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Botensilimab & Balstilimab: Redefining Immunotherapy in Cold Tumors

Agenus Corporate Overview | April 2026

Forward-Looking Statement

This presentation contains forward-looking statements that are made pursuant to the safe harbor provisions of the federal securities laws, including statements regarding Agenus' clinical development and regulatory plans (including the scope of any regulatory approval and the ability to obtain priority review) and timelines for product candidates including balstilimab, zalifrelimab, botensilimab, BMS-986442 (AGEN1777), AGEN2373, AGEN1571, and agenT-797; our commercialization plans and pipeline's potential to meet multiple blockbuster opportunities; anticipated safety, efficacy, potency, activity, superior responses, and durability; our goals, milestones and value drivers; anticipated commercial market opportunities (including partnering and licensing opportunities); our ability to collect milestone and royalty payments; our ability to continue to self-finance Agenus; our ability to develop first and best in class drug candidates, adjuvants, antigens and formulations; and our ability to meet manufacturing demands. Statements containing the words "may," "believes," "expects," "anticipates," "hopes," "intends," "plans," "will," "potential," or the negative of these terms and other similar words or expressions, are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements are subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in any forward-looking statement. These risks and uncertainties include, among others, the factors described under the Risk Factors section of Annual Report on Form 10-K for the fiscal year ended December 31, 2025, and our subsequent Quarterly Reports on Form 10-Q filed with the Securities and Exchange Commission and made available on our website at www.agenusbio.com. Agenus cautions investors not to place considerable reliance on the forward-looking statements contained in this presentation. Agenus makes no express or implied representation or warranty as to the completeness of forward-looking statements or, in the case of projections, as to their attainability or the accuracy and completeness of the assumptions from which they are derived. These statements speak only as of the date of this presentation, and Agenus undertakes no obligation to update or revise the statements, other than to the extent required by law. All forward-looking statements are expressly qualified in their entirety by this cautionary statement. Information that may be important to investors will be routinely posted on our website and social media channels.

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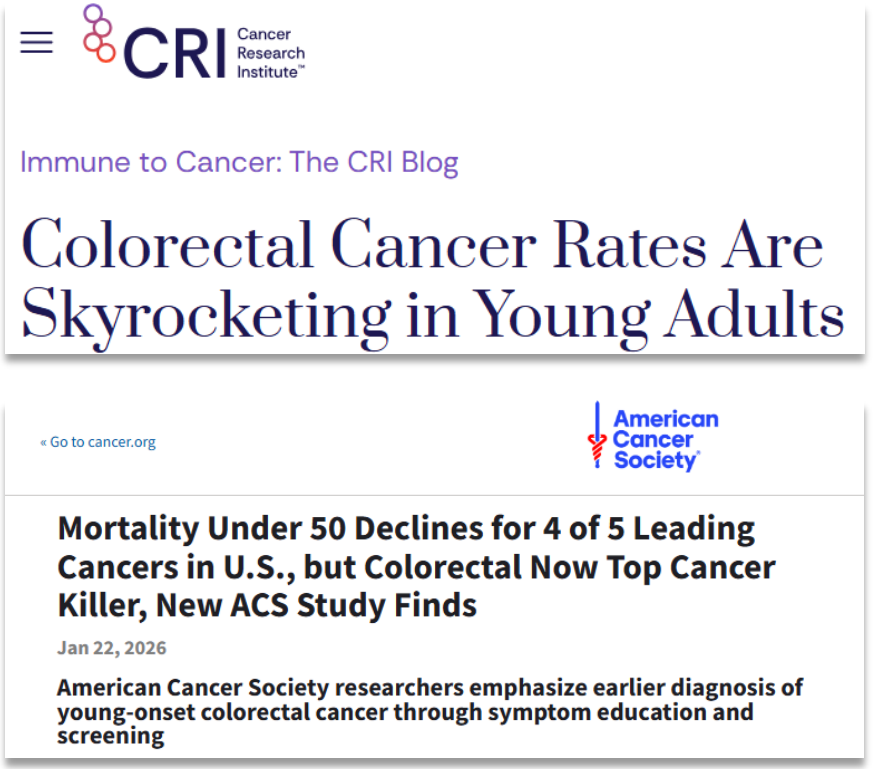
Colorectal Cancer (CRC) Faces Two Urgent Challenges: Rising Burden of Disease and Limited Innovation – Especially in Microsatellite Stable (MSS) Disease

