strategy through platform design

· **Clinical precedent:** Leverages antibody-drug conjugate (ADC) frameworks with established safety and efficacy.

· **Reduced development risk:** Built from components with known PK profiles and scalable manufacturing pathways.

· **Accelerated path to IND:** Modular platform and validated targeting streamline regulatory and translational progression.

· **Immuno-Oncology ready:** Engineered for tumor-selective delivery and compatibility with immune-modulating therapies.

1 provisional application to be filed in Q4 2025

Competitive advantage

Neoantigen induction	Sebastian BioPharma (SBP)	Greywolf Therapeutics	Neophore
Target pathway	Antigen presentation	Antigen presentation	Mismatch repair
Target molecule	**TAP**	ERAAP	PMS2
Induction of shared neoantigens	**Yes**	No	No
Type of drug	AOC	Small molecule	Small molecule
Targeting strategy	**Specific**	Non-specific	Non-specific
Stage	Preclinical	Phase 1[1]	Preclinical[2]

1. Greywolf Therapeutics presents first clinical data for GRWD5769, a first-in-class ERAP1 Inhibitor, at the 2024 American Society for Clinical Oncology (ASCO) Annual Meeting

2. NeoPhore presented preclinical data from our PMS2 program at the AACR Annual Meeting, San Diego, 5 - 10 April 2024. | Neophore

Market opportunity: Reinvigorating PD-1 in a $120B+ landscape

Immunotherapy market

· PD-1 inhibitors: **$62B today, $120B by 2034** [1]

· Global immunotherapy: **$486B by 2030** [2]

· **Patent cliff begins 2028:** Pharma seeks lifecycle-extending combos [3]

Unmet need

· Most solid tumors show **PD-1 resistance**

· Caused by **neoantigen deficiency** & immune evasion

· Existing combos: **Limited efficacy**

SBP advantage

Unlike current enhancers, iTAP is designed to overcome the main cause of low efficacy, tumor neoantigen deficiency by inducing potent, shared neoantigens.

This unique mechanism specifically targets the 70–80% of nonresponsive patients, enabling strong synergy with PD-1 antibodies even in tumors traditionally resistant to immunotherapy.

SBP offers a rare convergence of value: PD-1 lifecycle extension, ADC and RNA synergy, and platform scalability. With the 2028 patent cliff looming, now is the time to invest in the next wave of Immuno-Oncology innovation.

1. https://www.mordorintelligence.com/industry-reports/pd1-and-pdl1-inhibitors-market

2.https://www.grandviewresearch.com/industry-analysis/immunotherapy-drugs-market-report

3. https://www.biospace.com/business/5-pharma-powerhouses-facing-massive-patent-cliffs-and-what-theyre-doing-about-it

Where we stand today & Development path

Founder commitment & Runway

Founder-backed with ~$0.5M initial investment (Dr. Gilboa)
· Enables 12-month experimental runway
· Focused on platform validation and candidate selection
· Additional $0.5M (dilutive or non-dilutive) sought to complement initial capital and reach lead-to-hit milestone

Platform execution & Candidate advancement

· Lab operations launched: Established R&D footprint at InnoVenture Lab (April 2025)
· Accelerator graduation: Completed SCBio DRIVE program (June 2025), validating platform potential and strategic roadmap
· iTAP program progress: Advancing lead optimization ; 4 proprietary candidates under active evaluation
· Candidate differentiation: Each candidate assessed for TAP modulation, tumor-selective uptake, and delivery efficiency
Next milestone: Prioritization of top 2 candidates for IND-enabling studies

Funding & Strategic goals

Near-term goal: Raise $0.5M (dilutive or non-dilutive) to complete lead-to-hit milestone and extend early runway
· Mid-term goal: Secure $3–5M to enable IND-enabling studies, expand iTAP program, and prepare regulatory package
· Target outcome: IND-ready asset by end of Q2 2027
· Strategic leverage: Unlock value through candidate prioritization, early BD engagement, and modular platform scalability

Business & financial strategic planning underway to align milestones with investor readiness.

Clinical Validation Strategy

Trial design focused on early efficacy signals in PD-1 resistant tumors

SBP will initiate a **biomarker-guided basket trial in Q1 2028** to validate iTAP, our lead RNA interference therapeutic, restoring immune recognition in resistant tumors.

The clinical trial design includes a dedicated window at the recommended Phase 2 dose (RP2D) to evaluate single agent activity, enabling direct assessment of iTAP's immunologic impact prior to combination strategies.

