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# Botensilimab & Balstilimab: Redefining Immunotherapy in Cold Tumors

Agenus Corporate Overview | April 2026

# Botensilimab + Balstilimab ("BOT+BAL") is a Differentiated ICI Combo with Multiple Value Drivers Across Development, Registration, and Expansion Opportunities

## Late-Line BLA Submission Planned

Accelerated approval potential based on Phase 1b & Phase 2 late-line MSS mCRC NLM dataset

## Phase 3 Underway

Registrational, randomized controlled trial (RCT; "BATTMAN") with Overall Survival endpoint enrolling at ~100 sites across Canada, France, Australia & New Zealand

## Expansion in Early Disease Settings

Strong rationale for Phase 3 Neoadjuvant Colon Study based on significant pathologic responses and no relapses[a] in two Phase 2 investigator-sponsored trials (NEST and UNICORN)



ICI, immune checkpoint inhibitor; MSS mCRC NLM, microsatellite-stable metastatic colorectal cancer and no active liver metastases.

[a]Median follow-up 6–18 months.



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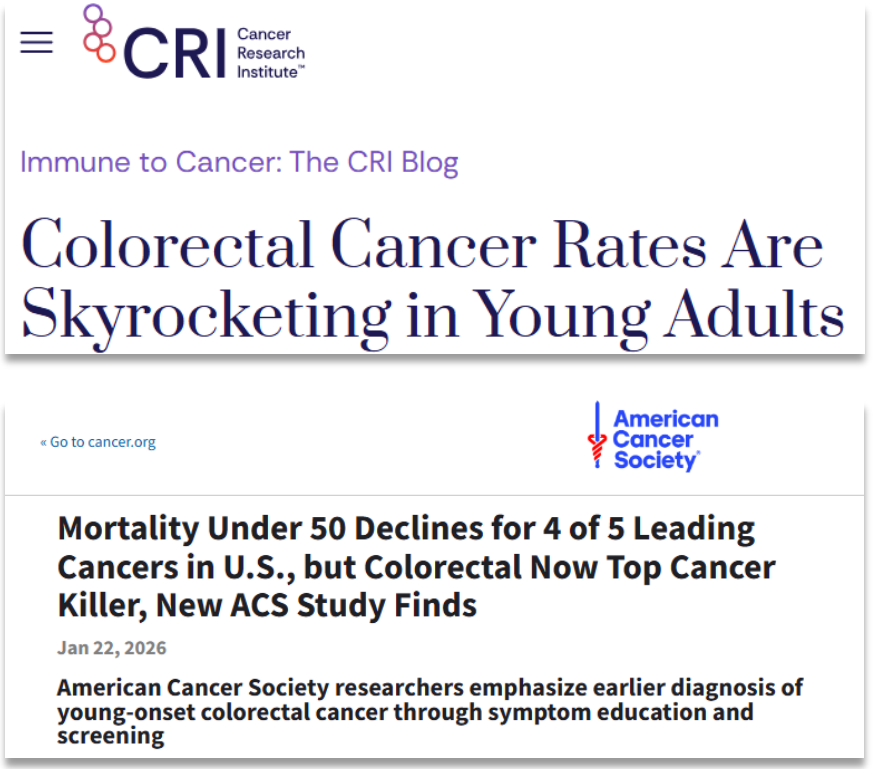
# Colorectal Cancer (CRC) Faces Two Urgent Challenges: Rising Burden of Disease and Limited Innovation – Especially in Microsatellite Stable (MSS) Disease

## 1 Rising CRC Burden

- Colorectal cancer (CRC) is now the leading cause of cancer-related death among Americans under 50[1]
- ~150k new cases annually in US[2]
- ~2M new cases annually worldwide[3]
- 16% 5-year survival rate for mCRC[4]

## 2 Most CRC lacks effective immunotherapy options

- Microsatellite stable (MSS) accounts for 85-95% of CRC cases[5,6]
- No major immune checkpoint inhibitor (ICI) advances in MSS CRC in >20 years[6]
- MSS CRC remains unaddressed by first-generation ICI[6]



CRI Cancer Research Institute

Immune to Cancer: The CRI Blog

Colorectal Cancer Rates Are Skyrocketing in Young Adults

« Go to cancer.org

American Cancer Society

**Mortality Under 50 Declines for 4 of 5 Leading Cancers in U.S., but Colorectal Now Top Cancer Killer, New ACS Study Finds**

Jan 22, 2026

**American Cancer Society researchers emphasize earlier diagnosis of young-onset colorectal cancer through symptom education and screening**



**1.** Siegel RL, et al. *JAMA.* 2026;335(7):632-634. **2.** Siegel RL, et al. *CA Cancer J Clin.* 2025;75(1):10-45. **3.** Bray F, et al. *CA Cancer J Clin.* 2024;74(3):229-263. **4.** National Cancer Institute. SEER Cancer Stat Facts: Colorectal Cancer. Bethesda, MD: National Cancer Institute. Available at: https://seer.cancer.gov/statfacts/html/colorect.html. **5.** Buchler T. *Front Oncol.* 2022;12:888181. **6.** Guven DC, et al. *Oncologist.* 2024;29(5):e580-e600.