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]

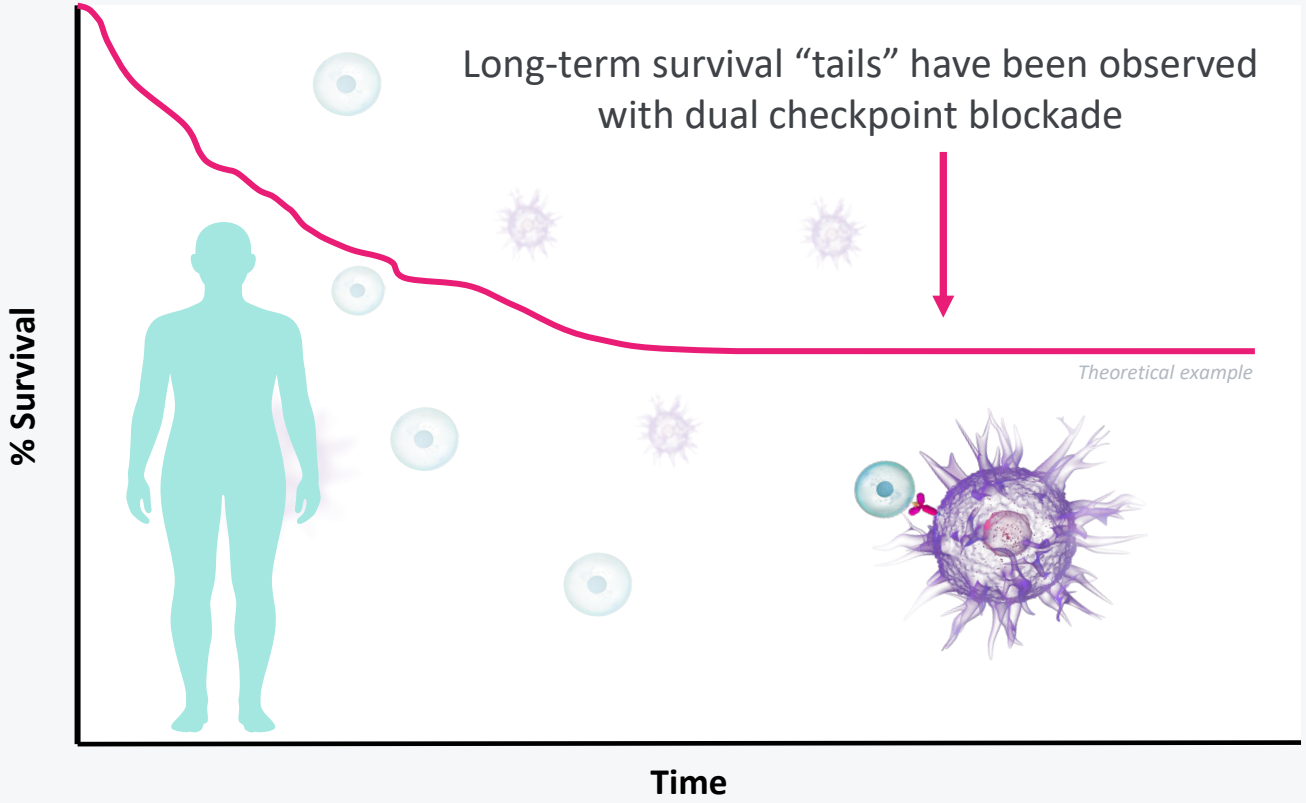
2 Most CRC lacks effective immunotherapy options

- 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]



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.

