

# Sebastian BioPharma

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A Tissue-Targeted Programmable RNA Interference Platform

*Advancing SBP-001 in IO-Resistant Colorectal Cancer*

# Executive Summary

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## Company Overview

Sebastian BioPharma is a preclinical oncology company developing **next-generation Antibody–Oligonucleotide Conjugates (AOCs)** designed to overcome the single-payload limitation of current platforms through modular, **dual-RNA delivery and intracellular co-modulation**.

## Technology Platform

**Proprietary dual-siRNA AOC platform** enabling precise stoichiometry, modular architecture, and **simultaneous modulation of two intracellular resistance pathways** from a single antibody conjugation site.

## Lead Program

**SBP-001** – Dual-siRNA AOC targeting **IO-resistant solid tumors (initial focus: colorectal cancer)**, designed for tumor-specific delivery with reduced systemic toxicity.

## Stage & Validation

- Dual intracellular targets validated | dual-siRNA cassette sequence locked
- In vitro + in vivo PD mouse models with subrogate drug
- Clear and differentiated MoA
- Human relevant in vitro PD | dual-target activity demonstrated
- **3 patents filed | 6 scientific publications**

## Team & Foundation

Co-founders are inventors of the IP with extensive drug development experience.

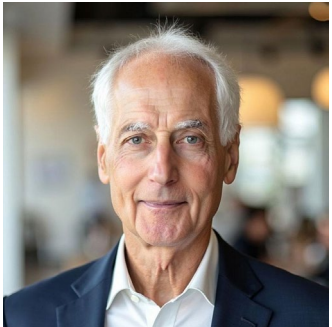
## Capital & Milestones

Initial Investment Commitment of up to \$800K of which \$630K are being currently deployed.

Raising a Total of **\$2.5M Pre-Seed → Drug Candidate Nomination and ~12-15 months Runway**

Seed Round of \$8-13M to be launched in ~12-15 months → IND Filing

# Founder Team with Proven Execution



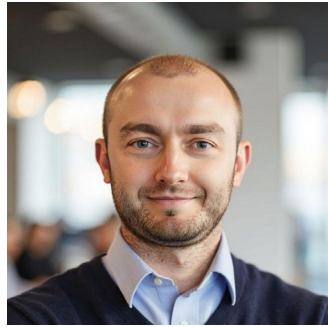
**Eli Gilboa, PhD**  
CSO & Founder

- Pioneer in RNA therapeutics; founder of Argos Therapeutics
- Decades of leadership in tumor immunology & translational discovery



**Greta Garrido, PhD, MSc**  
CEO & Co-Founder

- Advanced IO programs from discovery through IND
- Proven execution across translation, fundraising, and partnerships



**Brett Schrand, PhD**  
R&D, Associate Director

- Oligonucleotide therapeutics discovery & development
- Hands-on execution across in-vitro and in-vivo programs

## Validation

- **\$7.9M in non-dilutive funding** supporting target validation, MoA characterization, and in vivo efficacy
- Additional non-dilutive grant applications under review (Q3–Q4 2026)
- Graduate, SCbioDrive Accelerator (2025)
- Selected, Nucleate Activator (2026)

## Sebastian BioPharma (Launched January 2025)

- **Founder-led**, capital-efficient execution
- Fully operational lab workflows established
- Lead program advanced through key preclinical milestones



# Experienced Advisors Complementing our Expertise



## Business Advisory



**Carolina Alarco, MBA**  
Business Strategy



**Veronica Gibaja, MSc**  
Pre-Clinical & IND Support



**Fernanda Gamero, BSc**  
IR & Comms



**Gabriela Larenas, MSc**  
Biotechnology and  
Biomedical Sciences

## IP Advisory



**Seth Hudson, JD**



**Leon Pappas, MD, PhD, MSc**  
Clinical Advisor

## Scientific Advisory Board

## Incubated at



Beverly, MA

# Solid Scientific Foundation: Team Publications



These publications related to our platform and lead asset are the foundation of our work.

- **6 peer-reviewed publications in high-impact journals**
- **5+ publications supporting pipeline expansion**
- **All work authored by founding scientists**

Vol 465 | 13 May 2020 | doi:10.1038/nature08999 | nature

LETTERS

### Induction of tumor immunity by targeted inhibition of nonsense-mediated mRNA decay

Fernando Pastor<sup>1</sup>, Despina Kolonias<sup>1</sup>, Paloma H. Giangrande<sup>1</sup> & Eli Gilboa<sup>1</sup>

The main reason why tumours are not controlled by the immune system is that, unlike pathogens, they do not express potent tumour rejection antigens (TRAs). Tumour vaccination aims at stimulating a systemic immune response targeted to, mostly weak, antigens expressed in the disseminated tumour lesions. Main challenges in this field are the identification of TRAs and the development of adjuvants that enhance their immunogenicity. Here we describe a novel approach whereby a common set of new antigens are induced in tumour cells in situ by transient downregulation of the transporter associated with antigen processing (TAP). Administration of TAP siRNA conjugated to a broad-range tumor-targeting nucleolin aptamer inhibited tumor growth in multiple tumor models without measurable toxicity, was comparatively effective to vaccination against prototypic mutation-generated neoantigens, potentiated the antitumor effect of PD-1 antibody or F13 ligand, and induced the presentation of a TAP-independent peptide in human tumor cells. Treatment with the chemically-synthesized nucleolin-aptamer-TAP siRNA conjugate represents a broadly-applicable approach to increase the antigenicity of tumor lesions and thereby enhance the effectiveness of immune potentiating therapies.

nature COMMUNICATIONS

ARTICLE

<https://doi.org/10.1038/s41467-019-11728-2> OPEN

### Tumor-targeted silencing of the peptide transporter TAP induces potent antitumor immunity

Greta Garrido<sup>1</sup>, Brett Schrand<sup>1</sup>, Agata Leva<sup>1</sup>, Allem Rabasa<sup>1</sup>, Anthony Ferrantelli<sup>1</sup>, Diane M. Da Silva<sup>1</sup>, Francesca D'Ermo<sup>1</sup>, Koen A. Marjit<sup>1</sup>, Zhuran Zhang<sup>1</sup>, Deukwo Kwon<sup>1</sup>, Marcin Kortylewski<sup>1</sup>, W. Martin Kast<sup>1</sup>, Vikas Dudeja<sup>2,3</sup>, Thorald van Hall<sup>2,3</sup> & Eli Gilboa<sup>1,4</sup>

Neoantigen burden is a major determinant of tumor immunogenicity, underscored by recent clinical experience with checkpoint blockade therapy. Yet the majority of patients do not express, or express too few, neoantigens, and hence are less responsive to immune therapy. Here we describe an approach whereby a common set of new antigens are induced in tumor cells in situ by transient downregulation of the transporter associated with antigen processing (TAP). Administration of TAP siRNA conjugated to a broad-range tumor-targeting nucleolin aptamer inhibited tumor growth in multiple tumor models without measurable toxicity, was comparatively effective to vaccination against prototypic mutation-generated neoantigens, potentiated the antitumor effect of PD-1 antibody or F13 ligand, and induced the presentation of a TAP-independent peptide in human tumor cells. Treatment with the chemically-synthesized nucleolin-aptamer-TAP siRNA conjugate represents a broadly-applicable approach to increase the antigenicity of tumor lesions and thereby enhance the effectiveness of immune potentiating therapies.

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NATURE COMMUNICATIONS | (2019)10:3773 | <https://doi.org/10.1038/s41467-019-11728-2> | www.nature.com/naturecommunications

Cancer Immunology, Immunotherapy (2024) 7:9 | <https://doi.org/10.1007/s00262-023-03597-y>

RESEARCH

### Vaccination against neoantigens induced in cross-priming cDC1 in vivo

Emily S. Clark<sup>1</sup>, Ana Paula Benaduce<sup>1,3</sup>, Wasif N. Khan<sup>1</sup>, Olivier Martinez<sup>1,4</sup>, Eli Gilboa<sup>1,2,5</sup>

Received: 5 October 2023 / Accepted: 13 November 2023 / Published online: 17 January 2024

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**Abstract**  
The conventional type 1 dendritic cells (cDC1) play a pivotal role in protective immunity against pathogens and cancer. However, their low frequency in the blood and tissues limits their use in immune therapy. We have recently described a method to vaccinate against neoantigens that are induced in tumor cells by targeted delivery of a TAP siRNA to dendritic cells.

CANCER IMMUNOLOGY RESEARCH | RESEARCH ARTICLE

### Vaccination against Nonmutated Neoantigens Induced in Recurrent and Future Tumors

Greta Garrido<sup>1</sup>, Brett Schrand<sup>1</sup>, Agata Leva<sup>1</sup>, Allem Rabasa<sup>1</sup>, Anthony Ferrantelli<sup>1</sup>, Diane M. Da Silva<sup>1</sup>, Francesca D'Ermo<sup>1</sup>, Koen A. Marjit<sup>1</sup>, Zhuran Zhang<sup>1</sup>, Deukwo Kwon<sup>1</sup>, Marcin Kortylewski<sup>1</sup>, W. Martin Kast<sup>1</sup>, Vikas Dudeja<sup>2,3</sup>, Thorald van Hall<sup>2,3</sup>, and Eli Gilboa<sup>1,4</sup>

**ABSTRACT**  
Vaccination of patients against neoantigens expressed in recurrent tumors, recurrent tumors, or tumors developing in individuals at risk of cancer is posing major challenges in terms of which antigens to target and in limited to patients expressing neoantigens in their tumors. Here, we describe a vaccination strategy against antigens that were induced in tumor cells by downregulation of the peptide transporter associated with antigen processing (TAP). Vaccination against TAP downregulation-induced antigens overcomes the main limitation of vaccinating against mostly unique tumor-resident neoantigens and could represent a simpler vaccination strategy that will be applicable to most patients with cancer.

**Introduction**  
Neoantigen burden, mostly corresponding to randomly arising nonsynonymous mutations in tumor cells, is a major determinant of tumor immunogenicity, underscored by clinical studies showing that responsiveness to checkpoint blockade therapy correlates with the number of neoantigens expressed in the patients' tumor. Yet, many patients do not express, or express too few, tumor-resident mutation-derived neoantigens (1–3). Neoantigens expressed in a recurring tumor, a main challenge to clinical oncology (4–6), may differ from the neoantigens induced from a tumor many months or years earlier (7–11), and the question of which neoantigens will be expressed in a tumor that will emerge in a patient at risk of developing cancer cannot be predicted (12). Here, we describe a vaccination approach against antigens induced in recurrent, recurring, or future tumors by transient downregulation of the transporter associated with antigen processing (TAP), which overcomes the aforementioned limitations of targeting tumor-resident

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**Supplementary data** for this article is available at Cancer Immunology Research Online (<http://www.nature.com/cancerimmunologyresearch>).

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**Correspondence** Eli Gilboa, University of Miami Miller School of Medicine, 1550 MW 10th Avenue, Miami, FL 33136, USA. (email: egilboa@miamiami.edu)

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AACR Cancer Research | AACRJournal.org | 656

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Preprints are preliminary reports that have not undergone peer review. They should not be considered conclusive, used to inform clinical practice, or referenced by the media as validated information.