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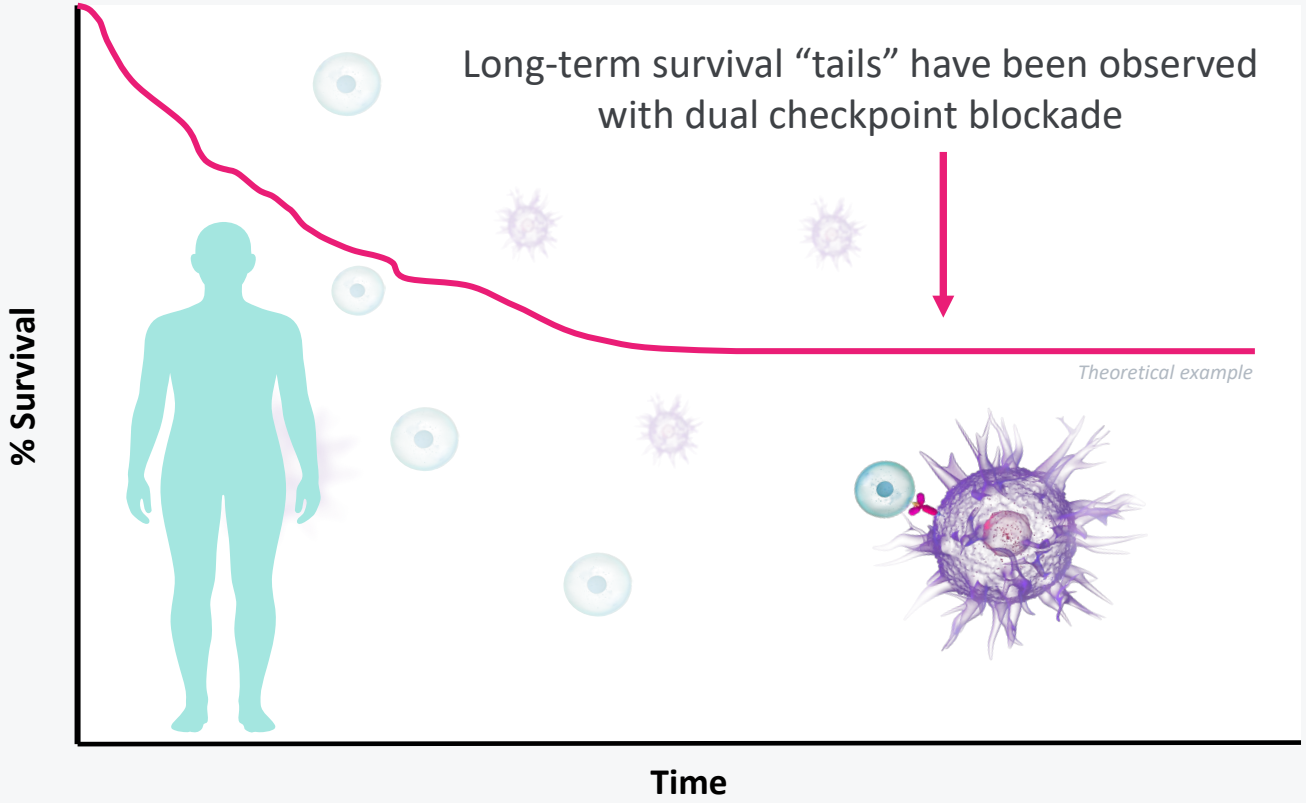
# Immunotherapy: A Proven Path to Long-Term Survival with Curative Potential




## Immunotherapy Approach

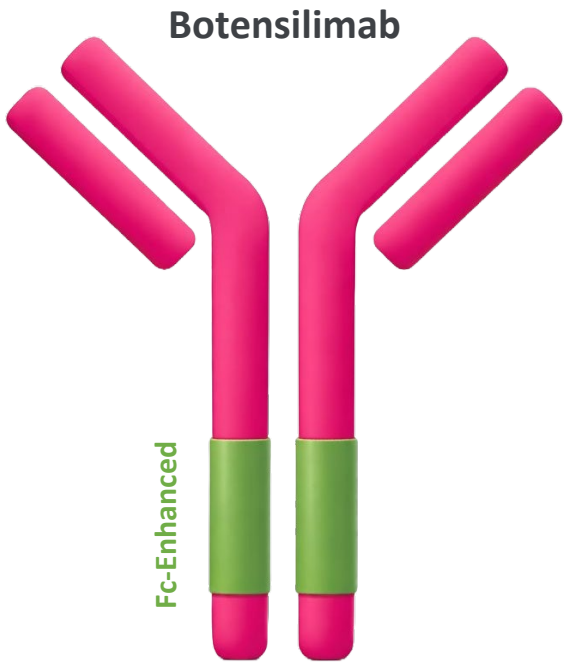
Immunotherapy can enable durable, treatment-free survival by activating the immune system to continuously kill cancer cells[1-2]

New immunotherapies are needed to “raise the survival tail” & enable long-term survival for more patients



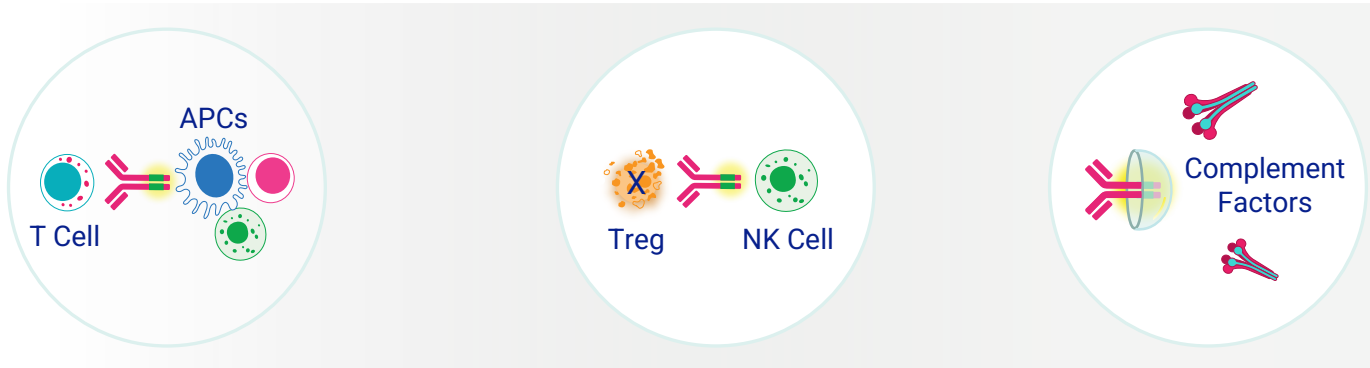
**1.** Larkin J, et al. *N Engl J Med*. 2019;381(16):1535-1546. **2.** Wolchok JD, et al. *N Engl J Med*. 2025;392(1):11-22. **3.** Haslam A, Olivier T, Prasad V. Int J Cancer. 2025;156(12):2352-2359.

