Sebastian BioPharma

A Tissue-Targeted Programmable RNA Interference Platform

Advancing SBP-001 in IO-Resistant Colorectal Cancer

Non-Confidential Deck

April 14th, 2026

Executive Summary

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

UNIVERSITY OF MIAMI *Exclusive IP licensor*

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

BioStrategy Advisors

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

MAYNARDNEXSEN

Seth Hudson, JD

Scientific Advisory Board

Massachusetts General Hospital
Founding Member, Mass General Brigham

HARVARD MEDICAL SCHOOL

Leon Pappas, MD, PhD, MSc
Clinical Advisor

Incubated at

innoventure labs
Go Further. Faster.

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*

Induction of tumour immunity by targeted inhibition of nonsense-mediated mRNA decay

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

Vaccination against neoantigens induced in cross-priming cDC1 in vivo

Vaccination against Nonmutated Neoantigens Induced in Recurrent and Future Tumors

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

Vaccination Against Pathogens Targeting Cell-Derived Cryptic Antigens

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**

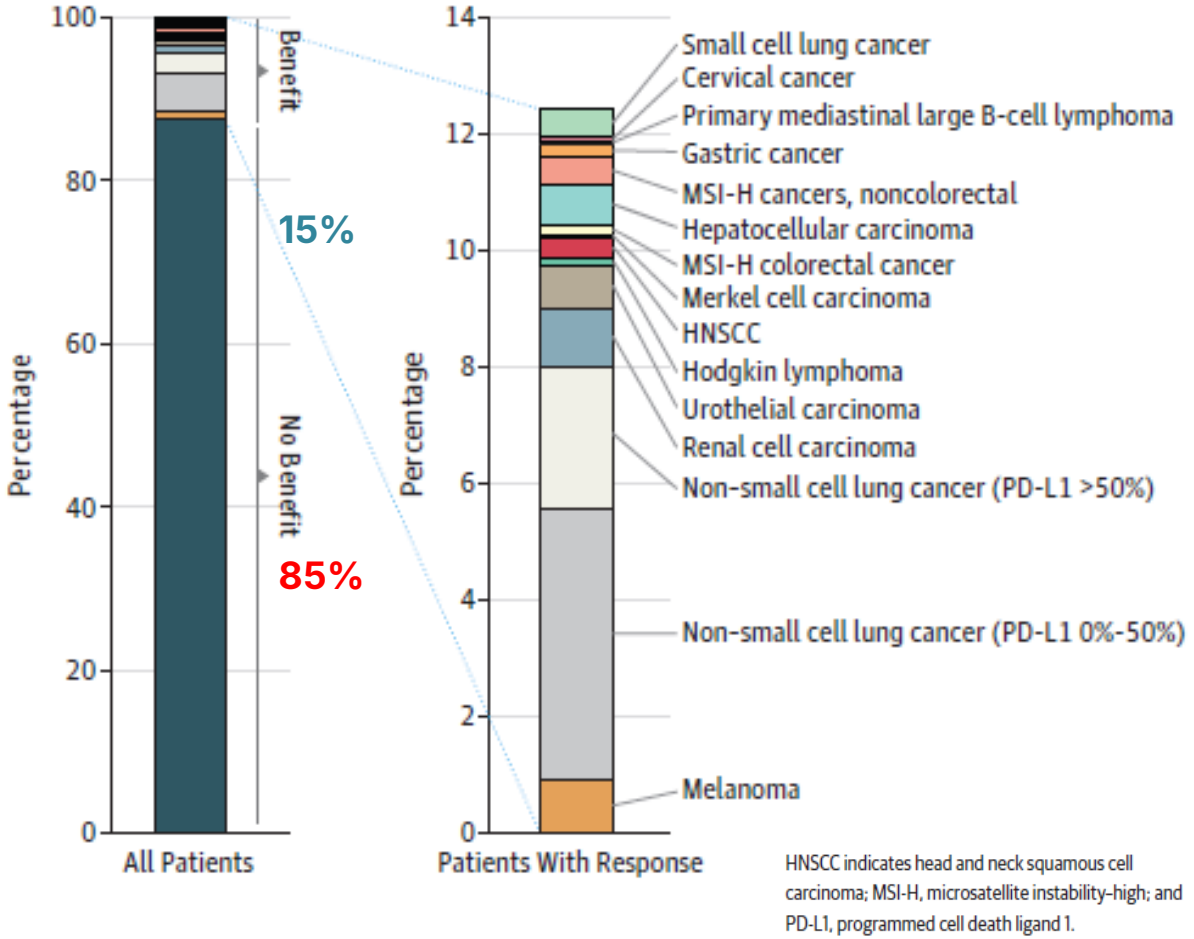
Application No.	Claims Covering	Priority Date/Filing Date	Publication No.	Title / Focus	Inventors	Assignee (Owner)	Status
18/906,621	Intracellular targets	June 9, 2017 October 4, 2024	US20250025489A1	Methods of Vaccination in Premalignant Settings — preventive immunotherapy for early neoplasia	Eli Gilboa, Greta Garrido, Brett Schrand, Agata Levay	Sebastian BioPharma (University of Miami)	Published /Pending
63/956,351	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
64/025,244	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 response 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



HNSCC indicates head and neck squamous cell carcinoma; MSI-H, microsatellite instability-high; and PD-L1, programmed cell death ligand 1.

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 Unmeet 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

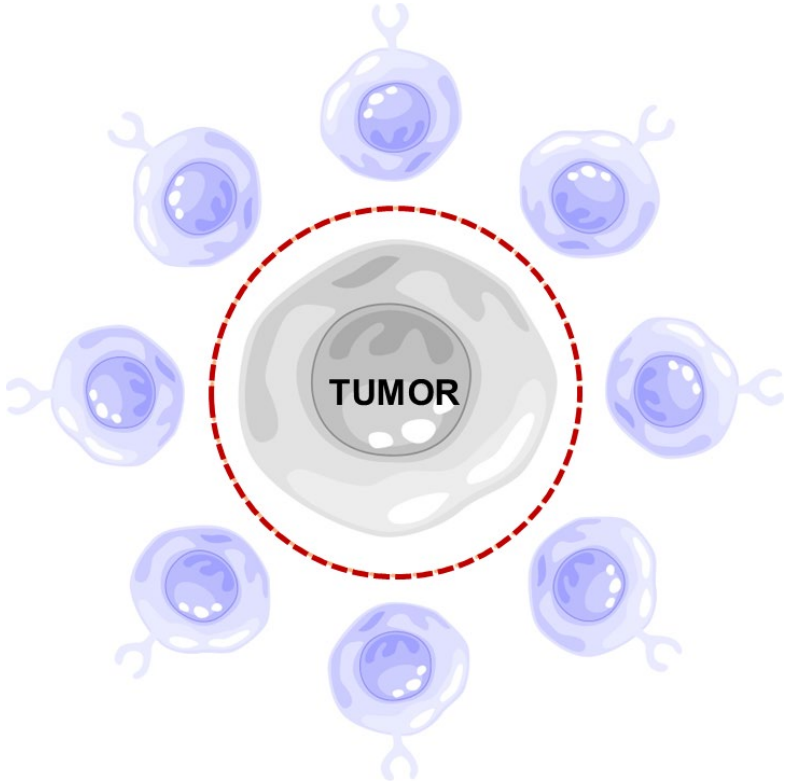
Established biomarker frameworks

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[1]

- Reduced antigen presentation
- Poor immune recognition

2. Immune exclusion[2]

- Suppressive tumor microenvironment
- Limited T-cell infiltration

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

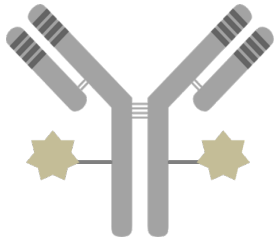
✓ **Resistance is multi-factorial requiring coordinated intervention.**