### KLF2 inhibition expands tumor-resident T cells and enhances tumor immunity

Eli Gilboa  
egilboa@med.miami.edu

University of Miami

The Journal of Infectious Diseases

MAJOR ARTICLE

IDSIA OXFORD

### Vaccination Against Pathogens Targeting Cell-Derived Cryptic Antigens

Emily S. Clark<sup>1</sup>, Greta Garrido<sup>1</sup>, Agata Leva<sup>1</sup>, Brett Schrand<sup>1</sup>, and Eli Gilboa<sup>1,2,3,4,5</sup>

**ABSTRACT**  
CD8<sup>+</sup> T-cell responses are an important component of a protective immune response in many pathogenic infections, including HIV and Herpesvirus such as cytomegalovirus (CMV) and Epstein-Barr virus (EBV). Identification of pathogen-encoded protective antigens, antigen heterogeneity, and progressive immune dysfunction are major barriers facing the development of effective CD8<sup>+</sup> T-cell-targeted vaccines. Here we tested the hypothesis that pathogen-infected cells can be sensitized to vaccination against host-derived antigens presented by the infected cells with reduced expression of TAP (transporter associated with antigen processing). In this study, we show the following: first, natural or targeted downregulation of TAP in CMV- and EBV- or HIV-infected cells, respectively, leads to the presentation of a cell-derived nonmutated cryptic epitope, initially described in tumor cells with reduced TAP expression; second, peripheral blood mononuclear cell-derived CD8<sup>+</sup> T cells enriched for multiple TAP downregulation-induced epitopes recognize TAP<sup>low</sup> CMV-, EBV-, and HIV-infected cells, leading to the depletion of TAP<sup>low</sup>-infected cells and the expression of activation markers in the T cells. This study describes a prototype of a universal drug formulation to vaccinate against tumors and pathogen-infected cells, dispensing with the need to identify pathogen- or tumor-specific antigenic targets and obtaining the limitations associated with antigenic heterogeneity and immune dysfunction characteristic of pathogens such as HIV.

**Keywords:** antibody targeting; CD8<sup>+</sup> T cells; HIV; peptide transporter TAP; siRNA; TAP downregulation-induced antigens.

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Correspondence: Eli Gilboa, PhD, Miller School of Medicine, University of Miami, 1550 MW 10th Ave, Medical Campus, P.O. Box 39700, Miami, FL 33136 (email: egilboa@miamiami.edu)

The Journal of Infectious Diseases

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• T-cell responses often correlate with good outcomes in non-human primate challenge models [3–6].

• Viral suppression in HIV controllers (spontaneous nonprogressors) is mediated by HIV-specific CD8<sup>+</sup> T cells with little evidence for contributions by humoral responses [7].

• While 2 pivotal clinical trials failed to provide adequate protection from HIV infection, subgroup analysis has revealed that increased levels of CD8<sup>+</sup> T-cell responses were associated with protection from infection or reductions in viral load [8, 9].

• Intra- and interpatient diversity of HIV is, however, a major barrier for developing not only humoral but also T-cell-directed vaccines [10, 17], leading to the emergence of escape variants [10–12]. The current strategies to prevent the emergence of antigenic resistance is to direct CD8<sup>+</sup> T-cell responses to mutationally constrained epitopes that require high fitness cost. Yet, identifying mutation-constrained epitopes that do not simply correlate with conserved sequences remains a challenge [1].

• Developing effective vaccines against viruses belonging to the Herpesviridae family represents an important unmet clinical need [13–17]. CD8<sup>+</sup> T-cell-directed vaccines capable of establishing long-lasting memory would be particularly effective to target latently infected cells undergoing periodic re-activation and initiating new cycles of infection. Despite broad efforts in academia and industry, except for several varicella

Vaccination Against Pathogens Targeting Cell-Derived Cryptic Antigens • HD • 1

# Robust Intellectual Property Portfolio

These patents protect the targets, design, mechanism, and delivery strategy of our platform & assets

- **Exclusive IP licensed from University of Miami**
- **2 company-owned patent application filed by Sebastian BioPharma**

Application No.	Claims Covering	Priority Date/Filing Date	Publication No.	Title / Focus	Inventors	Assignee (Owner)	Status
<b>18/906,621</b>	Intracellular targets	June 9, 2017 October 4, 2024	US20250025489A1	Methods of Vaccination in Premalignant Settings — preventive immunotherapy for early neoplasia	Eli Gilboa, Greta Garrido, Brett Schrand, Agata Levay	Sebastian BioPharma (University of Miami)	Published /Pending
<b>63/956,351</b>	Platform technology	January 8, 2026	Provisional	An Oligonucleotide(ODN)-Based Scaffold Attached to a Single Site on a Cell Targeting Ligand for the Delivery of Multiple Payloads	Greta Garrido, Eli Gilboa, Brett Schrand	Sebastian BioPharma	Filed
<b>64/025,244</b>	Composition of Matter for Assets	April 1, 2026	Provisional	Antibody-Oligonucleotide Conjugates Comprising Multi-siRNA Cassettes Targeting TAP1 and CTNNB1 for Treatment of Immune-Excluded Solid Tumors	Greta Garrido, Eli Gilboa, Brett Schrand	Sebastian BioPharma	Filed

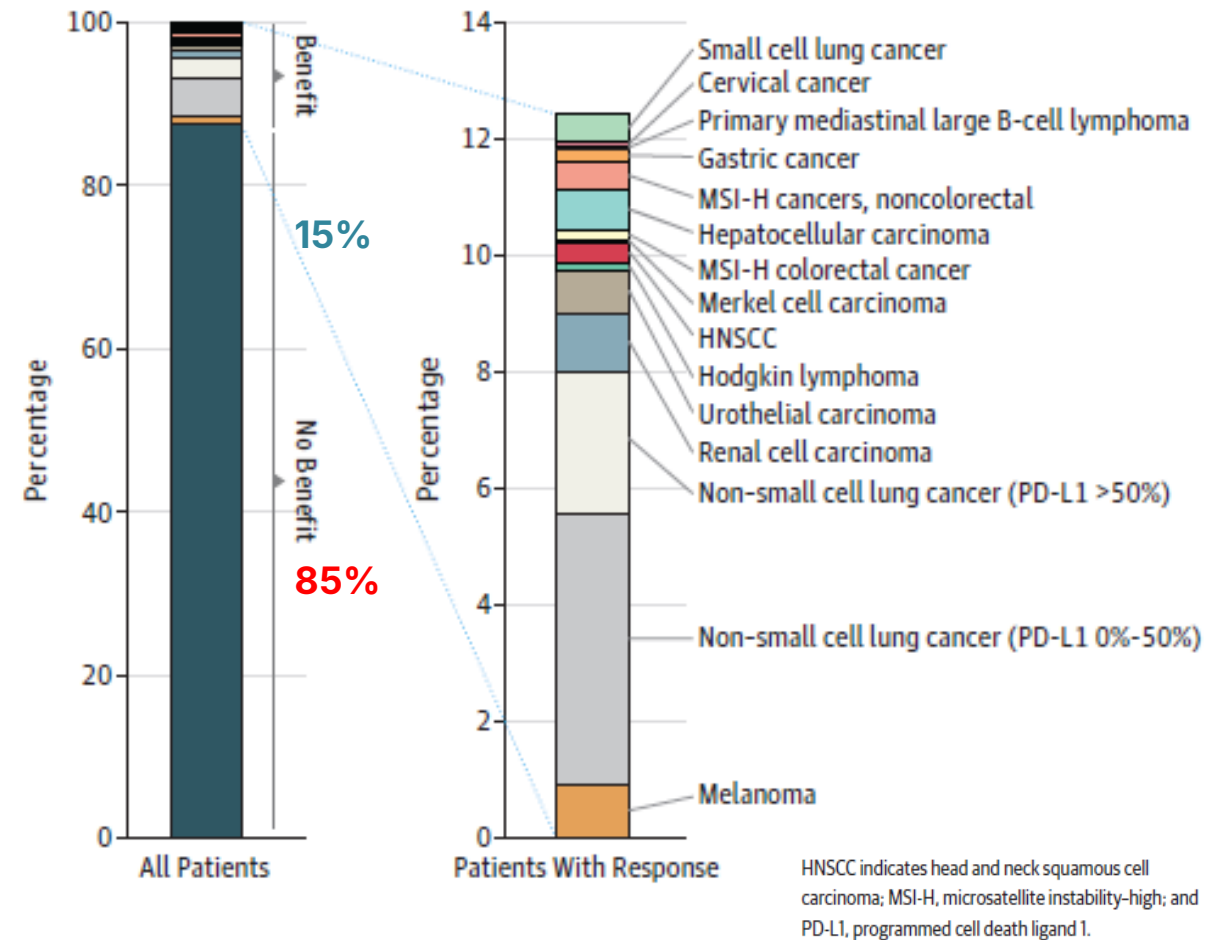
IP strategy expansion opportunities with ongoing company developments.

# Most Solid Tumors Fail Immunotherapy



- **85% of patients do not respond to immunotherapy**
- **Resistance** is driven by **multi-pathway tumor mechanisms**
- Combination therapies have **not meaningfully expanded benefit**
- The field lacks strategies that **simultaneously address intracellular resistance drivers**
- Our **dual-payload AOC platform** is built for **co-modulation of intracellular targets**

Percentage of US Patients who respond, by cancer type



Estimation of the Percentage of US Patients With Cancer Who Are Eligible for and Respond to Checkpoint Inhibitor Immunotherapy Drugs - PubMed

# Why Colorectal Cancer First



## High Unmet Need

**#2** cause of cancer death globally

**Fastest-growing** incidence in patients under 50

~**82.5%** do not benefit immunotherapy

SoC: chemotherapy ± targeted agents

**Large, refractory population**

## High Probability of Success

**Short PFS & OS** → rapid clinical readouts

**Well-characterized** resistance biology

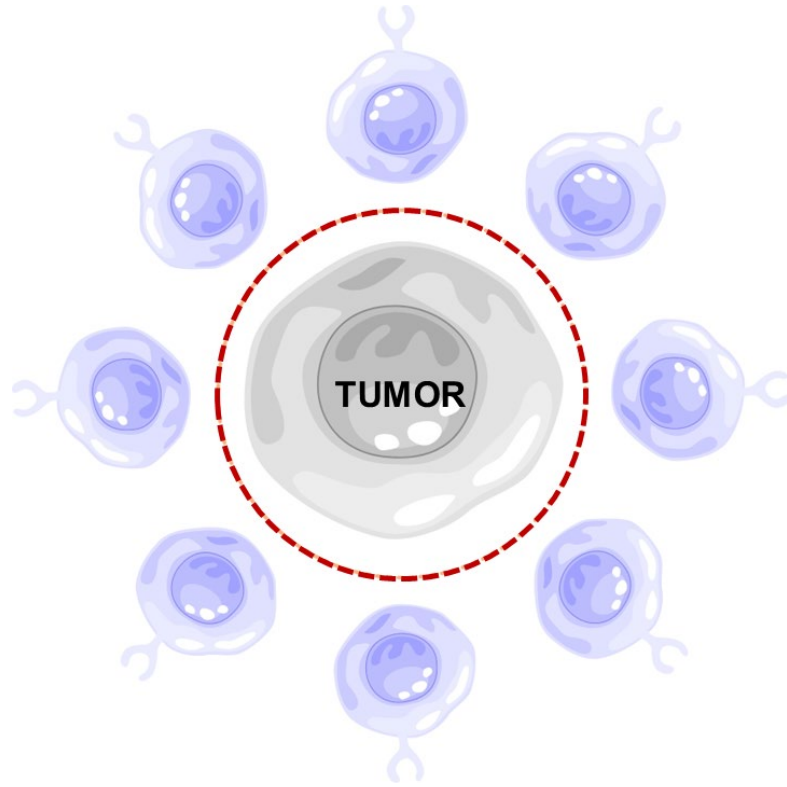
**Established** biomarker frameworks

**Efficient** patient stratification

**Clear translational path**

Strategic indication to demonstrate first-in-class technology & biology

# Why Immunotherapy Fails in Colorectal Cancer



☒ No response to immunotherapy

Immune resistance is driven by two barriers:

