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Botensilimab & Balstilimab: Redefining Immunotherapy in Cold Tumors

Agenus Corporate Overview | September 2026

Forward-Looking Statement

This presentation contains forward-looking statements that are made pursuant to the safe harbor provisions of the federal securities laws. These forward-looking statements include, but are not limited to, express or implied statements relating to the Company's expectations, hopes, beliefs, intentions or strategies regarding the future of its pipeline and business; the Company's strategic prioritization of BOT+BAL for the neoadjuvant treatment of MSS colon cancer; the potential benefits of treatment with the Company's product candidates, including without limitation BOT+BAL and the Company's other balstilimab, botensilimab, zalifrelimab, AGEN1777, AGEN2373 and AGEN1571 programs; the timing of the regulatory submission, design, enrollment, indication selection, dosing, timing of initiation, progress and timing of readouts and results of the Company's ongoing and planned clinical trials, including without limitation the Company's Phase 2 NEST and UNICORN trials and the Company's planned Phase 3 ROBBIN trial; anticipated safety, efficacy, potency, activity, superior response and durability outcomes with respect to the Company's ongoing and planned clinical trials; the Company's plans to discontinue financial support for the ongoing BATTMAN Phase 3 trial; expected regulatory timelines and filings; the Company's commercialization plans and anticipated commercial market opportunities (including partnering and licensing opportunities); the Company's ability to meet manufacturing demands; the closing of the Private Placement; the Company's agreement to register the resale of the securities sold in the Private Placement; the expected amount of proceeds from the Private Placement; and the Company's anticipated cash runway. 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.

Registration Enabling Opportunity for Neoadjuvant BOT+BAL in MSS Colon Cancer

The Set-Up	• Agenus' focus has been development of a next-gen Fc-enhanced anti–CTLA-4 (BOT) and anti–PD-1 (BAL) combination in late-line, metastatic MSS CRC and other advanced, metastatic solid tumors • Two separate ISTs (NEST and UNICORN) have tested neoadjuvant BOT+BAL for MSS colon cancer, where unprecedented pathologic response efficacy has translated to early and promising event-free survival (EFS)
Unprecedented Efficacy Data Across NEST and UNICORN	• Across NEST and UNICORN[5,6], n=52 MSS and MSI-H colon cancer patients treated with neoadjuvant BOT+BAL • For MSS colon cancer patients (n=38), ~30% pathologic complete response (pCR) rate, ~40% major pathologic response (MPR) rate, and 100% EFS after 9–18 months of median follow up • Well tolerated: Low rate of Grade ≥3 AEs, 1 delay to surgery (10 days) out of 52 patients treated • The demonstrated pathologic responses in NEST and UNICORN are likely to translate to a clinically meaningful EFS benefit in planned Phase 3 RCT as evidenced by results from prior trials in the neoadjuvant setting[4]
FDA Alignment, Phase 3 "ROBBIN" Trial	• Agenus has aligned with the FDA on this registrational trial ("ROBBIN[1]," n=850, Rand. 1:1, Primary Endpoint: EFS) • Study projected to start, first patient in by Q1 of 2027
Neoadjuvant MSS Colon Cancer: >$7B US TAM	• Neoadjuvant MSS colon cancer (~38k patients US, ~200k WW) is a >$7B TAM in the U.S. alone[2] • Moving priority program to neoadjuvant supports BOT+BAL pricing power: a robust I/O agent may deliver 4- to 10-fold greater value than major conventional oncology breakthroughs in the metastatic setting • No other active Phase 3 trials testing novel neoadjuvant therapies in MSS Colon Cancer[3]
Multiple Upcoming Catalysts	• Manuscript publications for updated data on NEST and UNICORN (anticipated 2H 2026) • Interim pathologic response rate readout at n=50 patients treated with BOT+BAL (anticipated 2H 2027) • Interim analysis for EFS (anticipated 2H 2029); Final analysis for EFS (anticipated 2H 2030)
Fully Funded through Projected Full Approval Timing	• July 2026 PIPE financing is expected to cover 100% of ROBBIN trial costs and all ongoing Agenus operational expenses through EOY 2031 (assuming full warrant exercise)