1 PD-1 Blockade in Tumors with Mismatch-Repair Deficiency - PMC

2 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

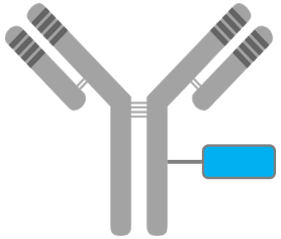
Complex genetic disease requires dual modulation | We are the first to solve that



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

☑ Targeted delivery

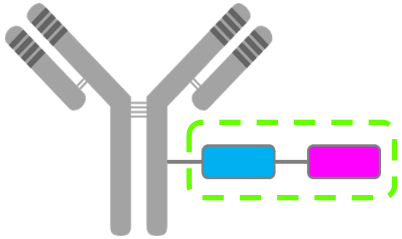
☒ *Cytotoxic payload*



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

☑ Precise gene modulation

☒ *One –Payload/Single-target intervention*



Sebastian BioPharma | Dual-Payload AOC Platform

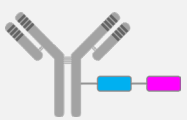
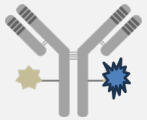
☑ Built on validated antibodies & linkers

☑ Proprietary dual-payload cassettes

☑ Modular & scalable

☑ **One drug, multi-pathway control**

Tissue-Targeted, Programmable Multi-Pathway Control

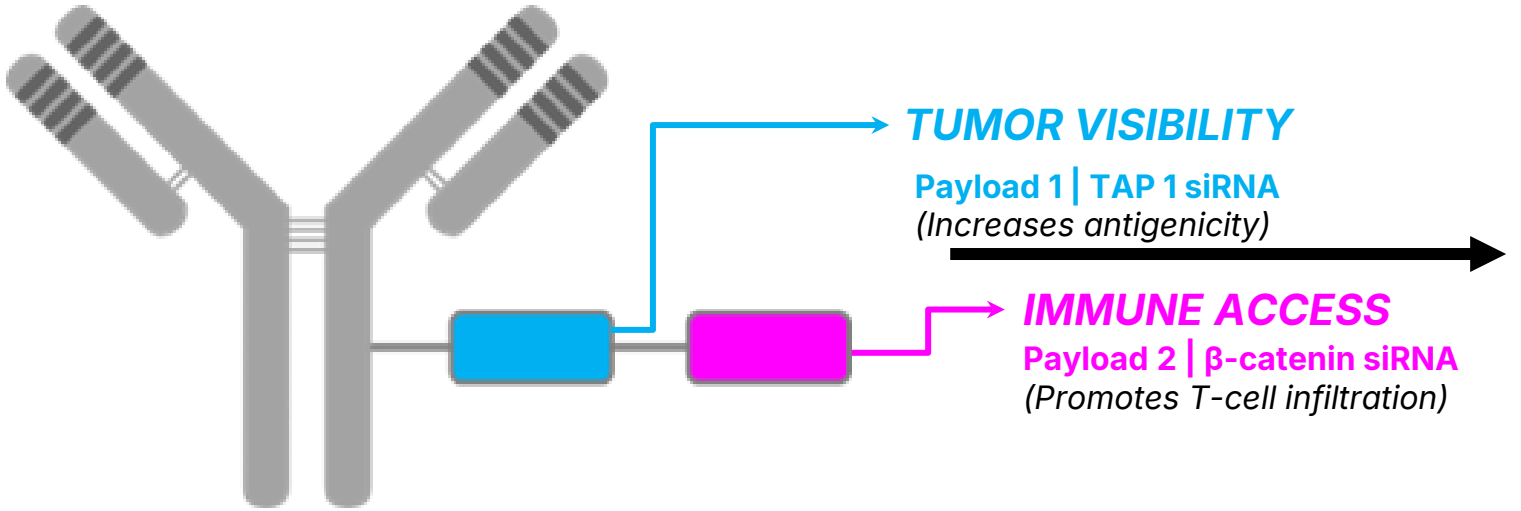
Features	Sebastian BioPharma Dual payload AOC	Dual payload ADC	LNP-RNA
			
Tissue specificity	✓	✓	✗
Gene modulation	✓	✗	✓
Coordinated multi-target control	✓	LIMITED by payload toxicity	✓
Payload programmability	✓	✗	✓
Systemic toxicity risk	LOW	HIGH	MODERATE

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

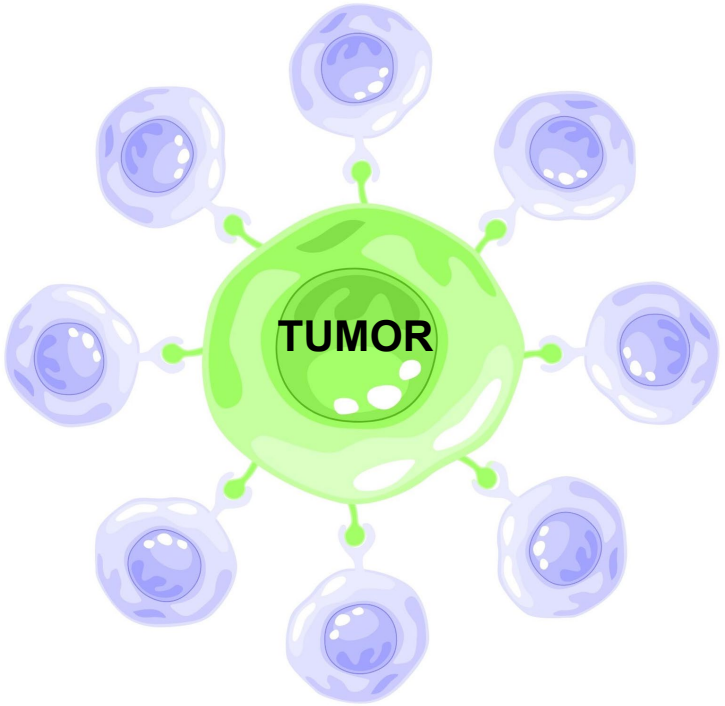


TUMOR VISIBILITY

Payload 1 | TAP 1 siRNA
(Increases antigenicity)

IMMUNE ACCESS

Payload 2 | β-catenin siRNA
(Promotes T-cell infiltration)



Capitalizing in ADC success for **EGFR and c-Met antibodies** in CRC

☑ **Anti-tumor response**

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.
Asset 1 SBP-001	**Colorectal (MSS CRC)**								
Asset 2 SBP-002	**Gastric**								
Asset 3 SBP-003	**Breast (Triple-negative)**								
Asset 4 SBP-004	**Endometrial**								



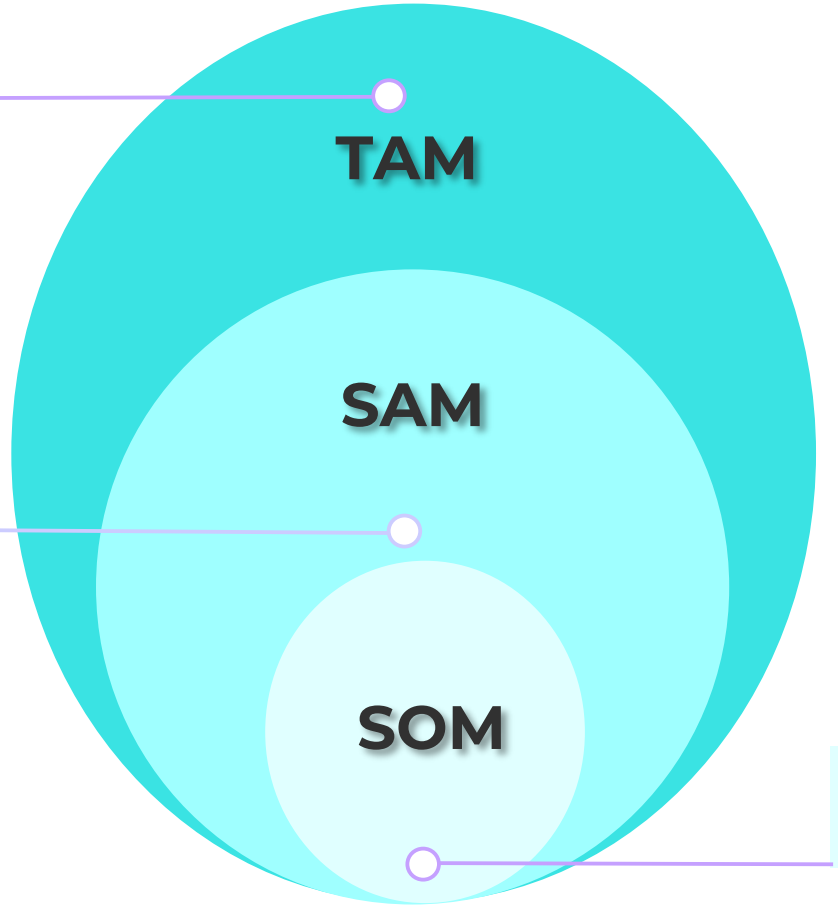

These four indications represent over **4M new cancer patients per year globally**