## 1. Tumor invisibility<sup>1</sup>

- Reduced antigen presentation
- Poor immune recognition

## 2. Immune exclusion<sup>2</sup>

- Suppressive tumor microenvironment
- Limited T-cell infiltration

✓ **Current therapies address these barriers independently or not at all.**

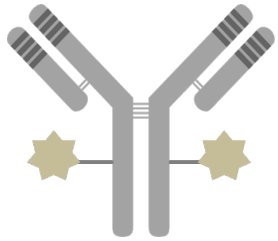
✓ **Resistance is multi-factorial requiring coordinated intervention.**

<sup>1</sup> PD-1 Blockade in Tumors with Mismatch-Repair Deficiency - PMC

<sup>2</sup> The Vigorous Immune Microenvironment of Microsatellite Instable Colon Cancer Is Balanced by Multiple Counter-Inhibitory Checkpoints | Cancer Discovery | American Association for Cancer Research

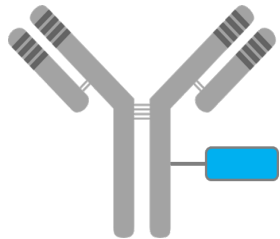
# Dual-Target Gene Modulation in One Drug

Complex genetic disease requires dual modulation | We are the first to solve that



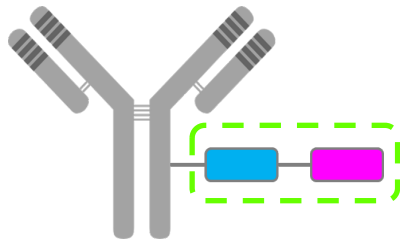
## ADCs (Antibody-Drug Conjugates) **VALIDATED**

- ✓ Targeted delivery
- ✗ *Cytotoxic payload*



## AOCs (Antibody-Oligonucleotide Conjugates) **EMERGING & TRACTION**

- ✓ Precise gene modulation
- ✗ *One -Payload/Single-target intervention*



## Sebastian BioPharma | Dual-Payload AOC Platform

- ✓ Built on validated antibodies & linkers
- ✓ Proprietary dual-payload cassettes
- ✓ Modular & scalable
- ✓ **One drug, multi-pathway control**

# Tissue-Targeted, Programmable Multi-Pathway Control



Sebastian BioPharma	Dual payload AOC	Dual payload ADC	LNP-RNA
Features			
Tissue specificity	✓	✓	✗
Gene modulation	✓	✗	✓
Coordinated multi-target control	✓	LIMITED by payload toxicity	✓
Payload programmability	✓	✗	✓
Systemic toxicity risk	LOW	HIGH	MODERATE

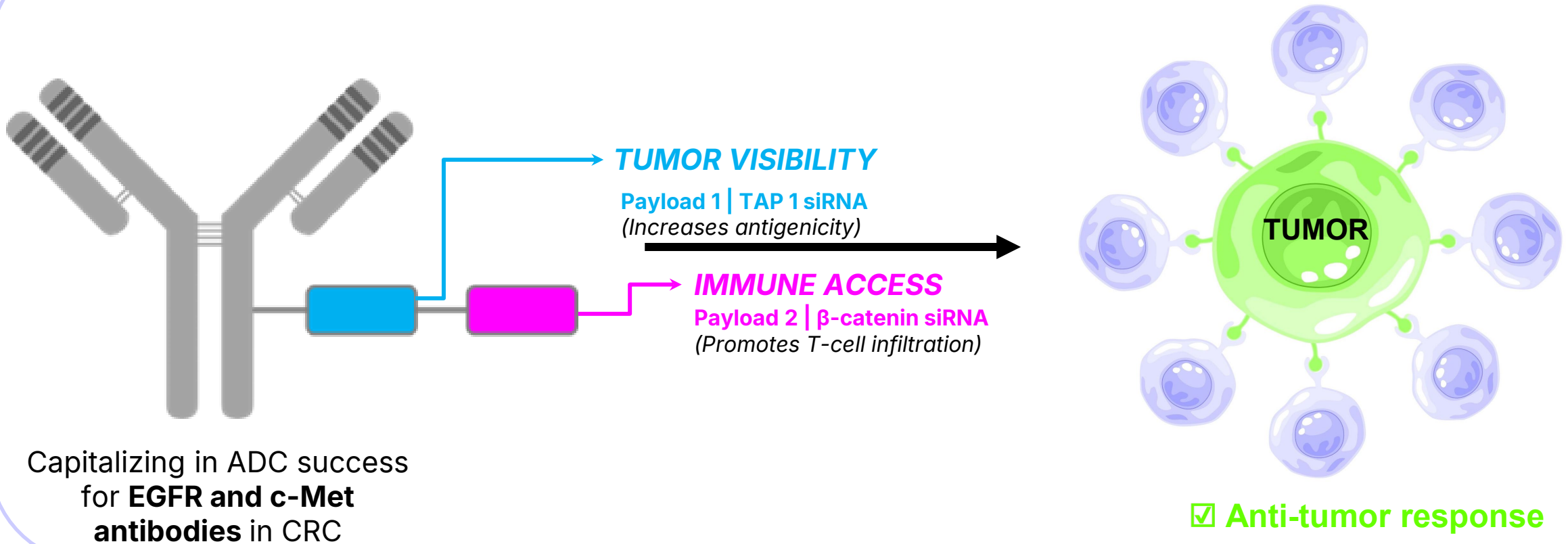
Uniquely combines tissue specificity with programmable multi-pathway control with reduced toxicity.

# SBP-001 | Targeting Tumor Invisibility & Immune Exclusion



## Mechanism of Action & Differentiation

### Dual-siRNA AOC | CRC-Specific Antibody



First clinical application of Sebastian BioPharma's dual-siRNA AOC platform

# SBP-001: Execution Progress & Readiness



Completed by 2026

\$7.9M non-dilutive + \$800 K (Angel/Founder)

## Validated Biology

- ✓ Dual intracellular targets validated
- ✓ Dual-siRNA cassette defined and sequence-locked

## Robust Preclinical Evidence

- ✓ In vitro + in vivo PD (mouse models/surrogate drug)
- ✓ Clear and differentiated mechanism of action

## Translational Readouts

- ✓ Human-relevant in vitro PD (EGFR and c-Met Abs)
- ✓ Dual-target activity demonstrated

## Manufacturing & CMC

- ✓ CDMO partners identified
- ✓ CMC strategy defined

## Execution

- ✓ Timelines and quotes in place
- ✓ Scalable path to DCN and early clinical





## Investor Readiness

- ✓ Data room ready for due diligence
- ✓ Materials prepared for partners and investors

Moving forward to **SBP-001's Drug Candidate Nomination** & Next value inflection point for our team

# Sebastian BioPharma's Pipeline

Large cancer patient populations, high unmet medical need

Assets/ Candidates	Programs/ Indications	Early discovery/ Target selection	Lead candidate optimization	Preclinical	Phase I	Phase II	Phase III	Regulatory approval	Comm.
<b>Asset 1</b> SBP-001	<b>Colorectal (MSS CRC)</b>								
<b>Asset 2</b> SBP-002	<b>Gastric</b>								
<b>Asset 3</b> SBP-003	<b>Breast (Triple-negative)</b>								
<b>Asset 4</b> SBP-004	<b>Endometrial</b>								

These four indications represent over **4M new cancer patients per year globally**

# TAM/SAM/SOM for SBP-001 & MSS CRC

TAM=Total Available Market

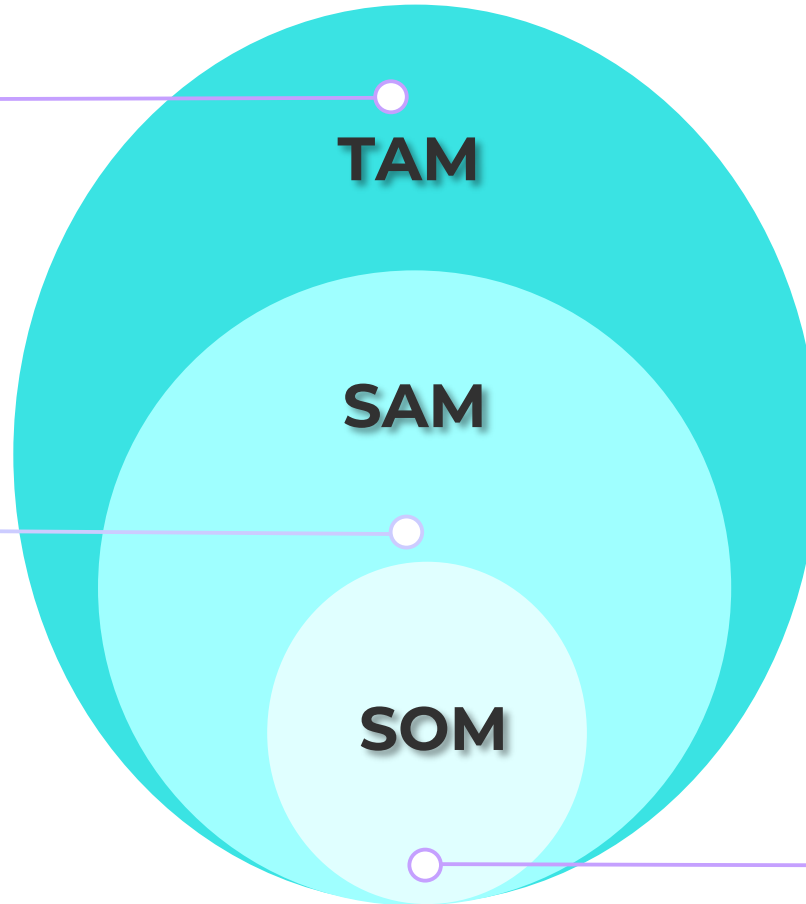
**\$13.4 Billion**

*The Global Colorectal Cancer (CRC) Market* potentially addressed by SBP-001  
**1.1 M new cases/year**

SAM=Serviceable Addressable Market

**\$6.24 Billion**

Focused on *MSS CRC* in the US & EU (82.5% of CRC cases) that are *immunotherapy resistant* (97.5% of MSS CRC cases).  
**338,153 new IO-R MSS CRC cases in US and EU**