1.ROBBIN: A Phase 3 Randomized, Open-Label Study of Botensilimab Plus Balstilimab In the Neoadjuvant Setting followed by Standard of Care Versus Standard of Care Alone in Previously Untreated High-Risk Stage II and Stage III Non–MSI-H/dMMR Colon Cancer (ROBBIN Study) ; 2. Epidemiology analysis based on data from SEER, CDC, and Clarivate ; 3. André T, Boni C, Mounedji-Boudiaf L, et al. Oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment for colon cancer. N Engl J Med. 2004;350(23):2343-2351. ; 4. Morton D, Seymour M, Magill L, et al. Preoperative chemotherapy for operable colon cancer. J Clin Oncol. 2023;41(8):1541-1552. ; 5. Hissong E, et al. Neoadjuvant Botensilimab (BOT) Plus Balstilimab (BAL) in Resectable Mismatch Repair Proficient (pMMR) and Deficient (dMMR) Colorectal Cancer (CRC). Poster presented at the ASCO Gastrointestinal Cancers Symposium. January 23-25, 2025. San Francisco, CA. Abstract #207 ; 6. Ghelardi F, et al. Neoadjuvant botensilimab and balstilimab in colorectal cancer. Poster presented at the ASCO Gastrointestinal Cancers Symposium. January 23-25, 2025. San Francisco, CA. Poster F20

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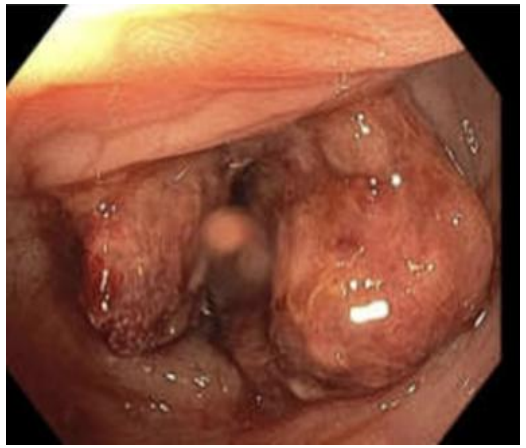
Novel Immunotherapy Approach with BOT+BAL

- Chemotherapy-free option
- Manageable safety profile
- Organ-sparing potential
- Safety and efficacy data from over 1,300 patients in metastatic and locally-advanced settings

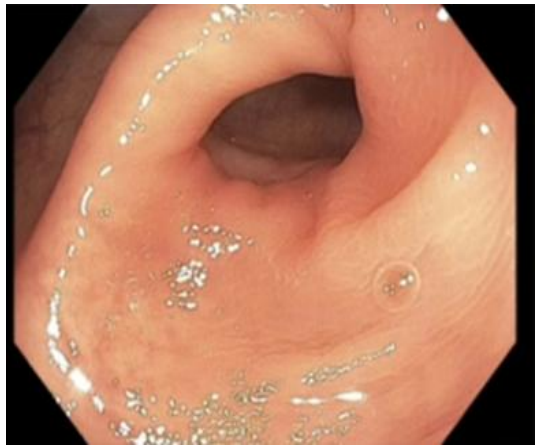
Example of 100% tumor regression from Neoadjuvant BOT+BAL in MSS Colon Cancer

After 1 dose of BOT + 2 doses of BAL with no concurrent nor prior therapy; from NEST[1] Phase 2 trial



MSS Colorectal Cancer

7 weeks



Shah M et al. Neoadjuvant Botensilimab/Bals□limab for localized mismatch repair proficient and deficient colon cancer: Results of the NEST phase 2 clinical trial. Clin Canc Res Aug 2026 ePub.

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]
- ~155,000 new cases annually in U.S.[2]
- ~2M new cases annually worldwide[3]

2 Most CRC lacks effective immunotherapy options

- Microsatellite stable (MSS) accounts for ~85% of early-stage CRC cases[5,6]
- No major advances in treatment of MSS colon cancer 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