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

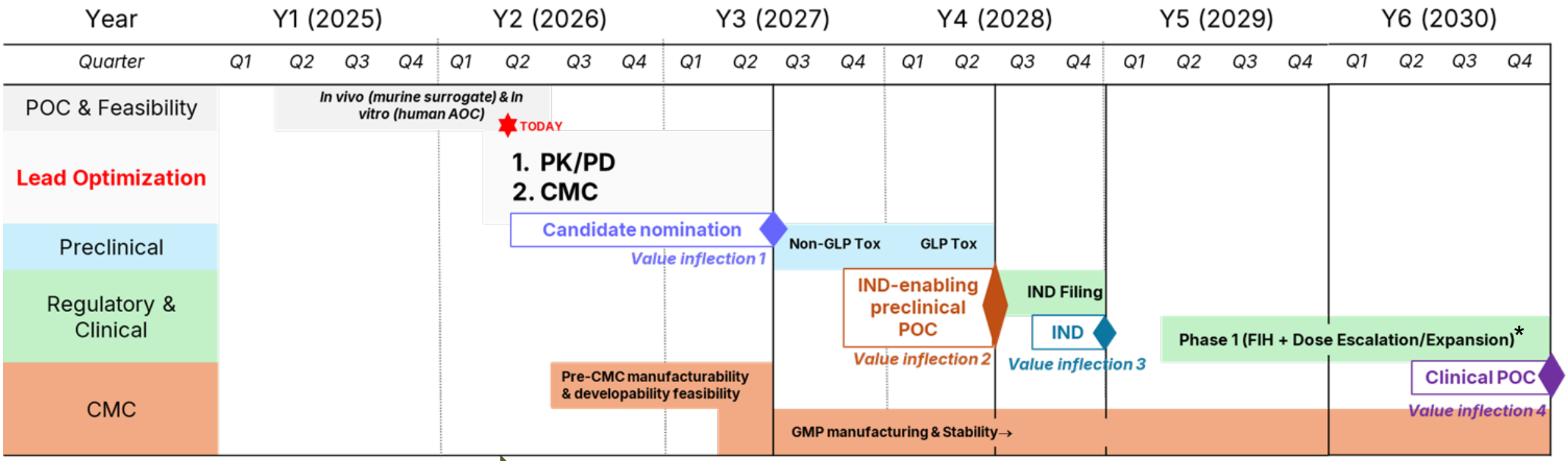
SOM=Serviceable Obtainable Market

$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-Pre-Seed (Founder-funded): **$800K**

Pre-Seed $2.5M

Seed (IND Filling): **$8-13M**

Series A (Phase 1): **$20-40M**

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.

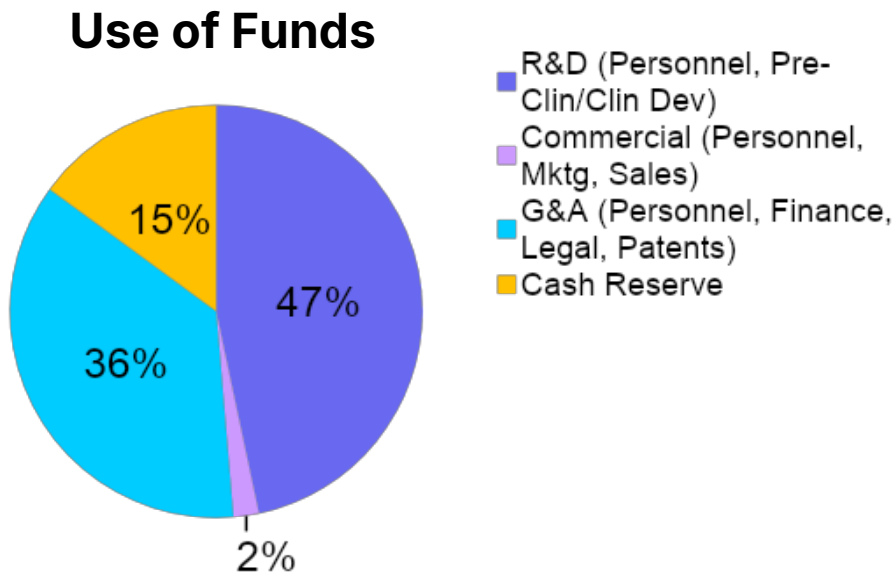
Angel-Specific/Early-Investor Terms:

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

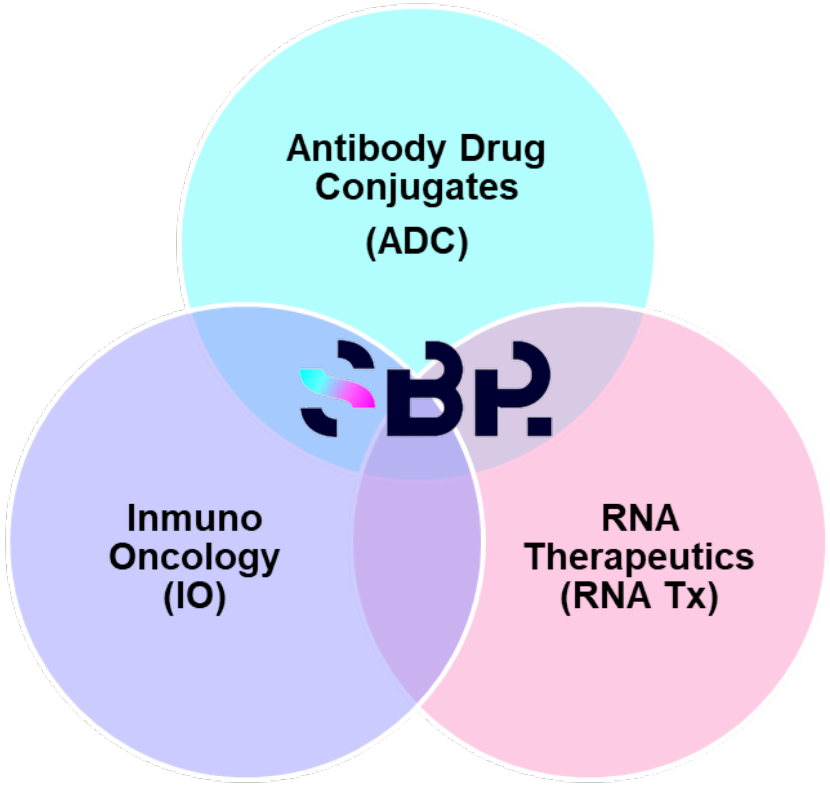
CATEGORY	Amount ($M)	%
R&D (Personnel, Pre-Clin/Clin Dev)	1.175	47
Commercial (Personnel, Mktg, Sales)	0.05	2
G&A (Personnel, Finance, Legal, Patents)	0.90	36
Cash Reserve	0.375	15
TOTAL	**$2.5M**	**100%**