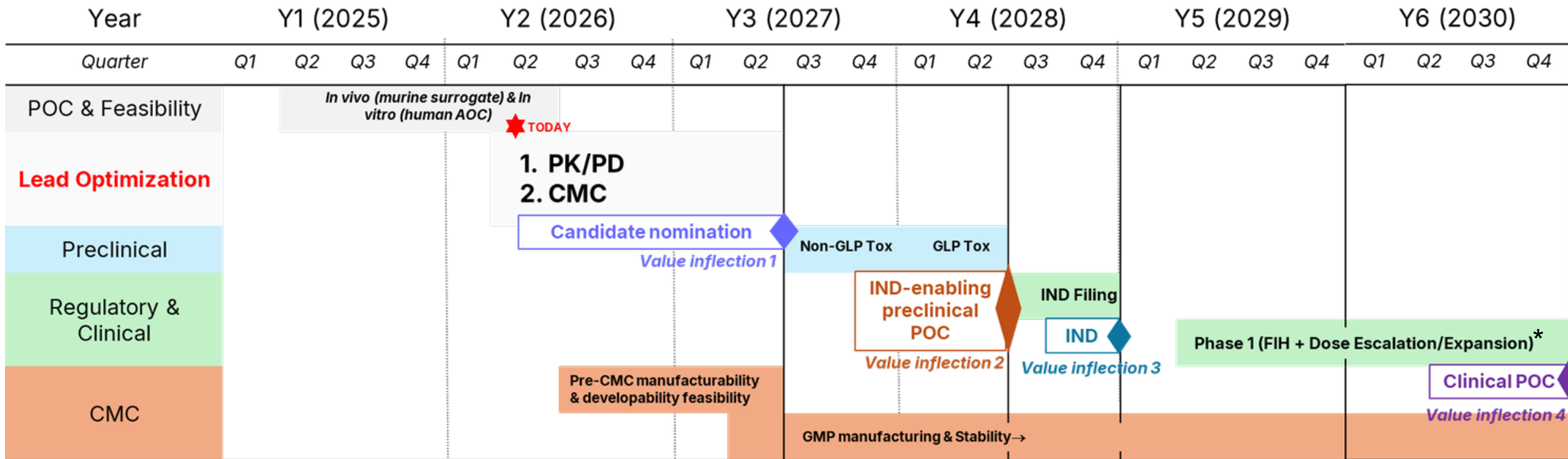
SOM=Serviceable Obtainable Market

**\$936.5 Million**

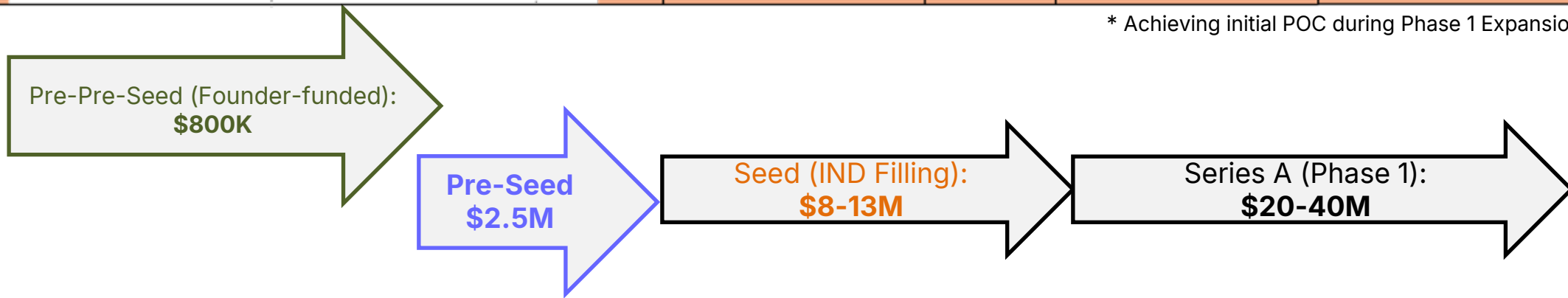
SOM (*15% of immunotherapy resistant MSS CRC patients* in US & EU):  
**52,024 patients in US and EU**

Detailed analysis available upon request.

# SBP-001: Development Plan to Clinical POC



\* Achieving initial POC during Phase 1 Expansion



# Pre-Seed Raise: Terms

---



Sebastian BioPharma is raising a **\$2.5M Pre-Seed Round** to get us to Drug Candidate Nomination and ~12-15 months Runway.

- Initial Investment of **\$800K from Angel/Co-Founder** (of which \$630K are deployed).
- Current runway until Aug/Sep 2026.
- A Seed Round of **\$8-13M** to be launched in ~12-15 months to get us to IND Filing.

## **Angel-Specific/Early-Investor Terms:**

- **SAFE with Valuation Cap of \$12.5M for 20% Equity**
- **Discount: 5%** (would consider 10–15% for large checks  $\geq$ \$100K)
- **Most Favored Nation (MFN): Not offered**, but negotiable
- **Pro-Rata Rights: Only for strategic investors or larger checks  $\geq$ \$100K**
- Equity Scenarios can be shared upon request

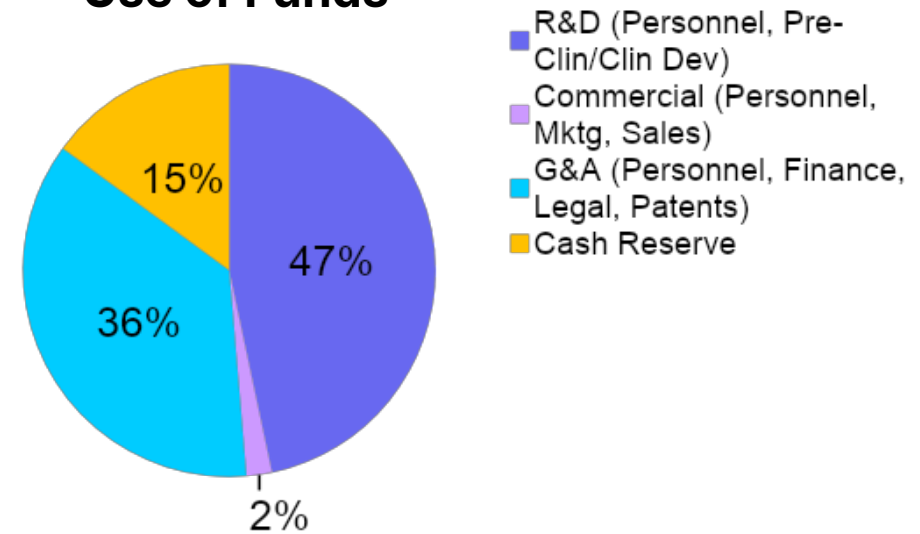
# Pre-Seed Raise: Use of Funds



Sebastian BioPharma is raising a **\$2.5M Pre-Seed Round** to get us to Drug Candidate Nomination and ~ 12-15 months Runway.

CATEGORY	Amount (\$M)	%
R&D (Personnel, Pre-Clin/Clin Dev)	1.175	47
Commercial (Personnel, Mktg, Sales)	0.05	2
G&A (Personnel, Finance, Legal, Patents)	0.90	36
Cash Reserve	0.375	15
<b>TOTAL</b>	<b>\$2.5M</b>	<b>100%</b>

Use of Funds

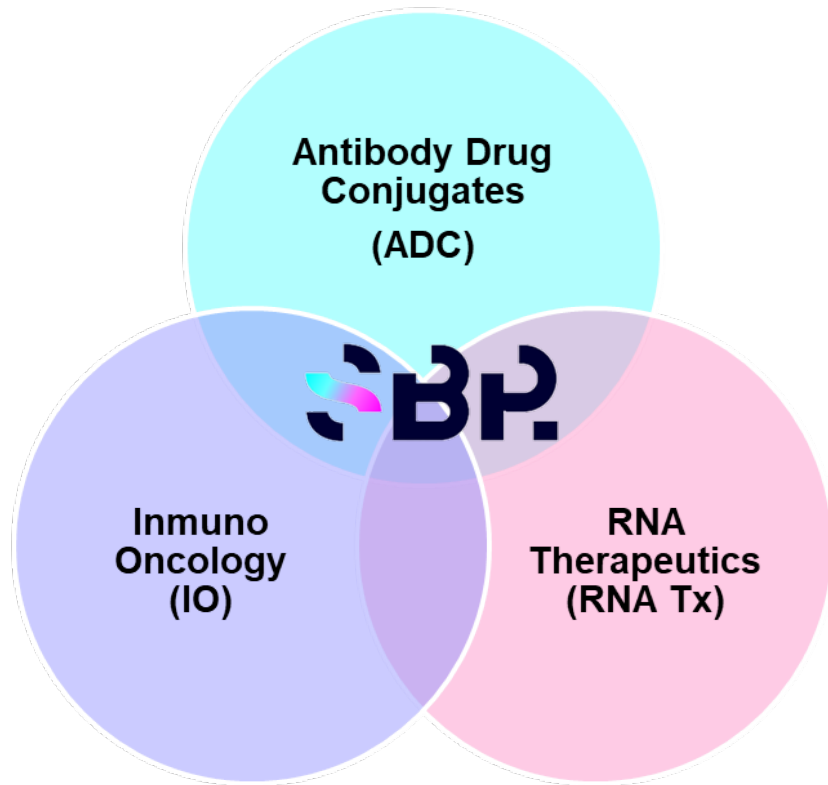


**Most of the capital is directed to R&D to advance SBP-001 to candidate nomination while strengthening IP protection to secure the platform**

# Exit Opportunities



SBP's assets are relevant across multiple buyer groups, not a single-buyer story. We sit at the intersection of these 3 popular modalities:



Anticipated engagement window: post-GLP Tox / IND-ready package (~48 months)

Companies potentially on the "buy-side" of Sebastian Bio:

- **Immuno-oncology players** → need solutions for MSS CRC and IO-resistant tumors



Bristol Myers Squibb™



MERCK  
INVENTING FOR LIFE



- **ADC companies** → need next-generation payloads

Johnson  
& Johnson

abbvie



- **RNA therapeutics companies** → need targeted delivery



NOVARTIS

IONIS

RECENT DEALS:

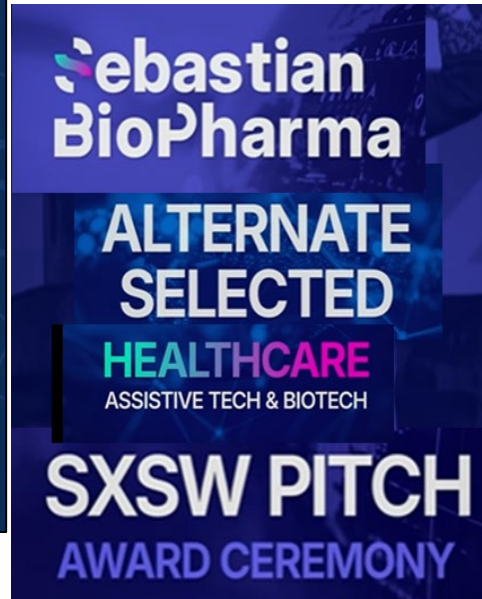
**Novartis → AOC validation:** Advanced Avidity AOC platform into registrational stage (Oct 2025)

**Eli Lilly → Dual-payload validation:** Acquired CrossBridge Bio (preclinical dual-payload ADC) (Apr 2026)

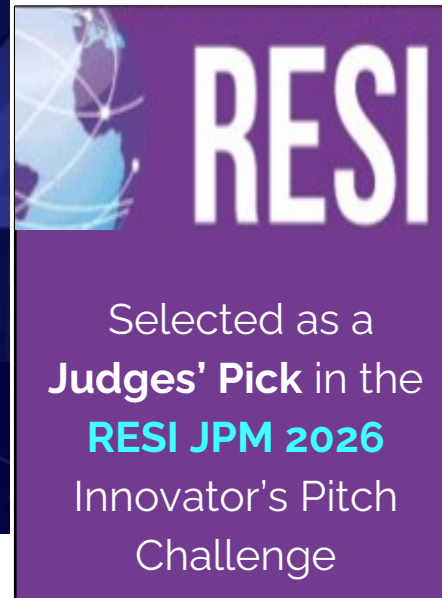
# Sebastian BioPharma in the Spotlight



April 2026



March 2026



January 2026



January 2026



June 2025

**Therapeutic Area:** Oncology | Colorectal Cancer

**Development Stage:** Early Preclinical Data + IP

**Technology Platform:** Dual-Payload Antibody Oligonucleotide Conjugate (AOC)

**Lead Program:** SBP-001 | First-in-class

## **Capital & Milestones:**

Operating with founder capital – \$800K | Runway until Aug/Sept 2026

**Raising a Total of \$2.5M Pre-Seed → Drug Candidate Nomination (~12-15 months Runway)**

Seed Round of \$8-13M to be launched in ~12-15 months → IND Filing

# Making Tumors Visible & Accessible So Immunotherapy Can Work

Thanks, let's talk.