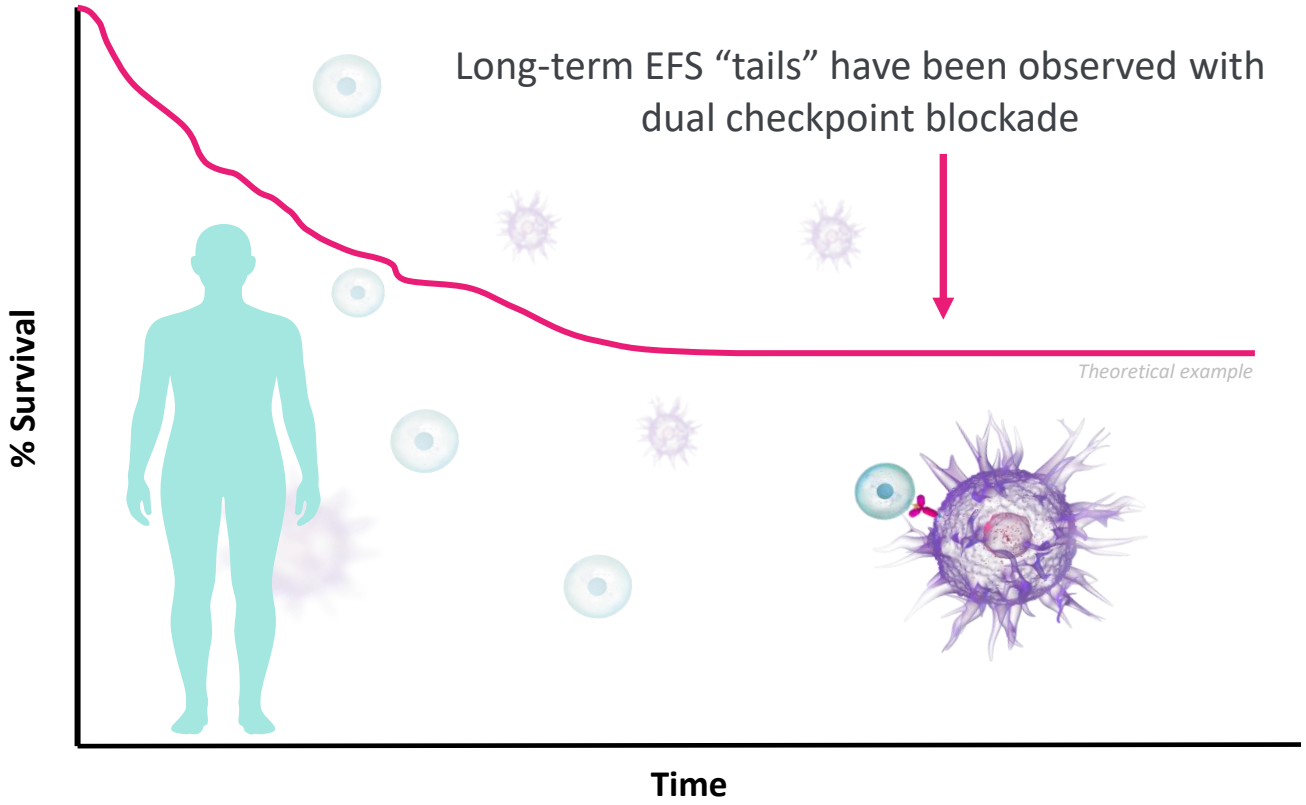
Mortality Under 50 Declines for 4 of 5 Leading Cancers in U.S., but Colorectal Now Top Cancer Killer, New ACS Study Finds

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.

Clinical Precedent Supports Next-Generation CTLA-4 in Neoadjuvant Treatment of “Cold” Tumors



Building on Clinical Success

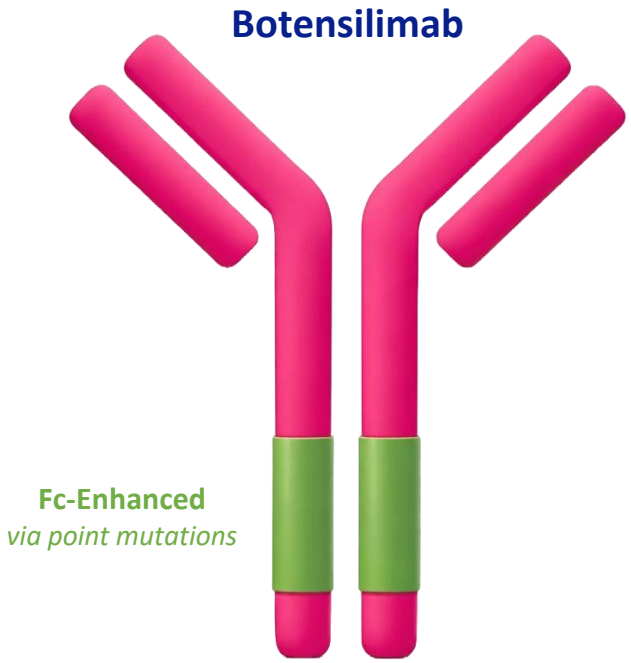
Neoadjuvant PD-1 and CTLA-4 blockade have demonstrated durable event-free survival (EFS) tails in "hot" tumors[1-3]

Perioperative PD-1 and CTLA-4 blockade has been incorporated into treatment guidelines for multiple "hot" tumor types[2-3]

Botensilimab is a next-generation Fc-enhanced CTLA-4 designed to broaden the benefit of neoadjuvant checkpoint blockade to more patients[4-6]