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 Roche

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

  Johnson & Johnson abbvie Pfizer

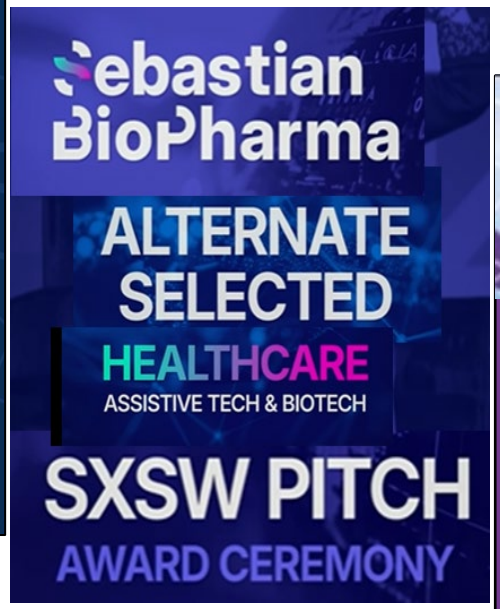
- **RNA therapeutics companies** → need targeted delivery

  Alnylam PHARMACEUTICALS NOVARTIS IONIS

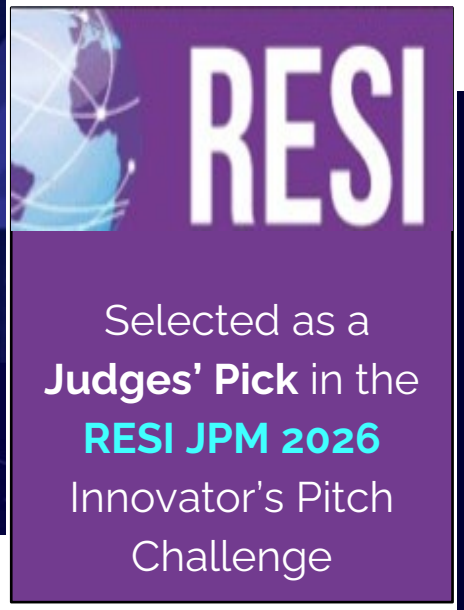
RECENT DEALS:
Novartis → AOC validation: Advanced Avidity AOC platform into registrational stage (Oct 2025)
Eli Lilly → Dual-payload validation: Acquired CrossBridge Bio (preclinical dual-payload ADC) (Apr 2026)

Sebastian BioPharma in the Spotlight

April 2026



March 2026



January 2026

January 2026

June 2025

Sebastian BioPharma | Snapshot

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 & Accesible
So Immunotherapy Can Work

Thanks, let’s talk.

www.sebastianbio.com
contact@sebastianbio.com

Additional Data & Analysis

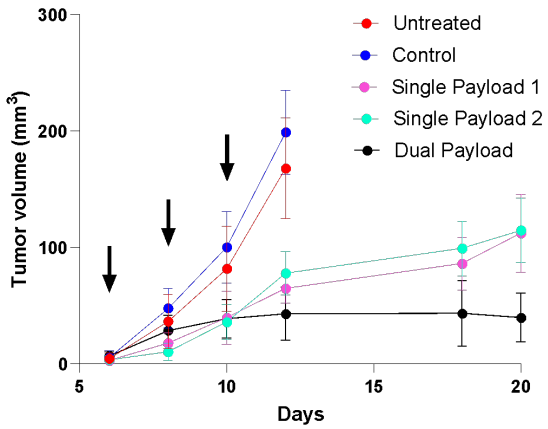
Pages 24-25: Selected Preclinical Data | SBP-001
Page 26: Risk and Mitigation Strategy | SBP-001
Pages 27-37: Why Sebastian BioPharma is a Different Kind of Bet

In Dual-siRNA Conjugate Demonstrates Synergistic In Vivo Efficacy

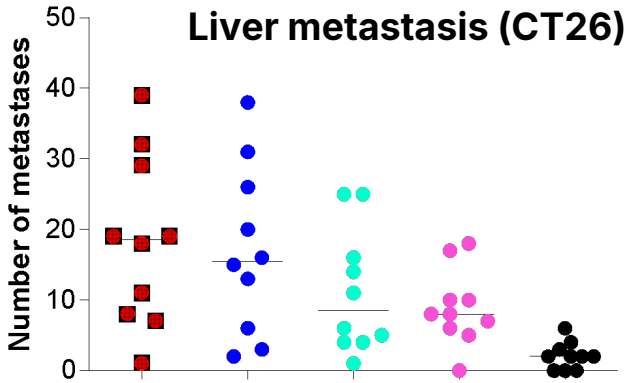
Dual payload drives synergistic tumor control

CRC

Primary tumor (MC38)

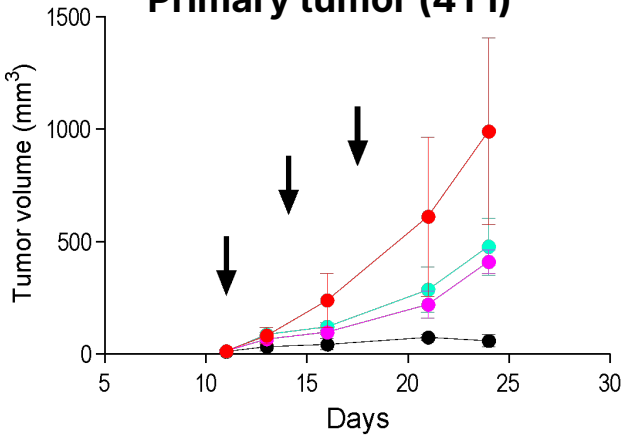


Liver metastasis (CT26)



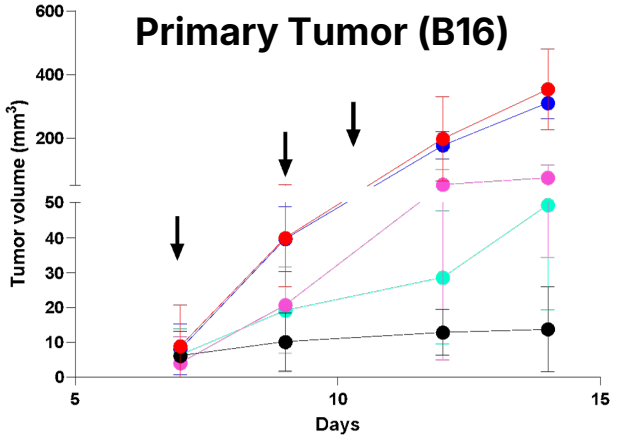
TNBC

Primary tumor (4T1)



Melanoma

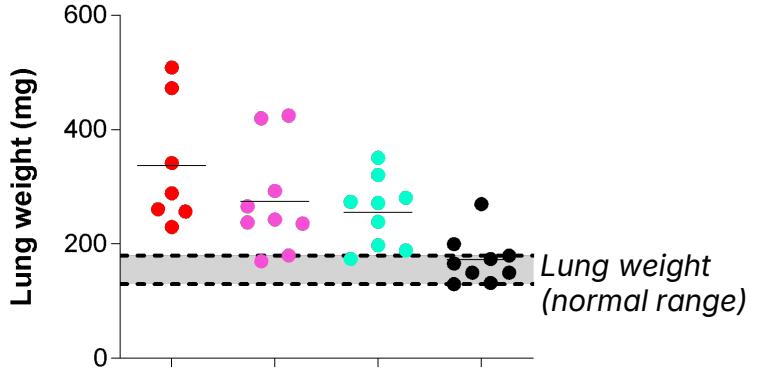
Primary Tumor (B16)



Black arrows indicate systemic dosing timepoints.