The trial will target a **defined patient population**: **TAP-positive, antibody-accessible, low-neoantigen tumors**, including CRC and other solid tumor types with high unmet need and strong potential for PD-1 synergy.

This strategy is designed **to deliver early proof-of-concept**, position iTAP as a first-in-class immunotherapy "enabler" and expand access for patients excluded from current immune therapies.

Colorectal cancer: A neoantigen-driven scenario

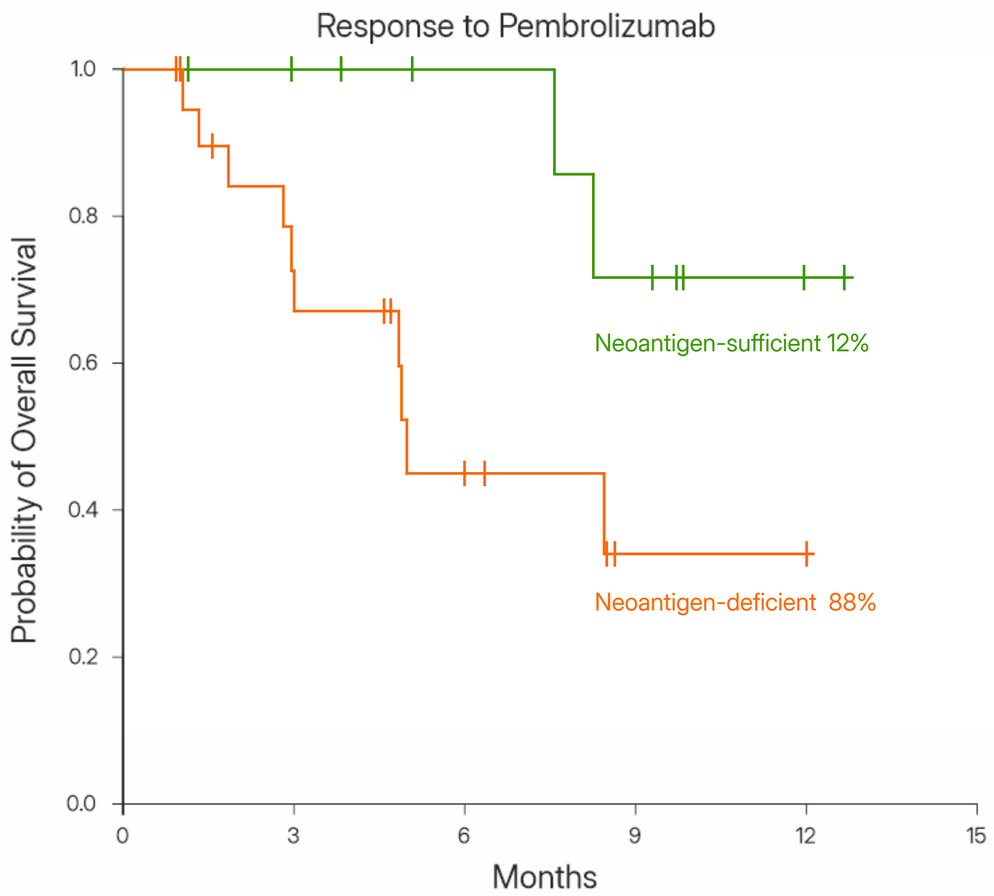
Focused population & Accelerated path to clinical proof-of-concept

2nd in cancer-related death in the U.S.

154,000+ new cases expected in 2025[1]

88% of CRC tumors lack neoantigens (microsatellite stability phenotype), rendering most patients resistant to PD-1 inhibitors

Only 14% of patients survive beyond 5 years[2]



Modified from Le et al., N Engl J Med 2015

1. https://cancerstatisticscenter.cancer.org/types/colorectum

2. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2024/2024-cancer-facts-and-figures-acs.pdf

Executive summary

Differentiated science
SBP's first-in-class TAP modulation induces neoantigen presentation, enabling PD-1 responsiveness in tumors that evade current immunotherapies.

Target population & Market opportunity
We're focused on microsatellite stable CRC and other resistant tumors, with potential to expand the $120B+ PD-1 market through strategic combinations.

Risk mitigation by design
Modular, multivalent antibody–oligonucleotide conjugates paired with rational drug design reduce translational risk, enable tissue-specific delivery, and offer built-in flexibility.

Execution strategy
Led by a team with FDA approvals and $50M+ raised, we've finalized our clinical plan and are actively recruiting the expertise needed to execute with speed and precision.

Sebastian Bio Pharma

Ready to deliver - science, strategy and value.

contact@sebastianbio.com | 786-717-0995
www.sebastianbio.com