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## Additional Data & Analysis

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Pages 24-25: Selected Preclinical Data | SBP-001

Page 26: Risk and Mitigation Strategy | SBP-001

Pages 27-37: Why Sebastian BioPharma is a Different Kind of Bet

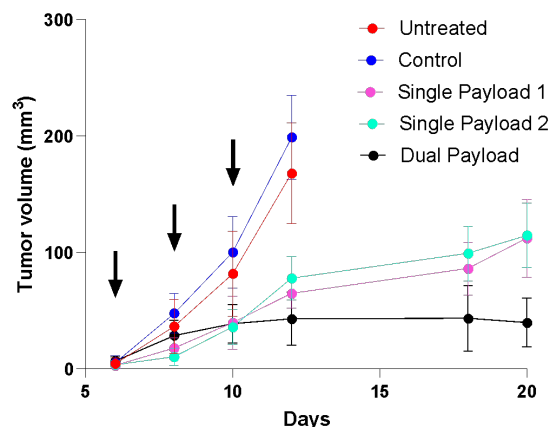
# In Dual-siRNA Conjugate Demonstrates Synergistic In Vivo Efficacy



Dual payload drives synergistic tumor control

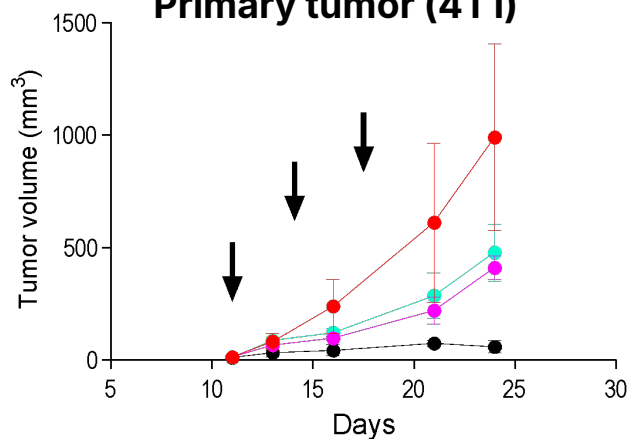
## CRC

### Primary tumor (MC38)



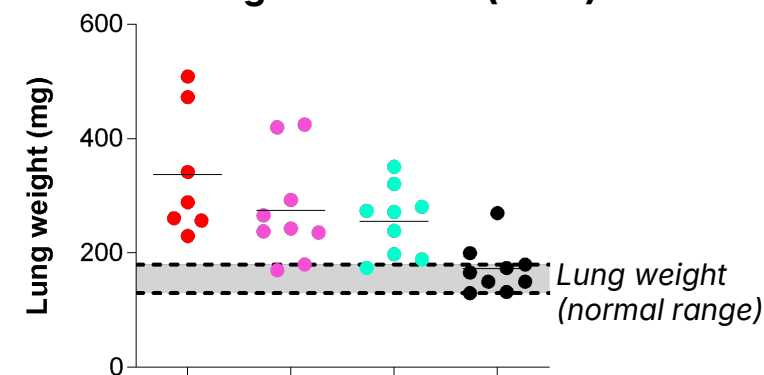
## TNBC

### Primary tumor (4T1)



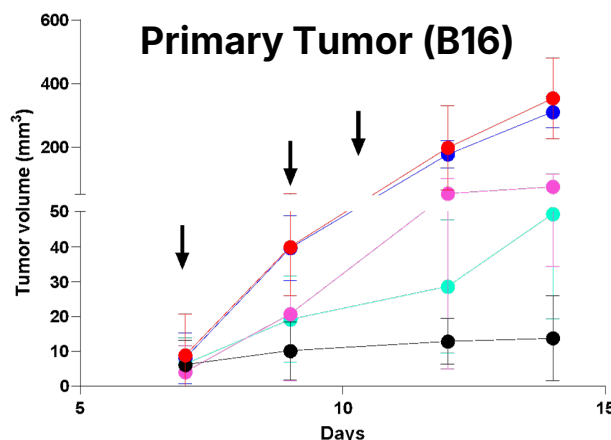
## NSCLC

### Lung metastasis (TC-1)



## Melanoma

### Primary Tumor (B16)



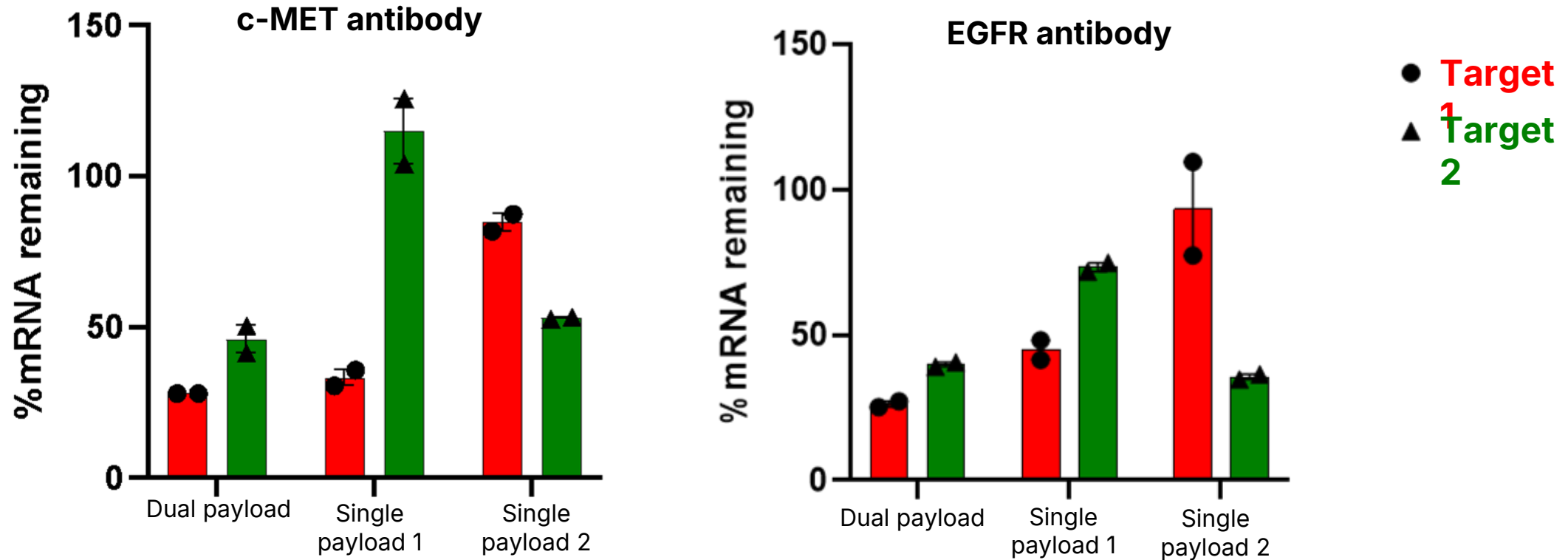
Black arrows indicate systemic dosing timepoints.

- ✓ Active in primary, metastatic & multiple tumor indications
- ✓ No measurable systemic toxicity
- ✓ Single-siRNA → partial tumor control
- ✓ Dual-siRNA → synergistic anti-tumor efficacy

# Concurrent Target Knockdown in Human CRC Cells



Dual payload enables simultaneous silencing of Target 1 and Target 2



✓ Concurrent, target-specific knockdown

✓ Activity preserved across clinically validated antibodies

**Two dual-payload AOC hits demonstrate superior efficacy and support advancement of SBP-001 toward DCN**

# Key Risks & Mitigation Strategy

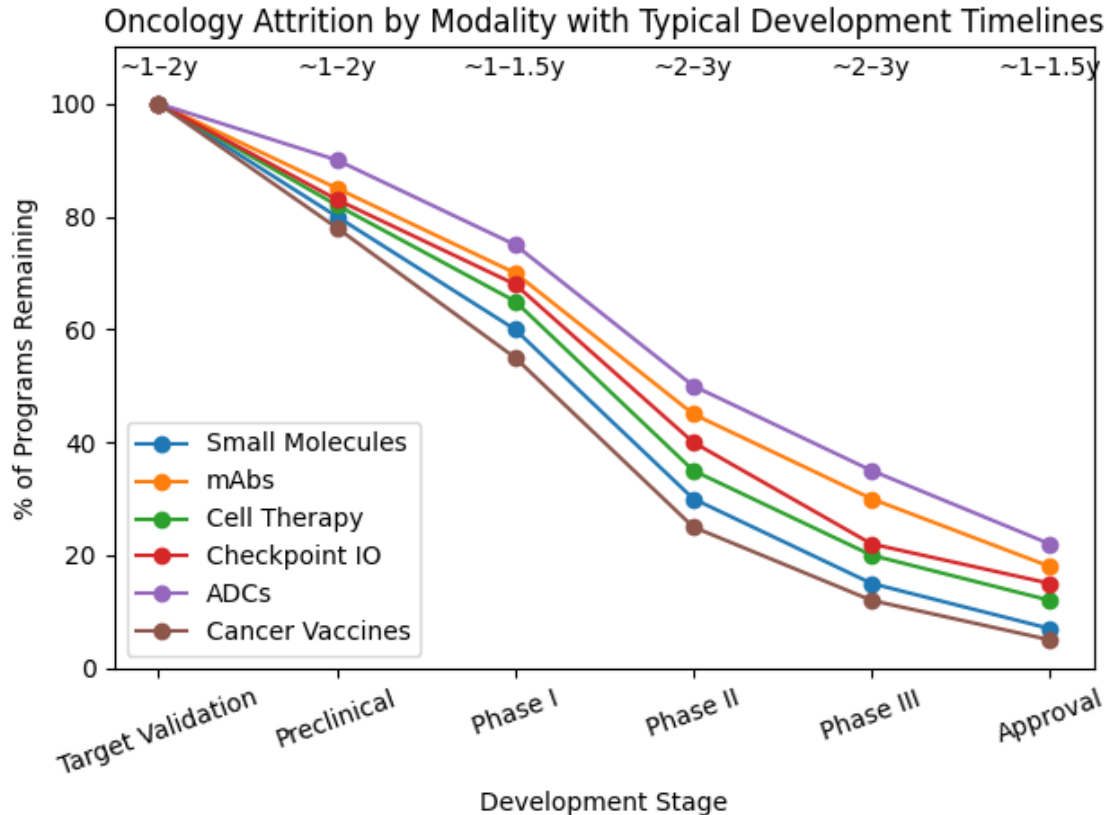
Risk	Status	Mitigation
<b>Dual-target biology (intracellular pathways)</b>	<b>De-risked</b>	In vivo efficacy and PD demonstrated using surrogate (murine) dual-modulation system; clear MoA supports synergistic biology
<b>Dual-payload AOC design</b>	<b>De-risked</b>	Dual-siRNA cassette sequence locked; AOC chemistry established and validated
<b>Targeted delivery (antibody selection)</b>	<b>Partially de-risked</b>	Strong delivery and in vitro PD demonstrated with EGFR and c-MET antibodies; ongoing lead optimization to select clinical candidate
<b>Translation to human</b>	<b>In progress</b>	Human CRC cell PD demonstrated; next step: PK/PD correlation in relevant models with defined experimental plan
<b>CMC &amp; manufacturability</b>	<b>Planned / initiated</b>	Pre-CMC strategy defined; CROs identified; development aligned with industry guidelines to support scalable manufacturing
<b>IND-enabling readiness</b>	<b>Planned / structured</b>	IND-enabling studies (including GLP tox) plan in place; regulatory consultants engaged; development aligned with IND submission requirements

Fully prepared for institutional diligence: data room, IP, and development documentation in place.