NSCLC

Lung metastasis (TC-1)

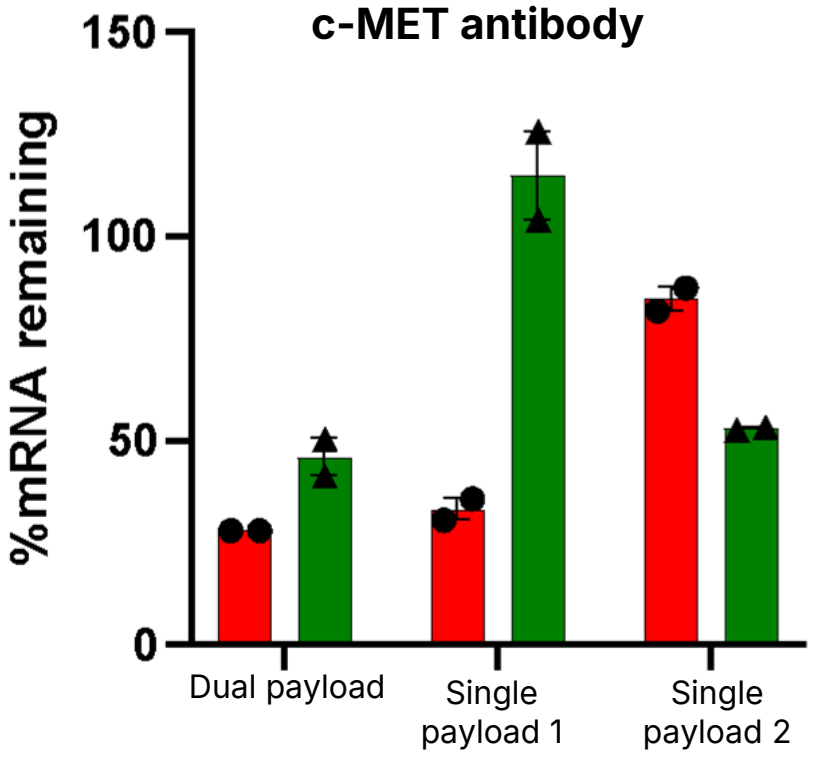


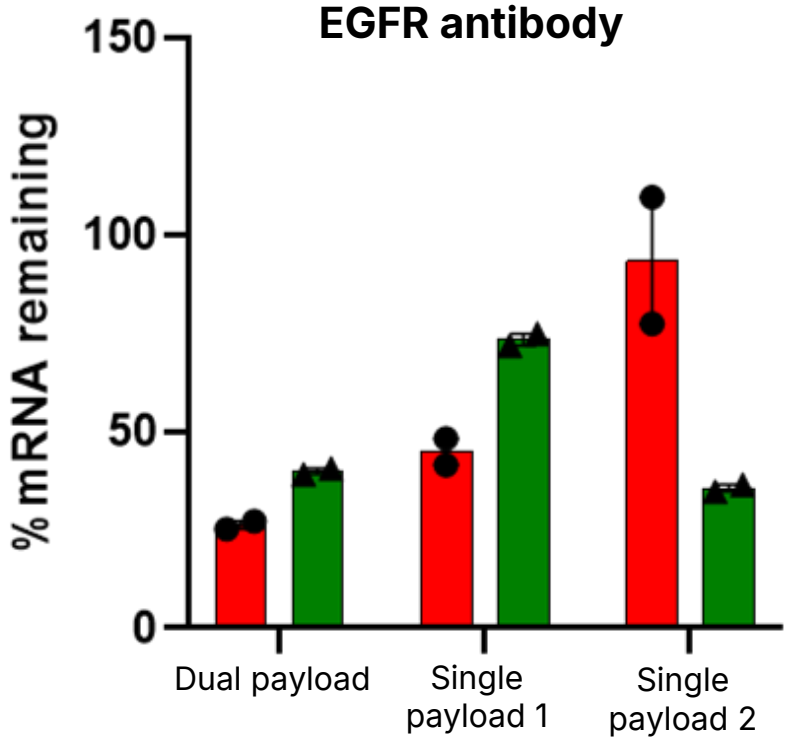
- ✓ Active in primary, metastatic & multiple tumor indications
- ✓ No measurable systemic toxicity
- ✓ Single-siRNA → partial tumor control
- ✓ Dual-siRNA → synergistic anti-tumor efficacy

Unpublished data.

Concurrent Target Knockdown in Human CRC Cells

Dual payload enables simultaneous silencing of Target 1 and Target 2





Target 1

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**

Unpublished data.

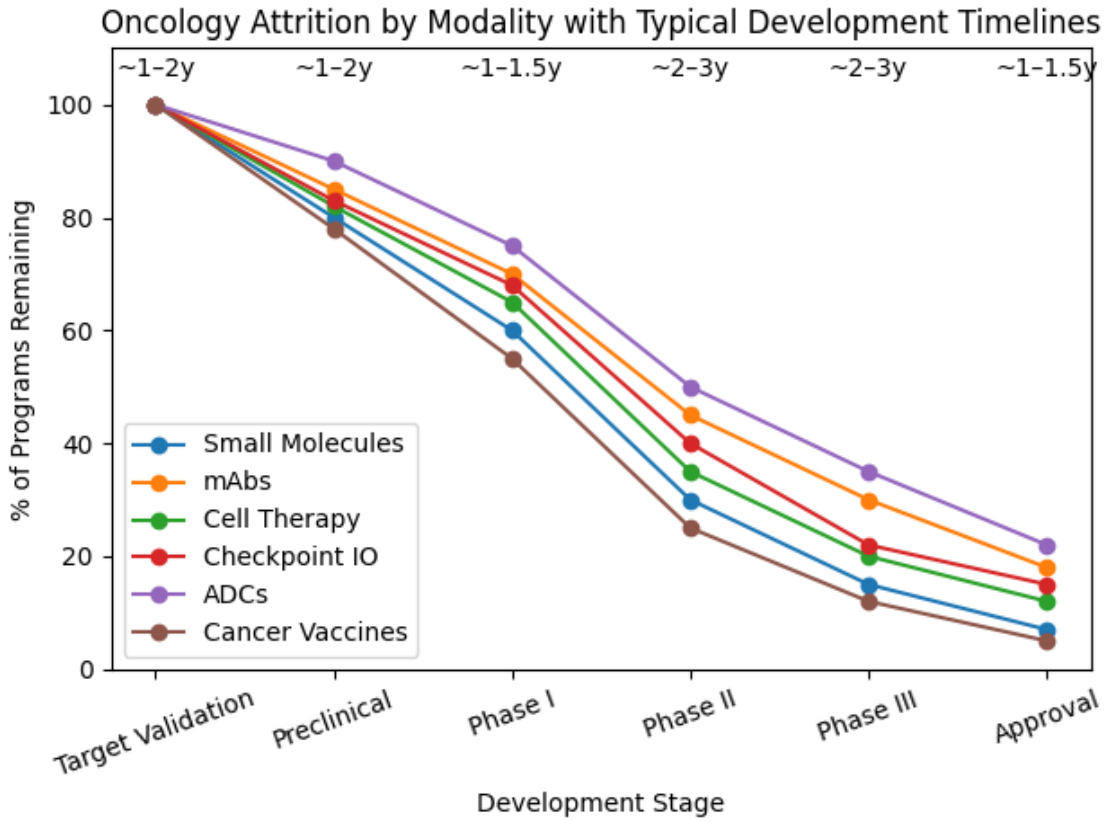
Key Risks & Mitigation Strategy

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



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.

- **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

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

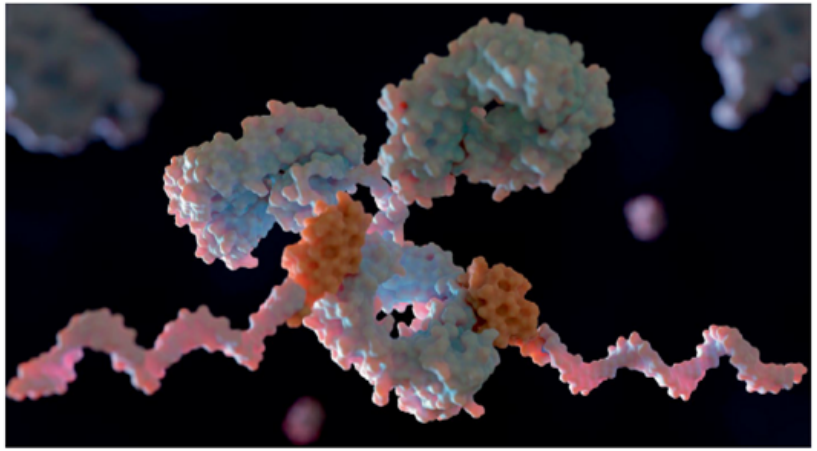
AOCs Recognized as the Next Drug Modality

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 dystrophia myotonica protein kinase (*DMPK*) 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 (*DUX4*) 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 *DMPK* mRNA conjugated to a cell-penetrating peptide for enhanced uptake	DM1	Phase 2
Dyne Therapeutics	Zeleciment rostudirsen (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)	*DMPK* 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 *DMPK* mRNA conjugated to a cyclic peptide that increases endosomal escape	DM1	Phase 1/2
Denali Therapeutics	DNL628	ASO targeting *MAPT* mRNA conjugated to a TfR1-binding antibody	Alzheimer's disease	Phase 1b
Aro Biotherapeutics	ABX1100	CD71-binding centryin 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.