# Botensilimab (BOT): A Differentiated Anti–CTLA-4 Designed to Overcome Resistance and Activate Anti-Cancer Immunity[1-5]




BOT ± BAL* is active in cold & treatment-refractory tumors

*Balstilimab (BAL): Agenus' PD-1 inhibitor with properties comparable to approved PD-1 inhibitors




Activates APCs/Myeloid Cells

Enhances T cell Priming, Activation & Memory

Reduces Intratumoral Regulatory T cells

Avoids Difficult-To-Treat Immune-Related AEs



**1.** Bullock AJ, et al. *Nat Med.* 2024;30(9):2558-2567. **2.** Waight JD, et al. *Cancer Cell.* 2018;33(6):1033-1047.e5. **3.** Chand D, et al. *Cancer Discov.* 2024;14(12):2407-2429. **4.** O'Malley DM, et al. *Gynecol Oncol.* 2021;163(2):274-280. **5.** O'Malley DM, et al. *J Clin Oncol.* 2022;40(7):762-771.



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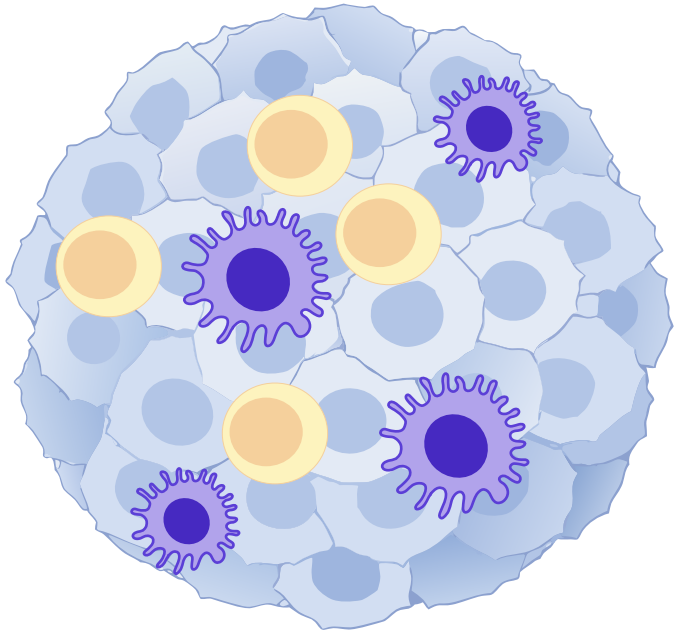
# BOT+BAL Is Uniquely Effective in Driving Durable Anti-Cancer Immunity and Converting Tumors from "Cold" (Immune Evading) to "Hot" (Immune Activated)

## "Cold" Tumors[1]

- Hidden from the immune system
- Poor/no response to approved immunotherapy

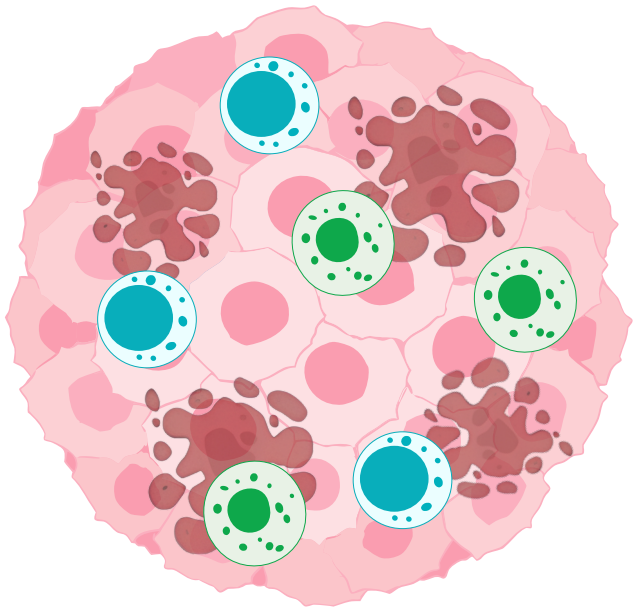


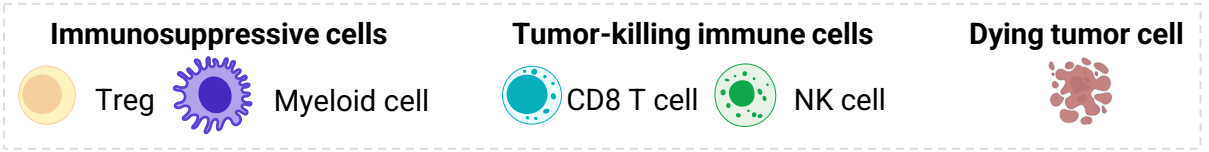
**BOT+BAL TURNS COLD TUMORS INTO HOT TUMORS[2-3]**

***BOT "lights up" the tumor, while BAL drives sustained anti-cancer killing response***

## "HOT" Tumors[2]

- Detectable by the immune system
- Sensitive to immunotherapy








**1.** Khosravi GR, et al. Cancer Commun (Lond). 2024;44(5):521-553. **2.** Chand D, et al. Cancer Discov. 2024;14(12):2407-2429. **3.** Waight JD, et al. Cancer Cell. 2018;33(6):1033-1047.e5.