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



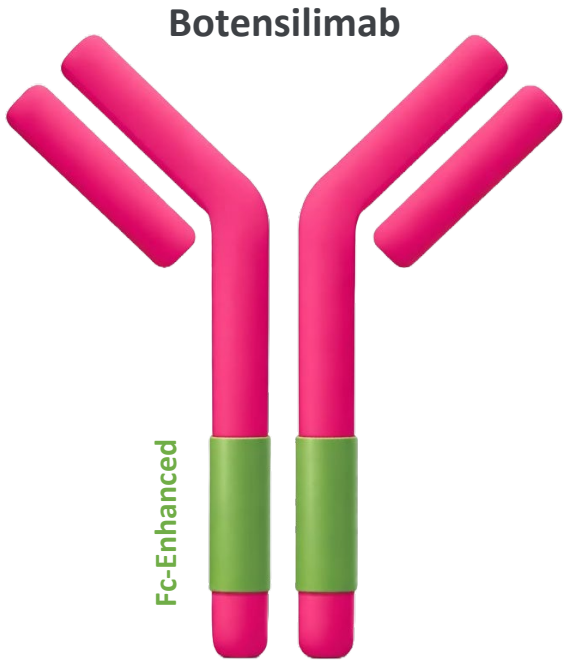
Immunotherapy Approach

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

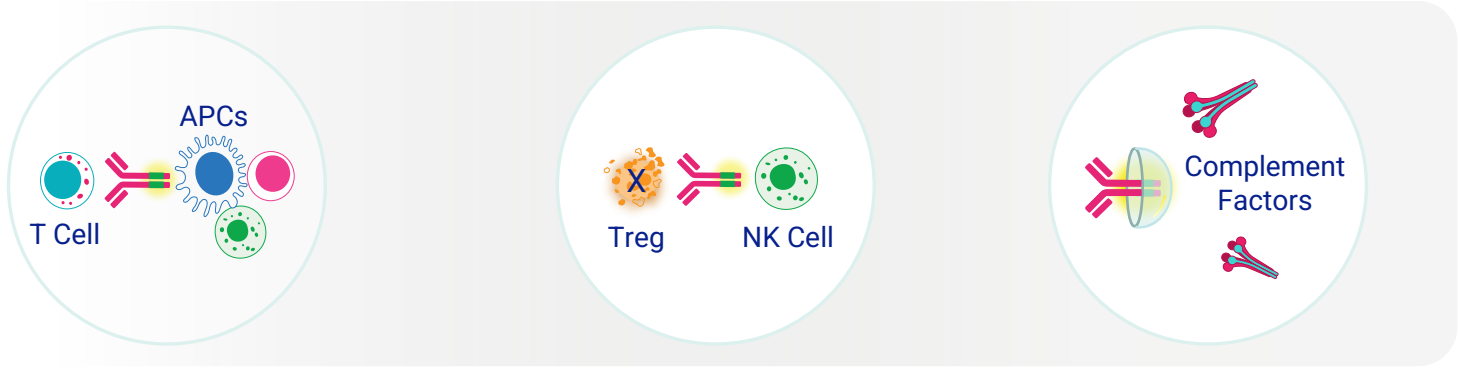
1. Larkin J, et al. *N Engl J Med*. 2019;381(16):1535-1546. **2.** Wolchok JD, et al. *N Engl J Med*. 2025;392(1):11-22. **3.** Haslam A, Olivier T, Prasad V. Int J Cancer. 2025;156(12):2352-2359.