**Core biology and delivery are de-risked — remaining work is disciplined execution toward IND and clinical candidate selection**

# Start with the Right Modality: ADC as a De-Risked

## Foundation *Modality is the primary driver of success in oncology and ADCs lead.*



- **ADCs** consistently show the **highest program retention and clinical success rates across development stages**
- Over the past decade, 10 ADCs have been approved for solid tumors (2013-2022), validating the approach
- This success is driven by a key advantage: antibodies as “magic bullets” enabling precise delivery of cytotoxic payloads

*Clinical attrition and timelines synthesized from BIO/Biomedtracker/Amplion, Wong et al. (Biostatistics, 2019), and Hay et al. (Nat Biotechnol, 2014), with modality-specific insights from Nature Reviews Drug Discovery and Evaluate Pharma. Clinical Development Success Rates 2006–2015 / 2011–2020.*

# Next-Generation ADCs Are Advancing Rapidly - AOCs Are the Next Step

*Innovation is accelerating the ADC paradigm.*

## Evolution of ADCs (Rapid Progress)

*From first-generation to next-gen innovation*

- **Improved linkers** → better stability and safety
- **Novel payloads** → beyond traditional cytotoxic
- **Higher DAR / optimized design** → increased efficacy

## Next-Generation ADC Trends

*Pushing beyond traditional limitations*

- **Dual-payload ADCs (early exploration)**
- **Immune-stimulating payloads**
- **Targeted delivery to new tissues**
- **Combination strategies to overcome resistance**

## AOCs: Expanding the ADC Paradigm

*From cytotoxicity → programmable biology*

- Replace cytotoxic payloads with **RNA-based therapeutics**
- Enable **precise gene-level modulation**
- Potential to address **multi-pathway disease biology**

**Sebastian BioPharma is building next-generation ADCs through AOCs, combining validated delivery with programmable RNA biology**

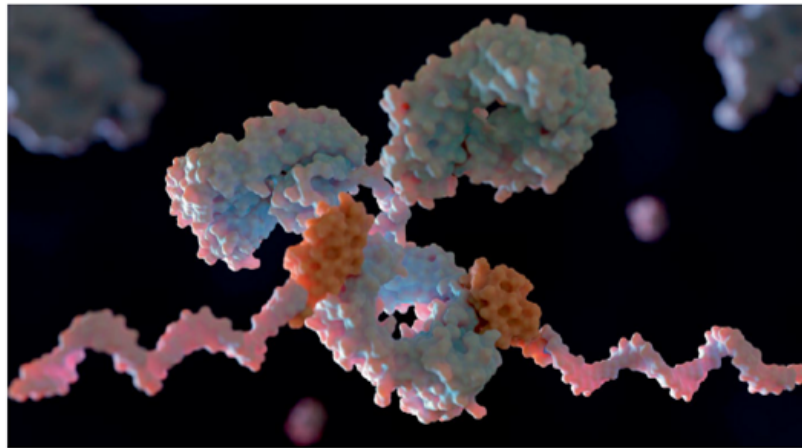
# AOCs Recognized as the Next Drug Modality

## Now with oligos: antibody–oligonucleotide conjugates are the new drug modality to watch

Developers have married gene-modulating oligonucleotides with the targeted precision of antibodies, and the first filings using such conjugates in Duchenne muscular dystrophy are imminent.

By Cormac Sheridan

In October, Novartis agreed to pay \$12 billion for Avidity Biosciences, drawing attention to a new therapeutic modality moving swiftly through clinical trials: the antibody–oligonucleotide conjugate (AOC). The Swiss pharma’s lavish bid – it was the second biggest deal of 2025 – for three late-stage AOCs is a sign of the growing interest in a platform that can deliver oligonucleotides with the precision of antibodies and elicit responses from patients that surpass those



Antibodies linked to siRNAs or ASOs promise to overcome the limitations of traditional oligo delivery.

Nature Biotechnology, January 2026

Table 1 | Selected antibody–oligonucleotide and peptide–oligonucleotide conjugate development programs

Developer	Drug candidate	Description	Indication(s)	Status
Avidity Biosciences	Delpacibart etedesiran (AOC 1001)	TfR1-targeting antibody conjugated to an siRNA directed at dystrophin myotonia protein kinase ( <i>DMPK</i> ) mRNA	Myotonic dystrophy type 1 (DM1)	Phase 3
Avidity Biosciences	Delpacibart-braxlosiran (AOC 1002)	TfR1-targeting antibody conjugated to an siRNA directed at double homeobox 4 ( <i>DUX4</i> ) mRNA	Facioscapulohumeral muscular dystrophy	Phase 3
Avidity Biosciences	Delpacibart zotadirsen (AOC 1044)	TfR1-targeting antibody conjugated to an exon-44-skipping PMO	Duchenne muscular dystrophy (DMD) amenable to exon 44 skipping	Phase 2
PepGen	PGN-EDODM1	PMO directed against the CUG repeat of <i>DMPK</i> mRNA conjugated to a cell-penetrating peptide for enhanced uptake	DM1	Phase 2
Dyne Therapeutics	Zeleciment rostdirsen (DYNE-251)	Exon-51-skipping-siRNA conjugated to an Fab that recognizes TfR1	DMD amenable to exon 51 skipping	Phase 1/2
Dyne Therapeutics	Zeleciment basivarsen (DYNE-101)	<i>DMPK</i> mRNA-directed ASO conjugated to an Fab that recognizes TfR1	DM1	Phase 1/2
Entrada Therapeutics	ENTR-601-44	Exon-44-skipping PMO conjugated to a cyclic peptide that increases endosomal escape	DMD amenable to exon 44 skipping	Phase 1/2
Vertex Pharmaceuticals, Entrada Therapeutics	VX-670	PMO directed against the CUG repeat of <i>DMPK</i> mRNA conjugated to a cyclic peptide that increases endosomal escape	DM1	Phase 1/2
Denali Therapeutics	DNL628	ASO targeting <i>MAPT</i> mRNA conjugated to a TfR1-binding antibody	Alzheimer’s disease	Phase 1b
Aro Biotherapeutics	ABX1100	CD71-binding centryrin conjugated to an siRNA targeting glycogen synthase 1 mRNA	Late-onset Pompe disease	Phase 1

ASO, antisense oligonucleotide; Fab, antigen-binding antibody fragment; PMO, phosphorodiamidate morpholino oligomer; TfR1, transferrin receptor-1. Sources: ClinicalTrials.gov; company websites; PubMed.

### AOCs are gaining recognition as a new class of therapeutics:

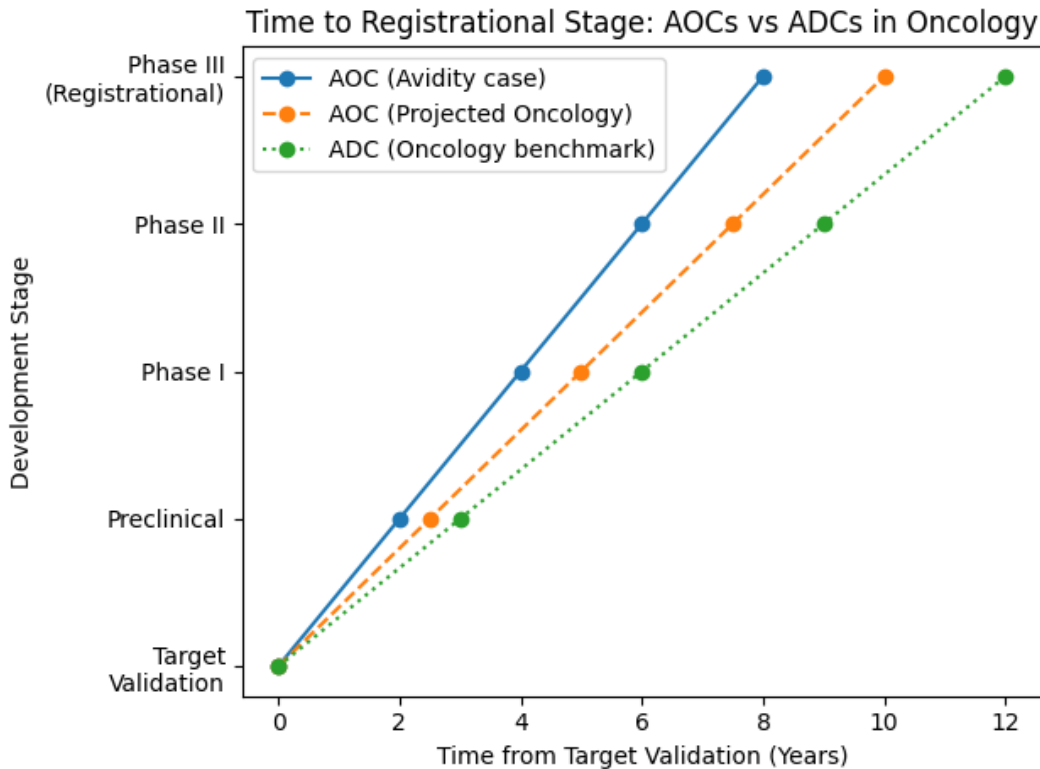
- Nature Biotechnology highlights AOCs as **“the new drug modality to watch”**
- Early clinical programs (Avidity, Dyne) are already advancing into **late-stage development**
- Large pharma (e.g., Novartis) is making **significant strategic investments in the space**

### The industry is beginning to converge on AOCs as the next evolution of targeted therapeutics

# AOCs: Faster Path to Value Than Traditional ADCs



AOCs combine validated delivery with faster clinical translation.