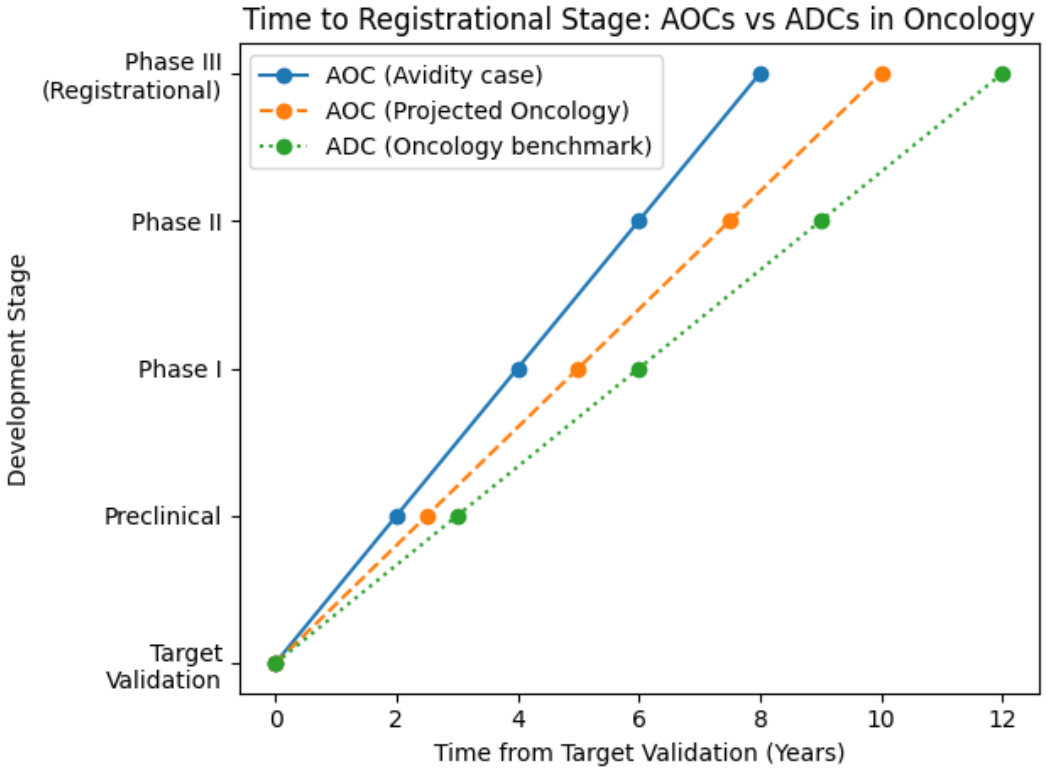
AOCs are gaining recognition as a new class of therapeutics:

- 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:

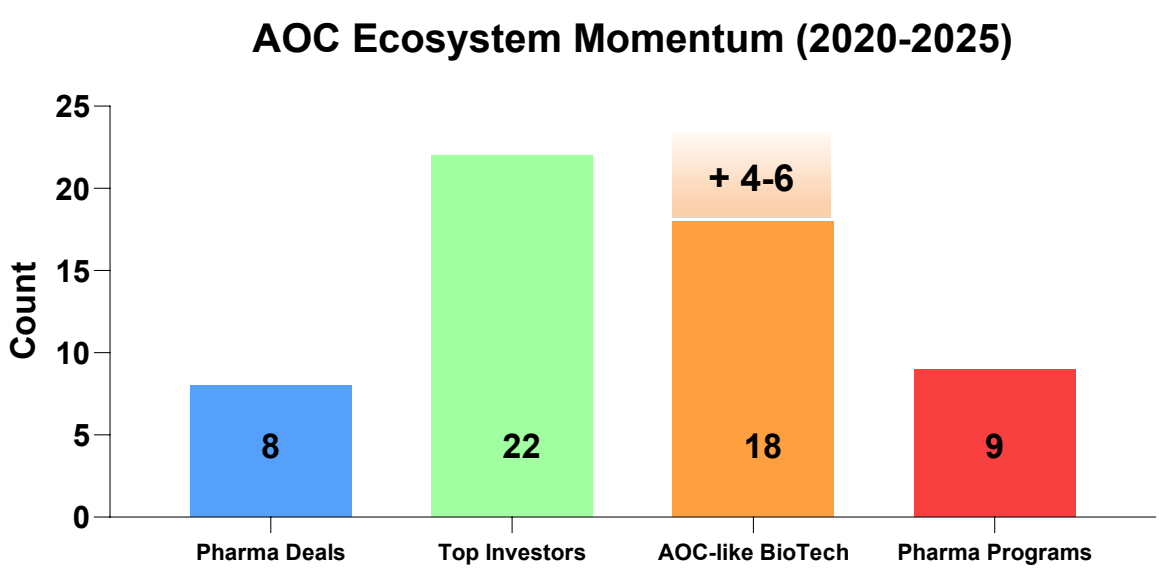
✓ Precise delivery + programmable RNA payloads → faster biological impact

✓ 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.



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

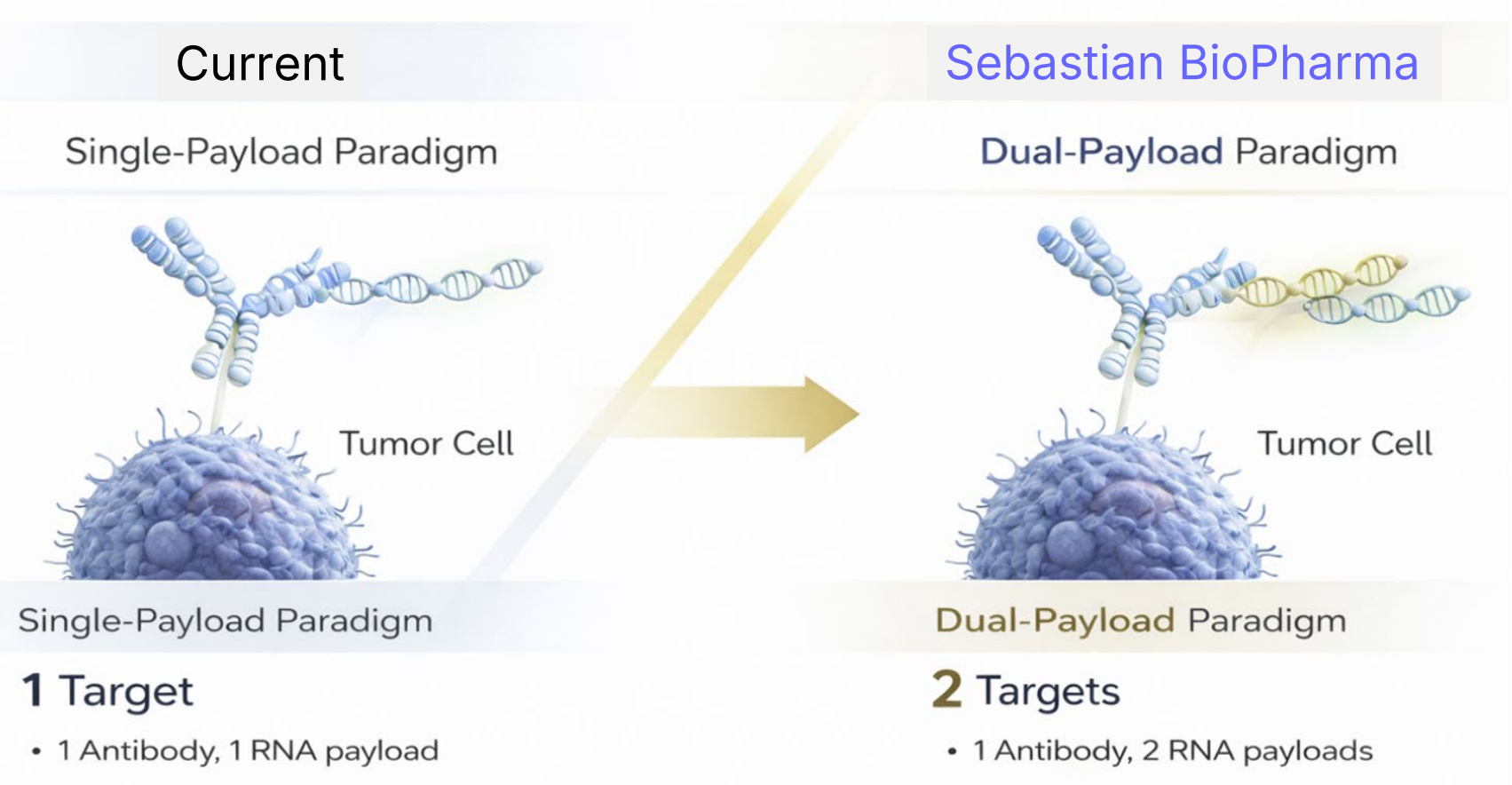
🟧 **Active AOC / AOC-like Companies**
Rapid expansion of dedicated players
- Core: Avidity, Dyne, Denali
- Additional: PepGen, Entrada, Aro, Manifold, Judo, City
- Emerging: Alnylam (extrahepatic push)