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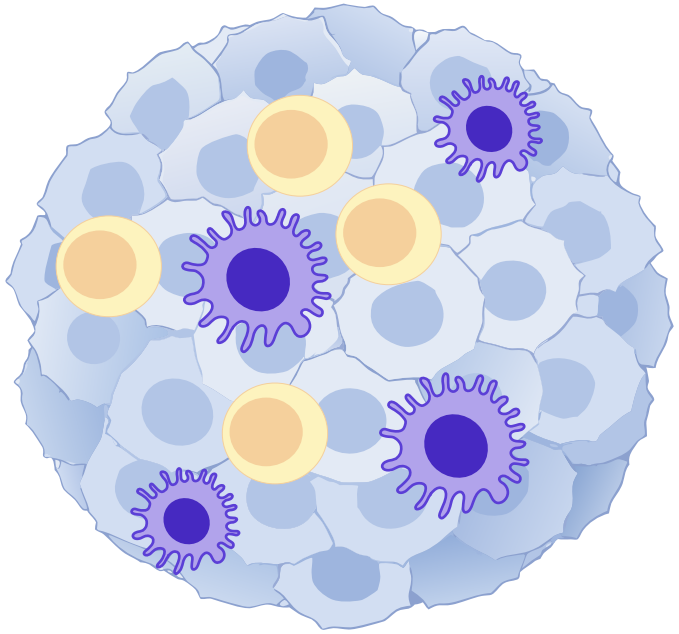
BOT+BAL Is Uniquely Effective in Driving Durable Anti-Cancer Immunity and Converting Tumors from "Cold" (Immune Evading) to "Hot" (Immune Activated)

"Cold" Tumors[1]

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

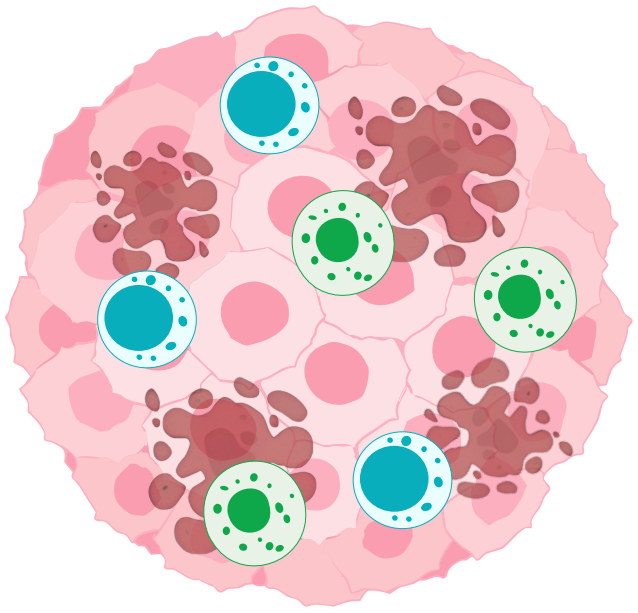


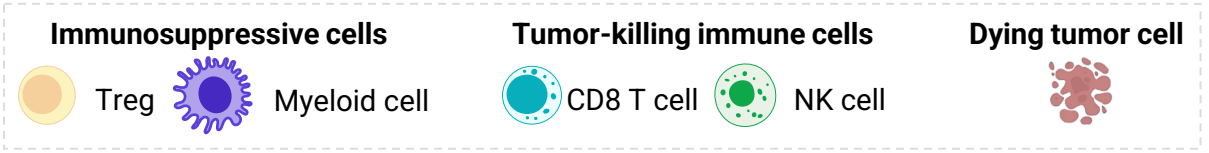
BOT+BAL TURNS COLD TUMORS INTO HOT TUMORS[2-3]

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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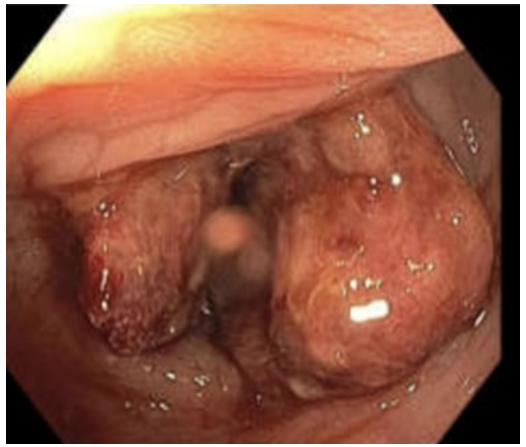
BOT + BAL