*AOC timelines based on Avidity Biosciences disclosures and Sheridan (Nat Biotechnol, 2026); oncology benchmarks from BIO/Biomedtracker, Hay et al. (Nat Biotechnol, 2014), Wong et al. (Biostatistics, 2019), and CSDD analyses.*

- AOC platforms have demonstrated rapid progression into late-stage development (Avidity, neuromuscular)
- Delivery-driven biology enables faster readouts vs traditional ADCs
- **No AOC yet validated in oncology**—but timelines are expected to translate

Key Advantage:

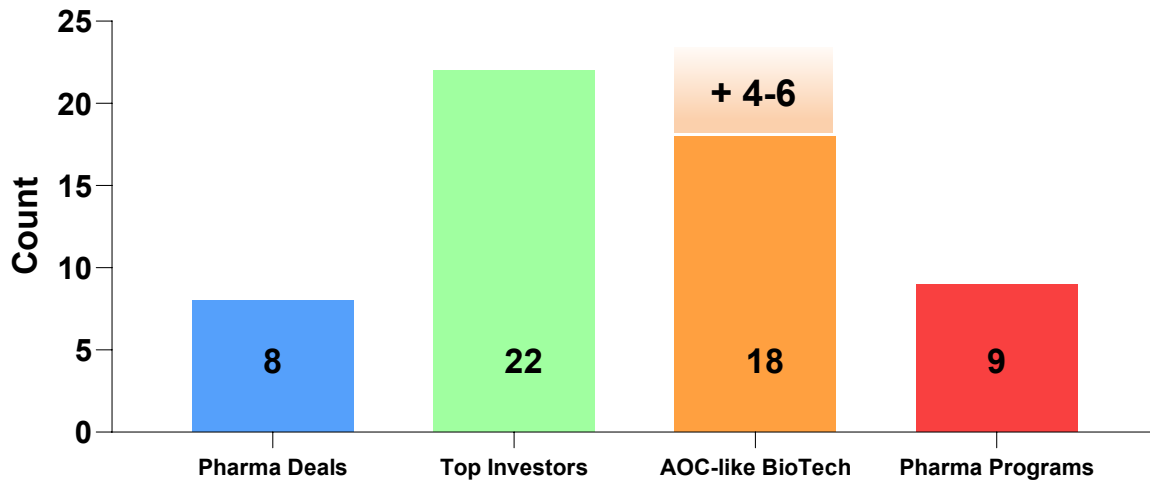
- ✓ Precise delivery + programmable RNA payloads → faster biological impact
- ✓ Faster path to Phase II/III = earlier value inflection, lower capital at risk

In oncology, time = risk. AOCs compress both.

# AOC Momentum Is Building

Capital, companies, and pharma are converging around AOCs.

**AOC Ecosystem Momentum (2020-2025)**



*Company disclosures, ClinicalTrials.gov, Nature Biotechnology (2026), Evaluate Pharma, and public pharma partnership announcements.*

**Pharma Deals / Strategic Engagements**  
Novartis, Roche, Lilly, Vertex, Bayer, AbbVie

**Top Investors**  
RA Capital, OrbiMed, Foresite  
Backing leading AOC players

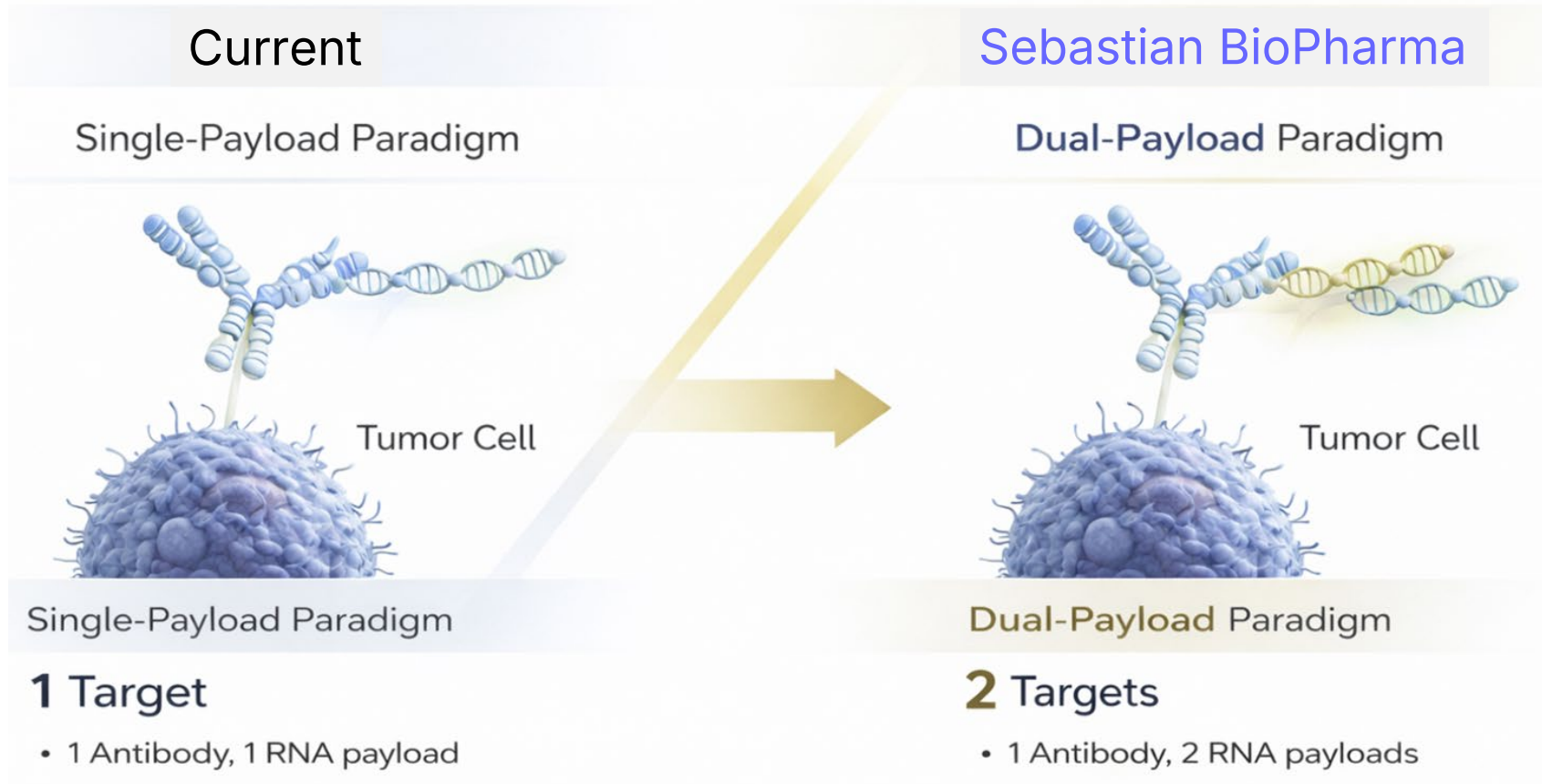
**Active AOC / AOC-like Companies**  
*Rapid expansion of dedicated players*

- Core: Avidity, Dyne, Denali
- Additional: PepGen, Entrada, Aro, Manifold, Judo, City
- Emerging: Alnylam (extrahepatic push)

**Pharma Programs**  
• Novartis, Ionis, Roche, Lilly, AbbVie, Novo Nordisk, Bayer  
*Internal and partnered pipelines emerging*

Pharma and investors are actively working to bring AOCs into oncology by evolving ADCs or building new delivery platforms

# Sebastian Introduces the First Dual-RNA Payload AOC Approach to Address Biological Complexity



**The industry is still solving one target at a time—no company has yet demonstrated tissue-specific delivery of two RNA payloads against distinct pathways**

# Cancer is Not a Single Bulb Problem

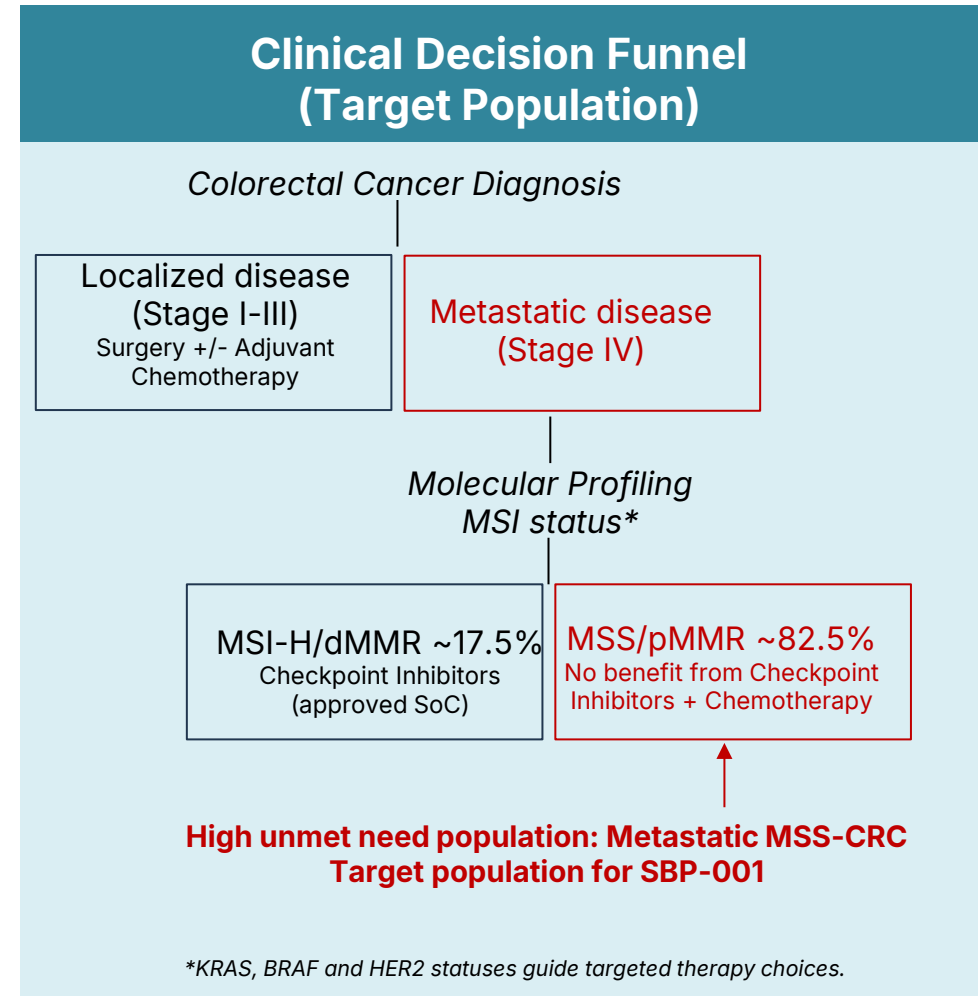


# Understanding CRC Biology Is Key to Understanding the Opportunity

Disease overview, unmet need, and target population.

- ~82.5% of colorectal cancer patients (MSS, pMMR) do not benefit from immunotherapy.
- Only ~17.5% of CRC patients are MSI-H/dMMR and eligible for checkpoint inhibitor monotherapy.
- CRC is the #2 cause of cancer-related death worldwide despite multiple lines of systemic therapy.
- >50% of CRC patients develop metastatic disease, where 5-year survival remains <15%.
- Standard chemotherapy-based regimens provide limited durability, with median PFS typically <1 year in metastatic MSS-CRC.

MSS = microsatellite stable; MSI-H = microsatellite instability-high; pMMR = proficient mismatch repair; dMMR = deficient mismatch repair.