🟥 **Pharma Programs**
- Novartis, Ionis, Roche, Lilly, AbbVie, Novo Nordisk, Bayer

Internal and partnered pipelines emerging

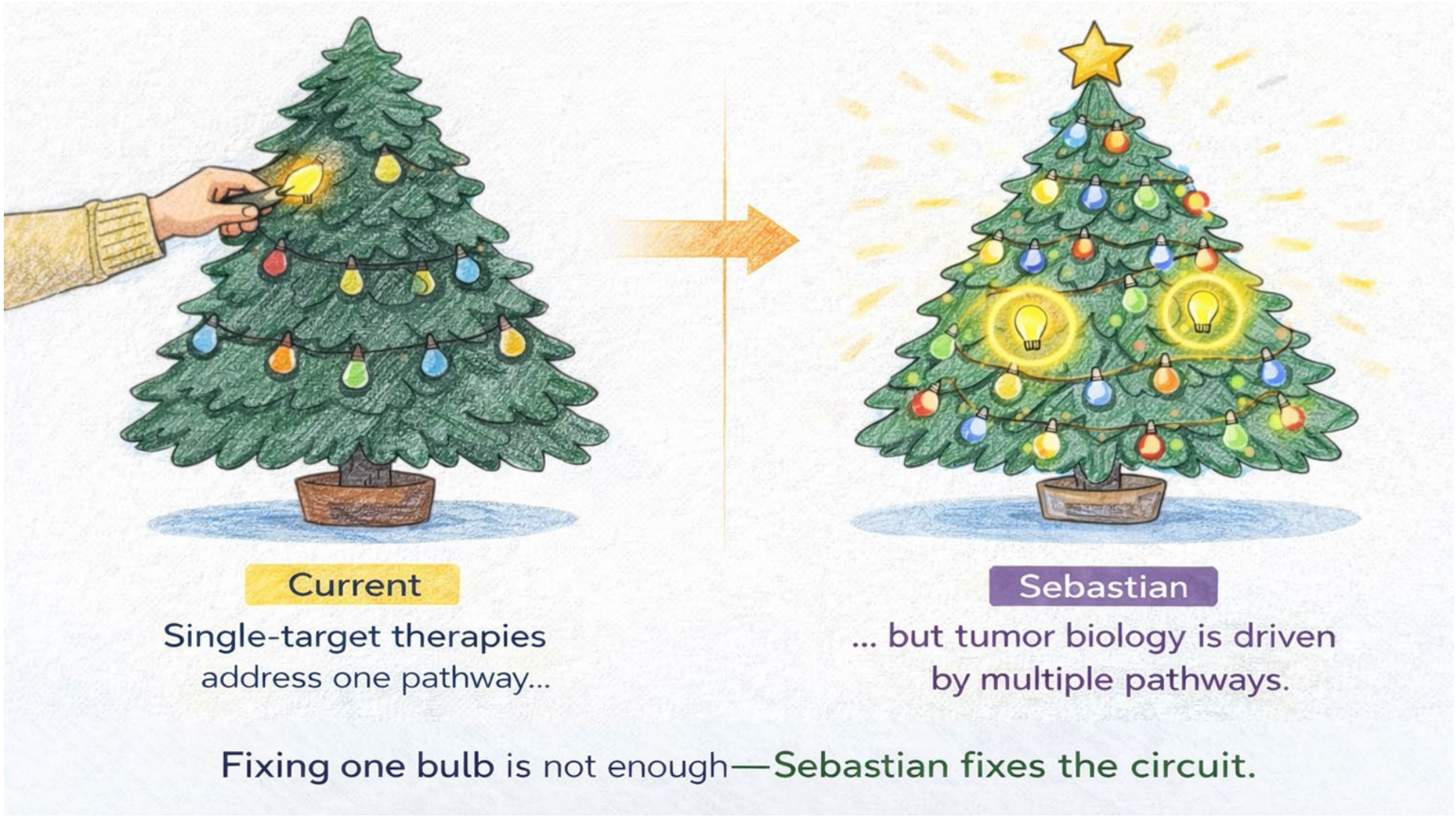
Pharma and investors are actively working to bring AOCs into oncology by evolving ADCs or building new delivery platforms