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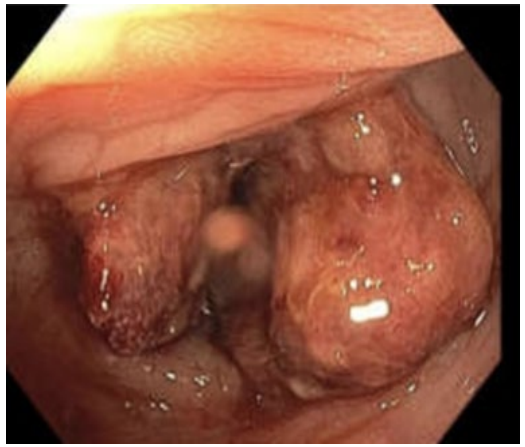
BOT + BAL

# Potential of Immunotherapy Approach with BOT+BAL

- Chemotherapy-free option
- Manageable safety profile
- Organ-sparing potential
- Considers quality of life (especially important in early-onset cancer)

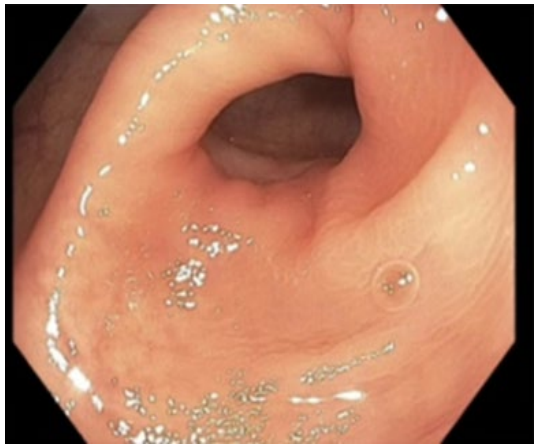
## Examples of 100% tumor regression

After 1 dose of BOT + 2 doses of BAL with no concurrent nor prior therapy; from ongoing neoadjuvant Phase 2 trials (NEST and NEOASIS)



**MSS Colorectal Cancer[5]**

**7 weeks**



**Merkel Cell Carcinoma[6]**

**6 weeks**

Single-patient images; images shared with patient consent.

**1.** Gordon MS, et al. Oral Presentation at ESMO Annual Meeting. Berlin, Germany. 2025. #1517MO. **2.** Schlechter BM, et al. Poster presented at the ESMO GI Congress. Barcelona, Spain. 2025. Poster #8P. **3.** Hissong E, et al. Poster presented at the ASCO GI Congress. Chicago, IL, USA. 2025. Abstract #207. **4.** Ghelardi F, et al. Poster presented at the ASCO GI Congress. Chicago, IL, USA. 2025. Poster #F20. **5.** Kasi P, et al. Oral presentation at the ESMO GI Congress. Munich, Germany. 2024. Presentation #743. **6.** Chalabi M, et al. Oral presentation at AACR. Chicago, IL, USA. 2025. Abstract #CT130.

# BOT+BAL Represents a Large and Growing Market Opportunity, with ~$10B+ in Peak Annual Global Revenue Potential in MSS CRC