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)

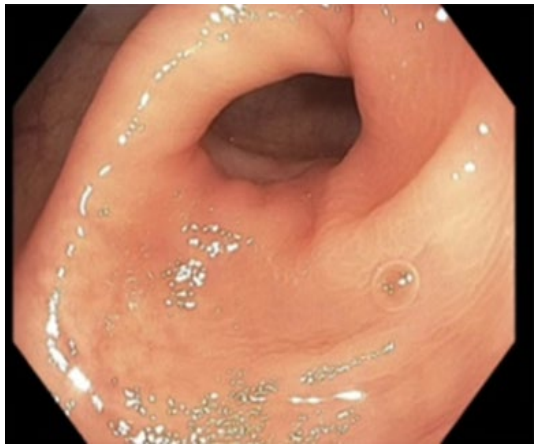
Examples of 100% tumor regression

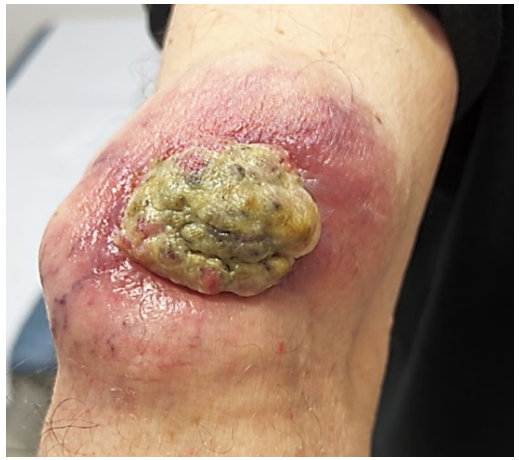
After 1 dose of BOT + 2 doses of BAL with no concurrent nor prior therapy; from ongoing neoadjuvant Phase 2 trials (NEST and NEOASIS)



MSS Colorectal Cancer[5]