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

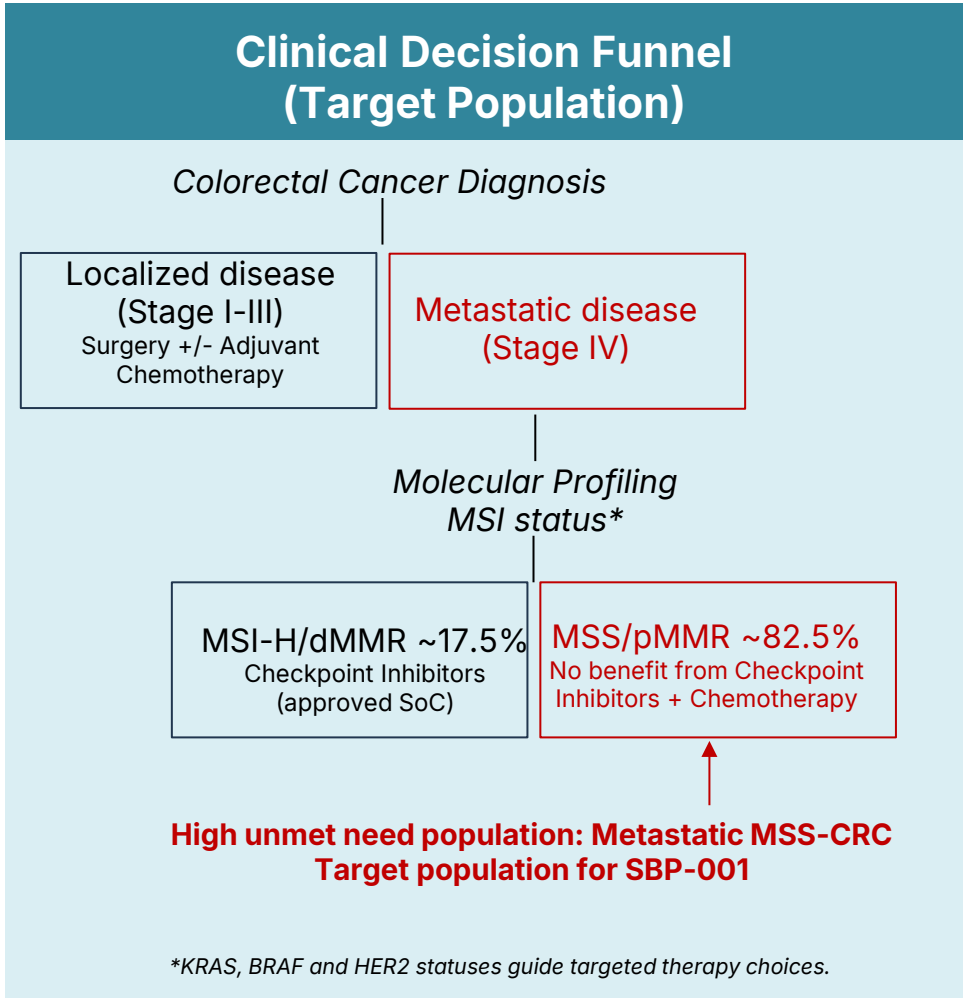


Understanding CRC Biology Is Key to Understanding the Opportunity

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.

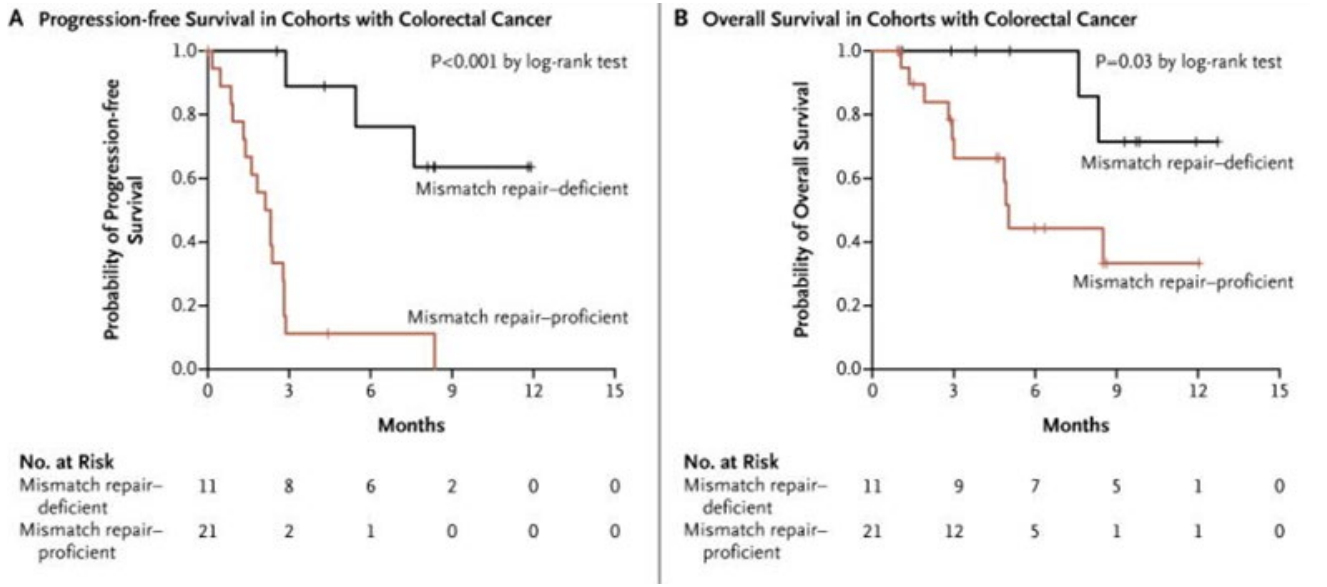


Tumor-intrinsic immune resistance in MSS-CRC is driven by lack of neoantigens and immune infiltration

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.



PD-1 blockade is effective in MSI-H/dMMR CRC but ineffective in MSS/pMMR CRC.

PD-1 Blockade in Tumors with Mismatch-Repair Deficiency - PMC

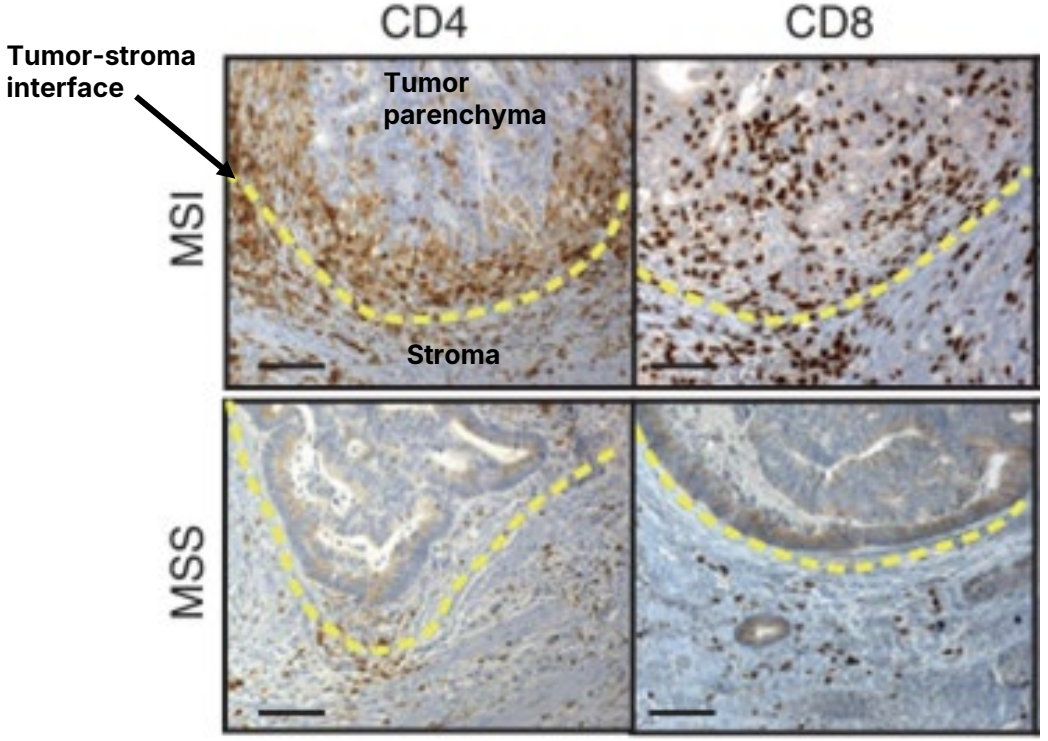
Differences between MSI-H and MSS tumors are driven not only by antigenicity, but also by immune infiltration, which plays a critical role in response to immune checkpoint blockade.

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⁺ and CD8⁺ 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⁺ and CD8⁺ 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:

Tumor Biology
Targeted Oncology Pathways
- EGFR (~40–50%)
- BRAF (~10%)
- KRAS G12C (~3–4%)
- HER2 (~2–3%)

❌ Limited durability
❌ Fragmented populations

Antigen Problem
Increase Antigen Presentation
- DNMTi / HDACi (↑ presentation)
- Temozolomide (↑ neoantigens)
- 6-thioguanine

❌ Weak or non-actionable neoantigens
❌ No effective immune activation

❌ No approach addresses BOTH:
- **Neoantigen** insufficiency
- **Immune** exclusion

Immune Activation
Force Immune Recognition
- Vaccines
- Bi-specifics (CEA-TCB, gpA33/CD3)

❌ Dependent on existing signal
❌ Limited clinical impact

Microenvironment
Overcome Immune Exclusion
- TGF-β (Bintrafusp alfa)
- Chemo + VEGF

❌ Systemic, non-specific
❌ Insufficient tumor penetration

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

Sebastian Approach

Dual-payload AOC platform

Simultaneous control of two pathways:

✓ **TUMOR INVISIBILITY** (Antigen problem)

✓ **IMMUNE EXCLUSION** (Microenvironment)