## Initial Entry

**Relapsed/Refractory MSS mCRC**

Annual patients
~10,000 US | 35,000 Global

## Near-Term Expansion

**Neoadjuvant MSS CRC**

Annual patients
~35,000 US | 200,000 Global

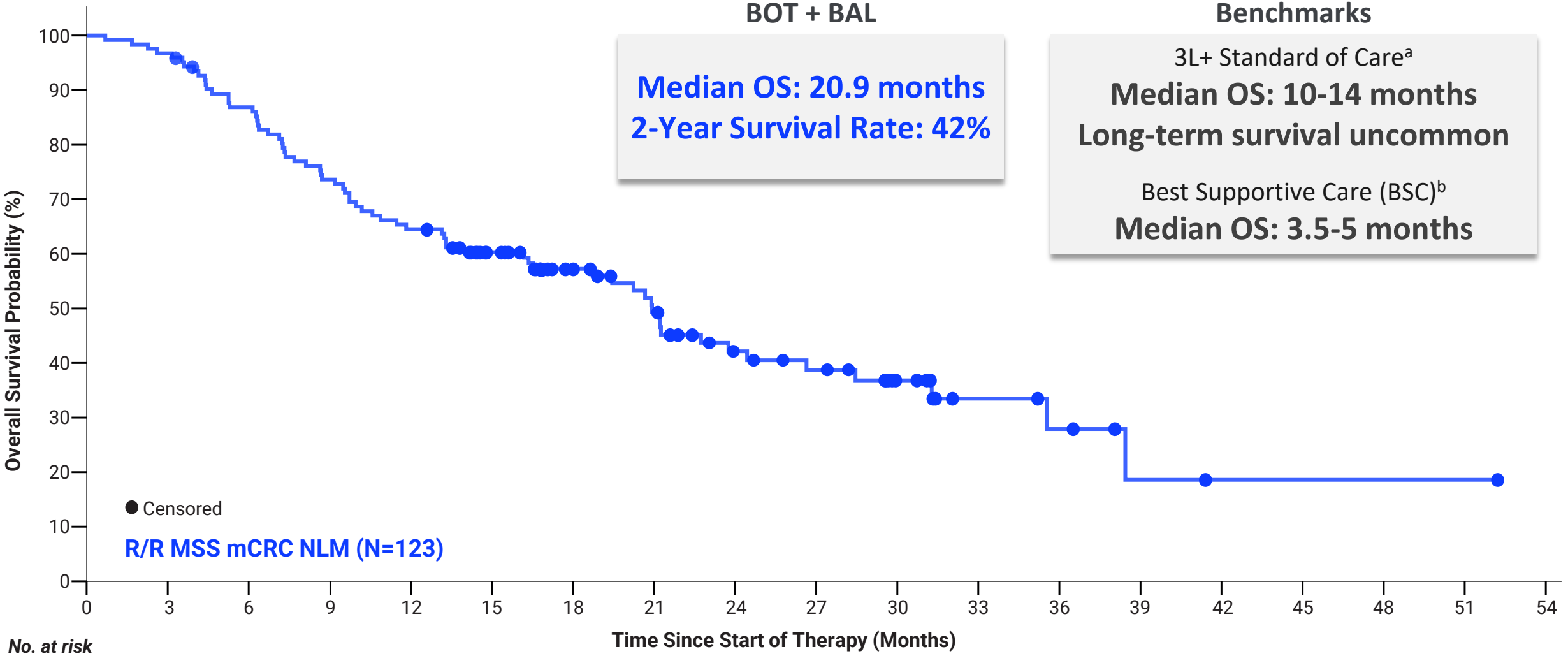
## Long-Term Value

**Pan Tumor**

Data in 9+ tumor types including NSCLC, HCC, ovarian, sarcoma, breast, and melanoma

# Durable Survival with BOT+BAL Beyond Historical Expectations in MSS mCRC, where ≥2 yr Survival is Rare

## BOT+BAL R/R MSS mCRC[1]




**BOT + BAL**

**Median OS: 20.9 months**
**2-Year Survival Rate: 42%**

**Benchmarks**

3L+ Standard of Care[a]
**Median OS: 10-14 months**
**Long-term survival uncommon**

Best Supportive Care (BSC)[b]
**Median OS: 3.5-5 months**

[a]Regorafenib, trifluridine/tipiracil ± bevacizumab, or fruquintinib in patients without active liver metastases.[2-4] [b]No systemic anticancer therapy; the control arm in ongoing BATTMAN Phase 3 RCT. Reference values from the CO.26 trial[5-6]


**1.** Schlechter BM, et al. Poster presented at the ESMO Gastrointestinal Cancers Congress 2025. Barcelona, Spain. 2025. Poster #8P. **2.** Cohen R, et al. Eur J Cancer. 2024;207:114160. **3.** Tabernero J, et al. Poster presented at the ASCO Annual Meeting. Chicago, IL, USA. 2024. Abstract #3584. **4.** Garcia-Carbonero R, et al. Poster presented at the ASCO Annual Meeting. Chicago, IL, USA. 2024. Poster 520P. **5.** Chen EX, et al. *JAMA Oncol.* 2020;6(6):831-838. **6.** Chen EX, et al. *JAMA Netw Open.* 2023;6(12):e2346094.

# Pan-Tumor Phase 1b: Expanded Safety Dataset Shows Manageable Tolerability Profile

***Selected BATTMAN (Ph3) Dose***

| Safety event, n (%) | 1 mg/kg (n=228) | | 2 mg/kg (n=183) | | Overall (N=411) | |
|---|---|---|---|---|---|---|
| **Any grade TRAE** | **85%** | | **86%** | | **85%** | |
| Grade 1-2 TRAEs | 57% | | 48% | | 53% | |
| Grade ≥3 TRAEs | 28% | | 38% | | 32% | |
| | **Grade 1 or 2** | **Grade ≥3** | **Grade 1 or 2** | **Grade ≥3** | **Grade 1 or 2** | **Grade ≥3** |
| **Any treatment-related imAE[a,b]** | 24% | 18% | 27% | 27% | 25% | 22% |
| **Most common (≥3%) treatment-related imAEs[a]** | | | | | | |
| Diarrhea/colitis[c] | 17% | **10%** | 21% | 19% | 19% | 14% |
| Thyroid[d] | 8% | **0%** | 8% | 0% | 8% | 0% |
| Hepatitis[e] | 2% | **1%** | 3% | 4% | 2% | 2% |
| Skin[f] | 1% | **1%** | 3% | 2% | 2% | 1% |
| Pneumonitis[g] | 1% | **1%** | 2% | 1% | 1% | 1% |

- Safety signals consistent across trials
- The most common imAEs were GI-related, which were reversible
- There was a low incidence of visceral toxicities outside the GI tract
- No treatment-related deaths were observed (grade 5)

Data cutoff: 13-MAR-2025. Safety analysis set (N=411; participants who received ≥1 dose of study drug).
[a]imAEs were medically adjudicated. [b]Grade 4 imAEs (n=1 each) of colitis (2 mg/kg group), autonomic neuropathy (1 mg/kg group), diabetic ketoacidosis (2 mg/kg group), and thrombocytopenia (1 mg/kg group) were reported; no other grade ≥4 imAEs occurred. [c]Grouped term that included preferred term events of autoimmune colitis, colitis, diarrhea, duodenitis, enteritis, enterocolitis, and immune-mediated enterocolitis. [d]Grouped term that included preferred term events of blood thyroid stimulating hormone increased, hyperthyroidism, hypothyroidism, immune-mediated hypothyroidism, immune-mediated thyroiditis, and thyroiditis. [e]Grouped term that included preferred term events of AST increased, ALT increased, autoimmune hepatitis, blood alkaline phosphatase increased, and immune-mediated hepatitis. [f]Grouped term that included preferred term events of immune-mediated dermatitis, lichen sclerosus, linear IgA disease, rash, rash erythematous, and rash maculo-papular that were treated systemically. [g]Grouped term that included preferred term events of immune-mediated lung disease, and pneumonitis.