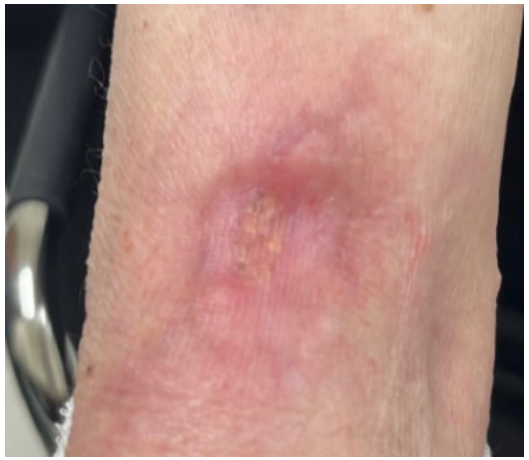
7 weeks





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

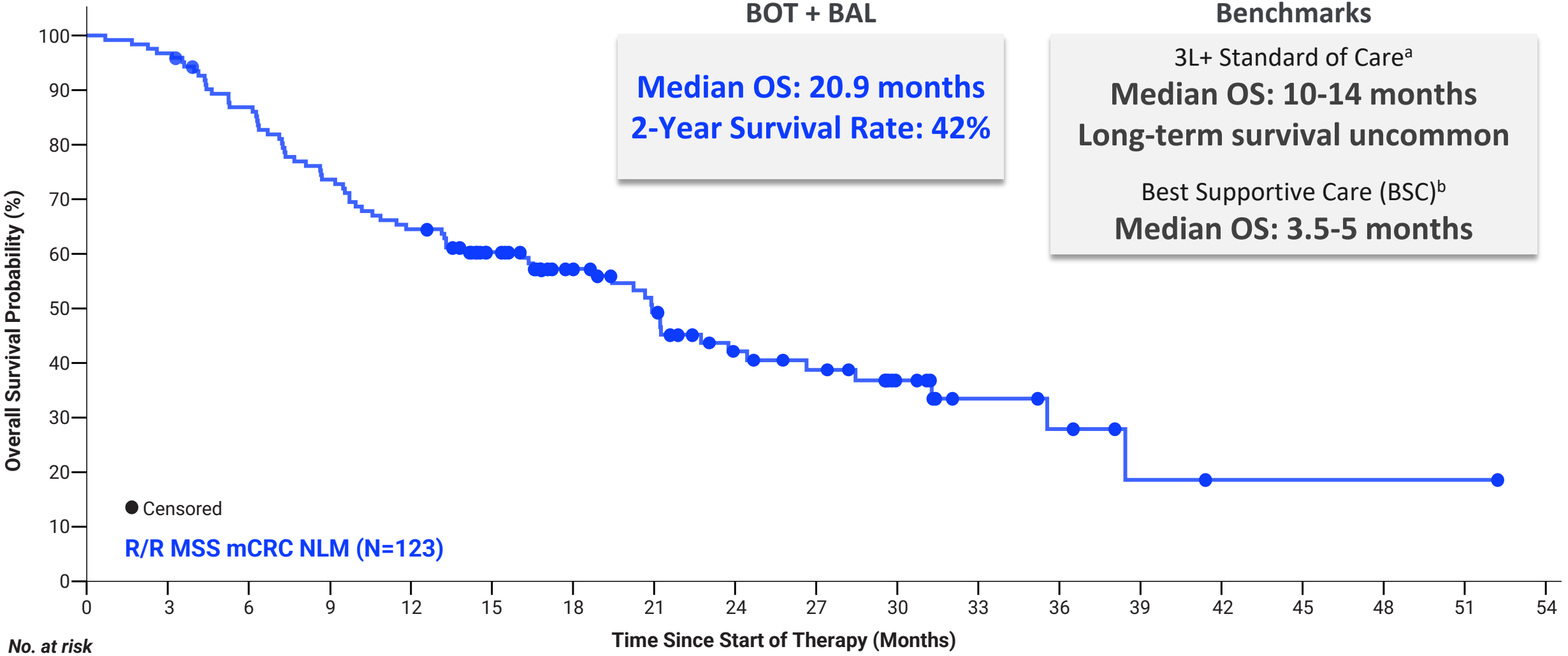
Long-Term Value

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

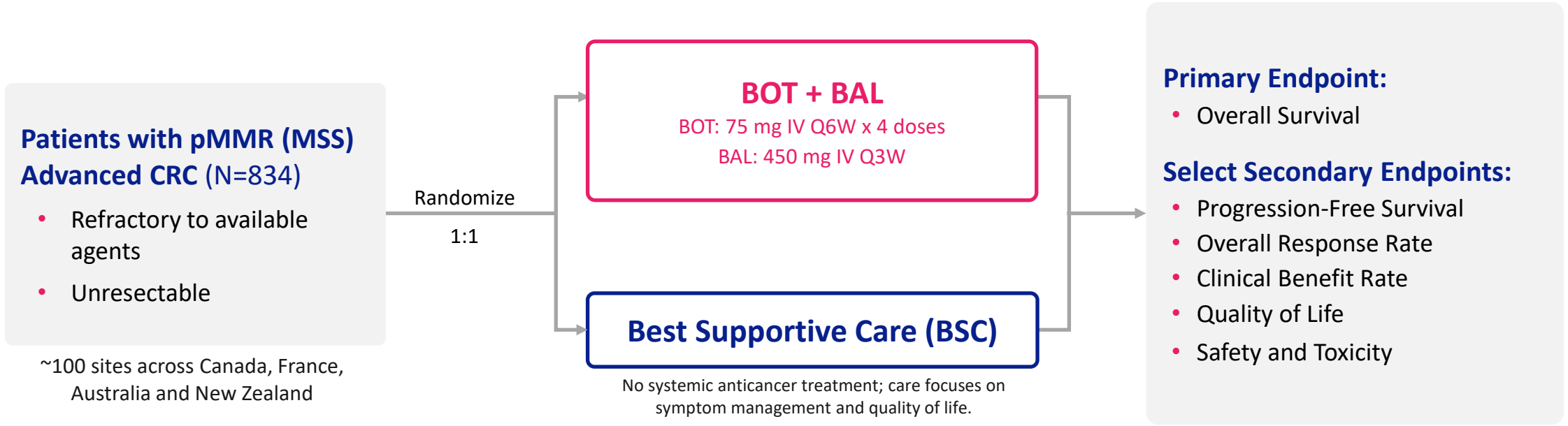
Safety event, n (%)	1 mg/kg (n=228)		2 mg/kg (n=183)		Overall (N=411)	
Any grade TRAE	**85%**		**86%**		**85%**	
Grade 1-2 TRAEs	57%		48%		53%	
Grade ≥3 TRAEs	28%		38%		32%	
	Grade 1 or 2	**Grade ≥3**	**Grade 1 or 2**	**Grade ≥3**	**Grade 1 or 2**	**Grade ≥3**
Any treatment-related imAE[a,b]	24%	18%	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)