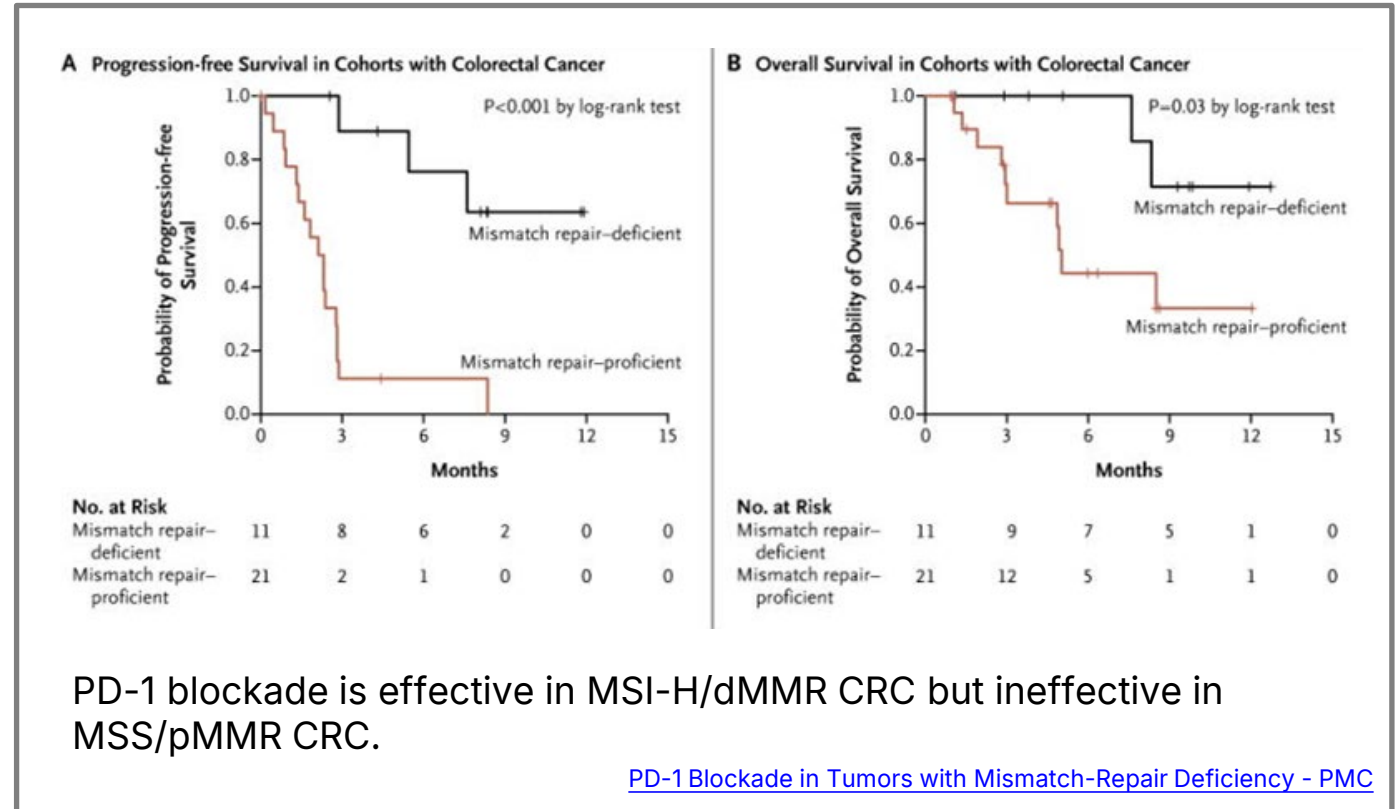


*Tumor-intrinsic immune resistance in MSS-CRC is driven by lack of neoantigens and immune infiltration*

# MSI Status Determines PD-1 Response in CRC

Tumor immune “invisibility” drives PD-1 failure in the majority of CRC patients.

- **PD-1 blockade is effective in MSI-H/dMMR CRC but not in MSS/pMMR CRC**, establishing MSI status as a determinant of response.
- **MSI-H and MSS-CRC differ primarily in tumor antigenicity**, with **MSS tumors exhibiting low neoantigen burden and impaired immune recognition**.
- **~95% of metastatic CRC is MSS**, making immunotherapy resistance the dominant clinical reality.



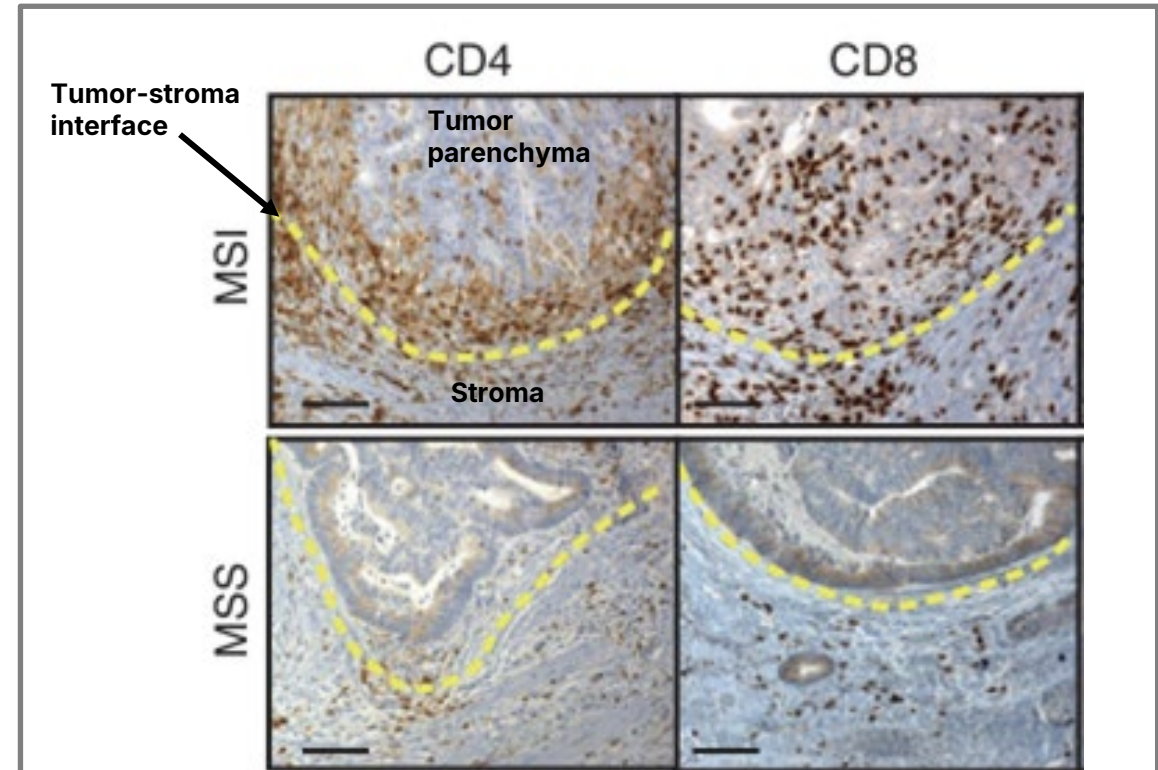
**Differences between MSI-H and MSS tumors are driven not only by antigenicity, but also by immune infiltration, which plays a critical role in response to immune checkpoint blockade.**

# Immune Infiltration Profile is Linked to MSI Status

Poor immune infiltration defines immunotherapy-resistant CRC.

- **MSI-H-CRC** tumors exhibit a **T-cell-inflamed phenotype**, with **dense intratumoral CD4<sup>+</sup> and CD8<sup>+</sup> T-cell infiltration**.
- **MSS-CRC** tumors are frequently **T-cell-excluded**, with **limited T-cell penetration** into the tumor parenchyma.
- Baseline **intratumoral T-cell infiltration** correlates with response to immune checkpoint blockade, whereas its **absence** predicts **primary resistance**.

**Immunotherapy response in CRC depends not only on tumor antigenicity, but also on permissive immune infiltration both of which distinguish MSI-H from MSS tumors**



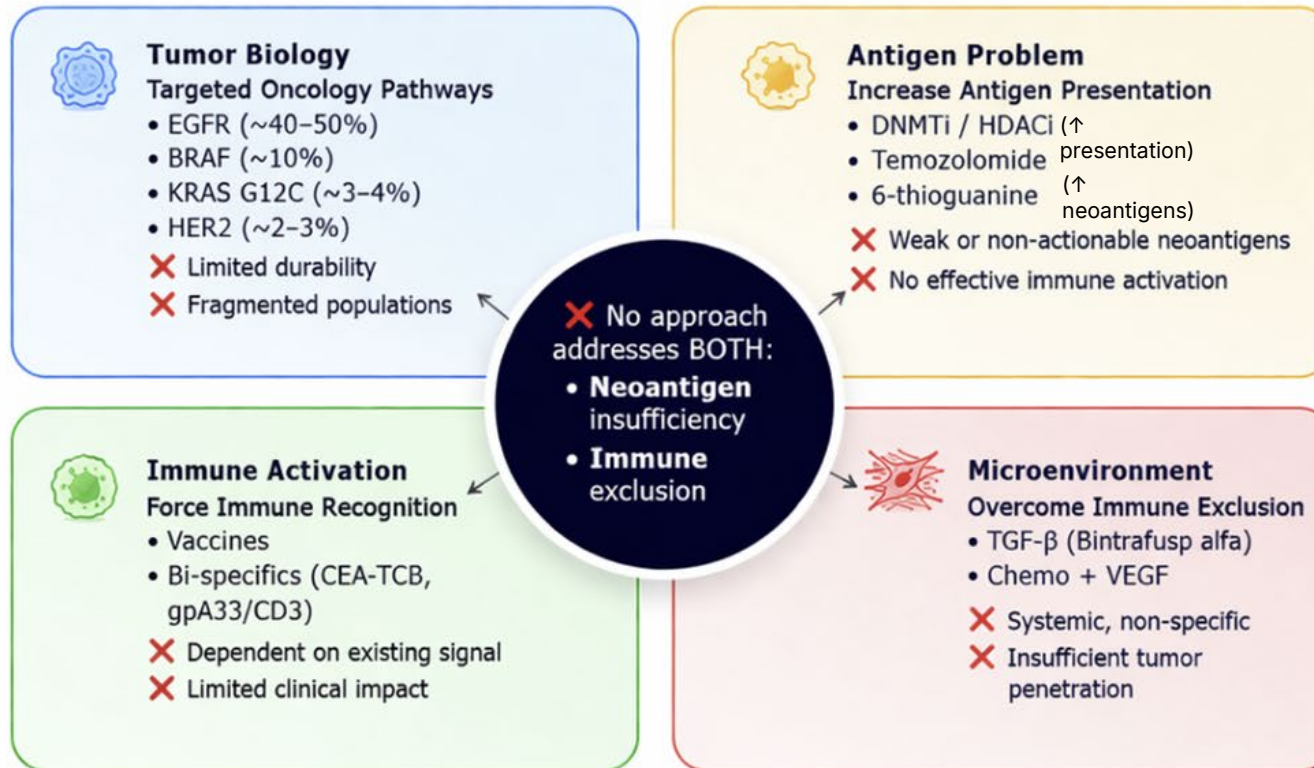
MSI-H CRC tumors show dense intratumoral CD4<sup>+</sup> and CD8<sup>+</sup> T-cell infiltration, whereas MSS tumors exhibit restricted T-cell localization, consistent with immune exclusion.

[The Vigorous Immune Microenvironment of Microsatellite Instable Colon Cancer Is Balanced by Multiple Counter-Inhibitory Checkpoints | Cancer Discovery | American Association for Cancer Research](#)

# Why 85% of CRC Remains Unsolved and Where We Break Through

Even with a high bar for what is game-changer in Oncology

What the field has tried on those patients:



The field has treated these problems separately —  
**Sebastian addresses them simultaneously in a single drug.**

**Sebastian Approach**

**Dual-payload AOC platform**

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Simultaneous control of two pathways:

- ✓ **TUMOR INVISIBILITY**  
(Antigen problem)
- ✓ **IMMUNE EXCLUSION**  
(Microenvironment)