Adapted from Gordon MS, et al. Oral Presentation at ESMO Annual Meeting. Berlin, Germany. 2025. #1517MO. Data cutoff: 13-MAR-2025.

# BATTMAN: Phase 3 RCT Designed to Confirm Survival Benefit in R/R MSS mCRC; FDA Aligned to Support Registration (NCT07152821)

**Patients with pMMR (MSS) Advanced CRC** (N=834)

- Refractory to available agents
- Unresectable

~100 sites across Canada, France, Australia and New Zealand

Randomize

1:1

**BOT + BAL**

BOT: 75 mg IV Q6W x 4 doses

BAL: 450 mg IV Q3W

**Best Supportive Care (BSC)**

No systemic anticancer treatment; care focuses on symptom management and quality of life.

**Primary Endpoint:**

- Overall Survival

**Select Secondary Endpoints:**

- Progression-Free Survival
- Overall Response Rate
- Clinical Benefit Rate
- Quality of Life
- Safety and Toxicity

# Strong Clinical Activity Observed Previously with BOT+BAL Compares Favorably to BSC Benchmarks, Supporting High Probability of Success for Phase 3 BATTMAN Trial

## R/R MSS Metastatic CRC

**BATTMAN** Primary Endpoint: Overall Survival (N=834)

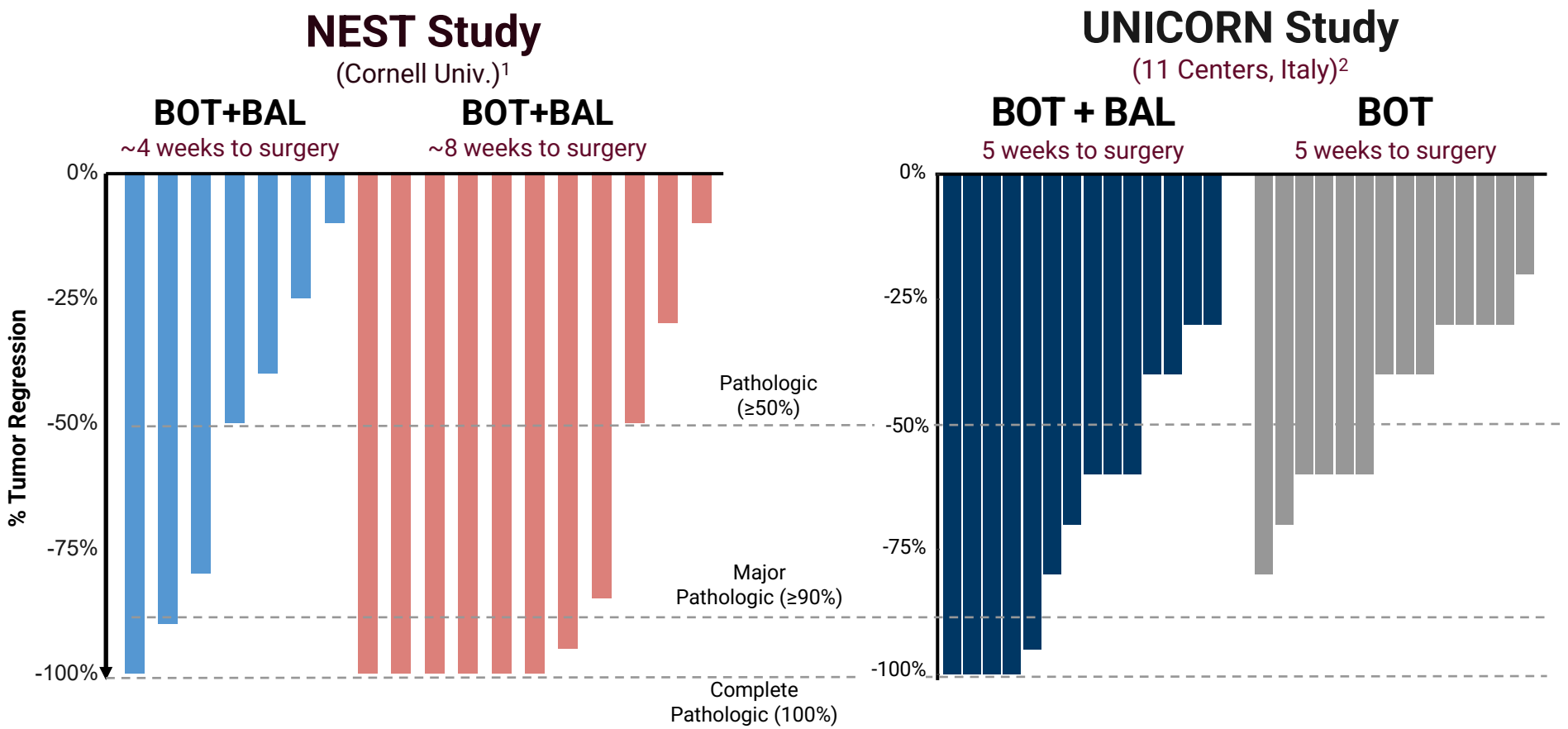
| Population | BOT+BAL Phase 1b Data | Best Supportive Care (BSC) Benchmark Data (CO.26 Study) |
|---|---|---|
| 3L+ without active liver mets (NLM) | **20.9 months** Median OS (n=123)[1] | ~5 months Median OS[a] |
| 3L+ with active liver mets (LM) | **7.5 months** Median OS (n=25)[2] | ~3.6 months Median OS[a] |

[a]Best supportive care arm in CO.26 trial conducted by CCTG; Chen EX, et al. *JAMA Netw Open.* 2023;6(12):e2346094.