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

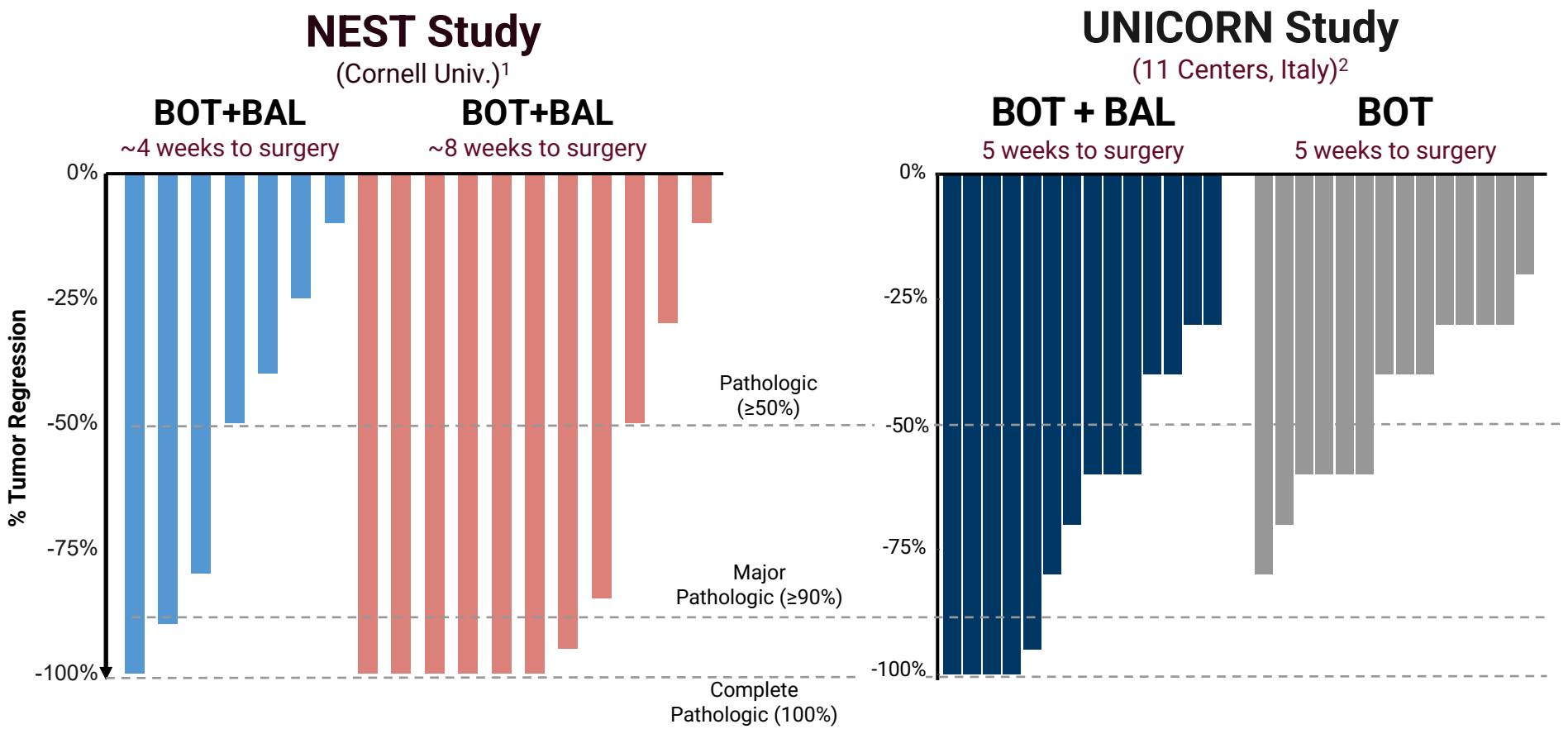
BATTMAN Primary Endpoint: Overall Survival (N=834)