**1.** Schlechter BM, et al. Poster presented at the ESMO GI Congress. Barcelona, Spain. 2025. Poster #8P. **2.** Bullock et al. *Nat Med.* 2024;30(9):2558-2567.

# Expanding From Late-Line R/R MSS mCRC into the Earlier Disease Neoadjuvant Setting with Curative Intent with BOT+BAL




**No recurrences to date** with any patients treated with BOT+BAL (median follow-up 6–18 months)



**1.** Hissong E, et al. Poster presented at the 2025 ASCO GI Congress. Chicago, IL, USA. Abstract #207. **2.** Ghelardi F, et al. Poster presented at the 2025 ASCO GI Congress. Chicago, IL, USA. Poster #F20.

# Consistently Favorable Safety Profile with BOT+BAL in Neoadjuvant CRC and No Impact on Surgical Feasibility

## NEST[1]

| | NEST-1 (n=10) | NEST-2 (n=14) |
|---|---|---|
| **Any Grade ≥3** | 2 (20%) | 1 (7%) |

*No delays in surgery due to imAEs*

## UNICORN[2]

| | Total population (n=56) |
|---|---|
| **Grade ≥3 imAEs** | 2 (4%) |

*1 surgery delay <4 weeks*

**Among 70 Patients:**

Low rate of grade ≥3 imAEs

No unresolved imAEs

One delay of less than 4 weeks due to treatment-related hyperthyroidism



**1.** Hissong E, et al. Poster presented at the ASCO Gastrointestinal Cancers Congress. Chicago, IL, USA. 2025. Abstract #207.
**2.** Ghelardi F, et al. Poster presented at the ASCO Gastrointestinal Cancers Congress 2025. Chicago, IL, USA. 2025. Poster #F20.



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# Strong BOT+BAL Neoadjuvant Activity Supports Rationale for Expansion into Phase 3 Trial

## Rational for Phase 3 RCT Neoadjuvant Trial in Stage III, Resectable, Locally Advanced MSS CRC

Primary Endpoint: Event-Free Survival

| Population | Prior BOT+BAL Phase 2 Data[1-2] | Historical Benchmark Data |
|---|---|---|
| Neoadjuvant (Stage III) MSS colon cancer | 0% recurrence at 6–18-month follow-up (n=38) | 28%–35% recurrence at 3 years[a] |
| | 36%–41% major pathological response rate | 8% major pathological response rate equivalent[b] |

[a]Adjuvant FOLFOX in MOSAIC trial; André T, et al. *N Engl J Med.* 2004;350(23):2343-2351.

[b]Neoadjuvant FOLFOX in the FOxTROT trial (based on complete plus marked regression rates); Morton D, et al. *J Clin Oncol.* 2023;41(8):1541-1552.



Major pathological response rate is defined as ≥90% tumor regression.

**1.** Hissong E, et al. Poster presented at the 2025 ASCO GI Congress. Chicago, IL, USA. Abstract #207. **2.** Ghelardi F, et al. Poster presented at the 2025 ASCO GI Congress. Chicago, IL, USA. Poster #F20.



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# BOT+BAL Clinical Activity Observed Across Multiple Metastatic Solid Tumor Types

| Clinical Outcome | Pan Tumor Population (Efficacy Evaluable)[1] n=339 | Previously Reported MSS mCRC NLM | |
|---|---|---|---|
| | | R/R Patients[2] n=123 | Late-Line R/R Patients[2] n=37[b] |
| **24-month OS** (95% CI) | **39%** (33–45) | **42%** (32–52) | **43%** (25–59) |
| **Median OS** (95% CI) | **17.2 months** (14.8–20.9) | **20.9 months** (16.2–26.6) | **16.2 months** (9.7–NR) |
| **Confirmed ORR** n (95% CI) | **17%** 58 (13–22) | **20%** 24 (13–28) | **19%** 7 (8–35) |
| **DCR[a]** n (95% CI) | **66%** 222 (60–71) | **69%** 85 (60–77) | **70%** 26 (53–84) |

**>9 tumor types** with activity

**2-year OS of 39–43% across cohorts[1,2]**

**Consistent efficacy across overall R/R and late-line MSS mCRC cohorts[2]**



[a]DCR defined as complete response, partial response, or stable disease for ≥6 weeks. [b]Previously received at least one regimen of regorafenib, trifluridine/tipiracil ± bevacizumab, or fruquintinib.

**1.** Gordon MS, et al. Oral Presentation at ESMO Annual Meeting. Berlin, Germany. 2025. #1517MO. Data cutoff: 13-MAR-2025.

**2.** Schlechter BM, et al. Poster presented at the ESMO Gastrointestinal Cancers Congress. Barcelona, Spain. 2025. Poster #8P. Data cutoff: 13-Mar-2025.



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# Zydus Partnership Strengthens Balance Sheet, Reduces Burn, and Supports Manufacturing Readiness

**$91M upfront cash payment** from Zydus to Agenus for California-based BioCDMO facilities including equity investment completed in January, 2026[1]

**First $20M of $50M in contingent payments** triggered in March 2026 to Support BOT+BAL manufacturing needs

**Exclusive manufacturing rights:** Zydus to produce BOT/BAL at former Agenus West facility, optimized for monoclonal antibody production

**5% royalty** on net sales of BOT and BAL in India and Sri Lanka

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**Sharper financial profile**

Transaction-related benefits and operating discipline reduced annualized **operating burn** to approximately **$50M**

1. $16M equity investment in Agenus at $7.50 per share

# $4.2M in Initial BOT+BAL Paid Access Income in FY 2025, $3.2M Q4 2025 Demonstrates Early Interest From Physicians and Patients

## Program Expansion

### AAC Expanded to 3 Tumor Types, NPP to New Markets

The French regulatory authority approved BOT+BAL for paid reimbursement in MSS CRC, sarcomas, and ovarian cancer in January 2026

## High Interest

### Documented HCP and Patient Interest

France AAC and self-pay markets indicate that patients and physicians will seek BOT+BAL where access is available

## Regulatory context

### Unmet Need Remains Evident

Paid pre-approval use does not substitute for clinical evidence, but it underscores urgency of access and real-world interest in treatment



Source: https://investor.agenusbio.com/news/news-details/2026/Agenus-Announces-Upcoming-AACR-2026-Presentation-Evaluating-Botensilimab-Plus-Balstilimab-in-First-Line-MSS-Metastatic-Colorectal-Cancer/default.aspx



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# Compelling Efficacy and Unmet Need Support BLA Submission for Accelerated Approval in R/R MSS mCRC NLM

## Large Safety Database

### >1,200 patients treated with BOT+BAL combo

- **Consistent safety** across trials

## Efficacy Benefit

### Consistent long-term efficacy in R/R MSS mCRC NLM setting

- **N=245 patients** across Ph1+Ph2
- **21.2 mo mOS** (vs. SOC mOS of 10–14 mo)
- **42%** 2-yr survival rate
- **19% ORR** (vs. SOC reported ORR of 3–8%)

## Regulatory Context

### Rapidly evolving FDA; focus on patient access

**Urgency is building:** FDA leadership is calling for innovation, as CRC has become the leading cause of cancer deaths in Americans under 50 yrs of age

**Rationale supporting a BLA submission through accelerated approval pathway**

- Ongoing Phase 3 BATTMAN trial will be meaningfully enrolled by time of potential PDUFA date
- Mature data demonstrating long-term survival that is unprecedented relative to existing therapies
- Clear and growing patient unmet need validated by Paid Compassionate Access programs
- Changes at FDA focused on innovative therapies

# Clinical Momentum, Early Interest, and Long-term Durability Reinforce BOT+BAL Opportunity

## Clinical Momentum

- **Phase 3 BATTMAN trial is underway** with first patient in, activated sites, and ongoing screening
- **Neoadjuvant data** in MSS CRC and other solid tumors continuing to mature favorably
- Existing sponsored data and ongoing ISTs supporting **expansion** across metastatic and neoadjuvant settings

## Market Interest & Commercial Readiness

- **Early HCP and patient interest** demonstrated through French AAC and NPP programs
- Near-term **realized income** through paid access pathways
- Zydus partnership **strengthens balance sheet and secures manufacturing** and submission support

## Long-Term Value & Durability

- **Expansion opportunities** across multiple tumor types in metastatic and neoadjuvant settings, including MSS CRC, ovarian, sarcoma, breast, HCC, and NSCLC
- **Patent life** for BOT and BAL through 2036–2038, with extensions to 2040–2042

# Recent and Upcoming 2026 Catalysts

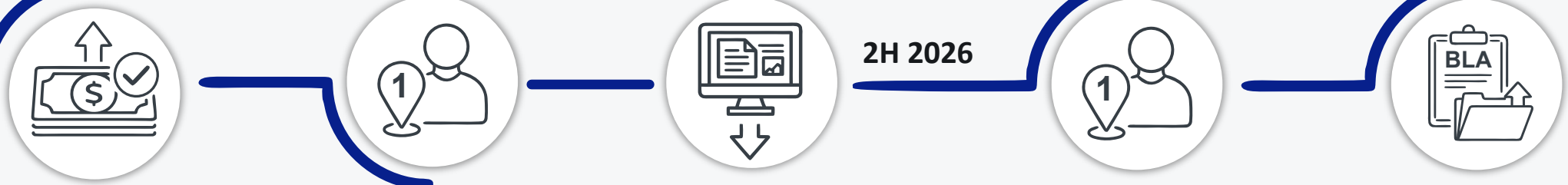
Zydus transaction closure: first $20M contingent payment triggered

**GOAL:** Start Phase 3 RCT, BOT+BAL in Neoadjuvant MSS CRC

BLA filing in R/R MSS mCRC NLM

**1H 2026**

**2H 2026**




AAC Program expansion to mSarcomas and mOvarian Cancer

First patient in, BATTMAN Phase 3 RCT (R/R MSS mCRC)

**BOT+BAL Publication Data Updates (FY 2026):**

- Pan-tumor biomarker data (AACR-IO)
- Ph2 in 1L MSS CRC (AACR)
- Ph2 GEJ (+AgenT-797; AACR)
- 3-yr OS in refractory MSS mCRC NLM
- 3-yr OS in ovarian, sarcoma, and pan tumor
- Ph2s neoadjuvant MSS CRC (NEST & UNICORN)
- Ph2 MSS mCRC NLM

# Expanding the Possibility of a Treatment Path for Metastatic Disease Less Dependent on Chemotherapy and Surgery

Latest Local News Live Shows ... CBS NEWS

HealthWatch | Eat Move Sleep Love Mental Health Health Essentials Spotlight On: Gut Health

HealthWatch

**A young dad's colon cancer spread to his lungs with no warning. He says a clinical trial led to a miracle.**

By Kerry Breen

Updated on: March 14, 2026 /

Add CBS News on Google

Spencer Laird and his daughter Madison.

- Patient testimony underscores what a potential alternative to chemotherapy can mean for patients and their families
- The goal is to expand the possibility of a treatment approach that may reduce dependence on chemotherapy and surgery
- We thank the investigators, researchers and patient volunteers that make innovation possible
- Read the CBS national news coverage