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

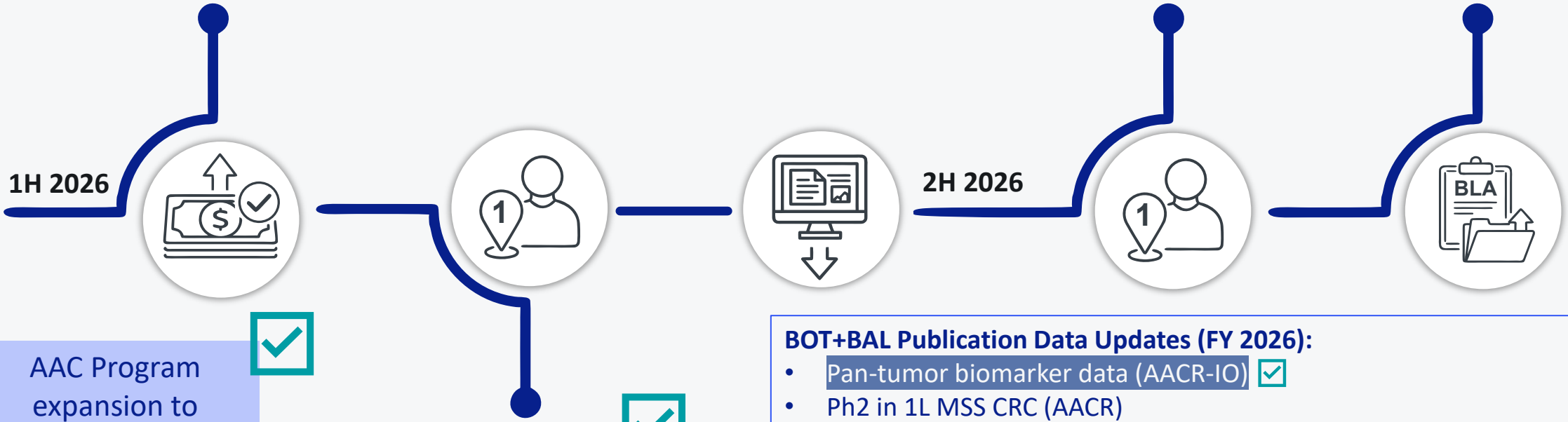
- **Expansion opportunities** across multiple tumor types in metastatic and neoadjuvant settings, including MSS CRC, ovarian, sarcoma, breast, HCC, and NSCLC
- **Patent life** for BOT and BAL through 2036–2038, with extensions to 2040–2042

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



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

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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 /

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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

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