1. Blank CU, et al. *N Engl J Med*. 2024;391(18):1696-1708. **2.** Malik A. New NCCN guidelines add treatment options for NSCLC. *EMJ*. Published November 18, 2025. https://www.emjreviews.com/respiratory/news/new-nccn-guidelines-add-treatment-options-for-nsclc/ **3.** Hollasch M. Neoadjuvant therapy NCCN recommendations take the melanoma field in a new direction. OncLive. Published November 22, 2024. Accessed July 1, 2026. https://www.onclive.com/view/neoadjuvant-therapy-nccn-recommendations-take-the-melanoma-field-in-a-new-direction **4.** Chand D, et al. *Cancer Discov*. 2024;14(12):2407-2429. **1.** Hissong E, et al. Neoadjuvant Botensilimab (BOT) Plus Balstilimab (BAL) in Resectable Mismatch Repair Proficient (pMMR) and Deficient (dMMR) Colorectal Cancer (CRC). Poster presented at the ASCO Gastrointestinal Cancers Symposium. January 23-25, 2025. San Francisco, CA. Abstract #207 . **6.** Ghelardi F, et al. Neoadjuvant botensilimab and balstilimab in colorectal cancer. Poster presented at the ASCO Gastrointestinal Cancers Symposium. January 23-25, 2025. San Francisco, CA. Poster F20

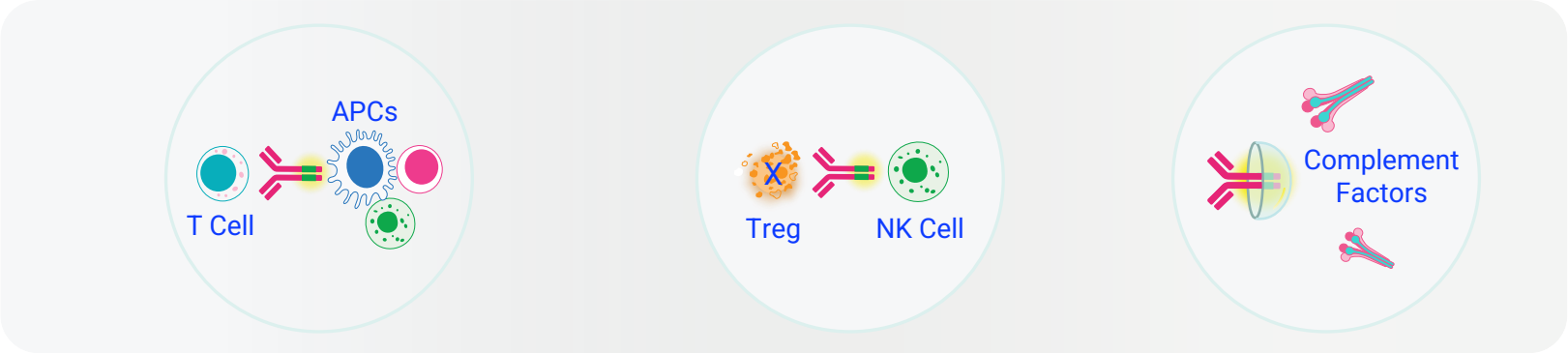
Botensilimab (BOT): A Differentiated Anti–CTLA-4 Designed to Overcome Resistance and Activate Anti-Cancer Immunity[1,2]



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

*Balstilimab (BAL): Agenus' PD-1 inhibitor with properties comparable to approved PD-1 inhibitors[3,4]

BOT's Fc-enhanced design supports multifaceted immune activation:



Activates APCs/Myeloid Cells

Enhances T cell Priming, Activation & Memory

Reduces Intratumoral Regulatory T cells

Avoids Difficult-To-Treat Immune-Related AEs

BOT+BAL converts "cold" tumors into "hot" tumors and has demonstrated clinical activity across 9+ cold and ICI-refractory tumor types[1,2,5,6]

1. Waight JD, et al. *Cancer Cell.* 2018;33(6):1033-1047.e5. **2.** Chand D, et al. *Cancer Discov.* 2024;14(12):2407-2429. **3.** O'Malley DM, et al. *Gynecol Oncol.* 2021;163(2):274-280. **4.** O'Malley DM, et al. *J Clin Oncol.* 2022;40(7):762-771. **5.** Gordon MS, et al. Oral Presentation at ESMO Annual Meeting. Berlin, Germany. 2025. #1517MO. **6.** Atkins MB, et al. Poster presented at Annual ASCO Congress. Chicago, IL, USA. 2026. Poster 259.

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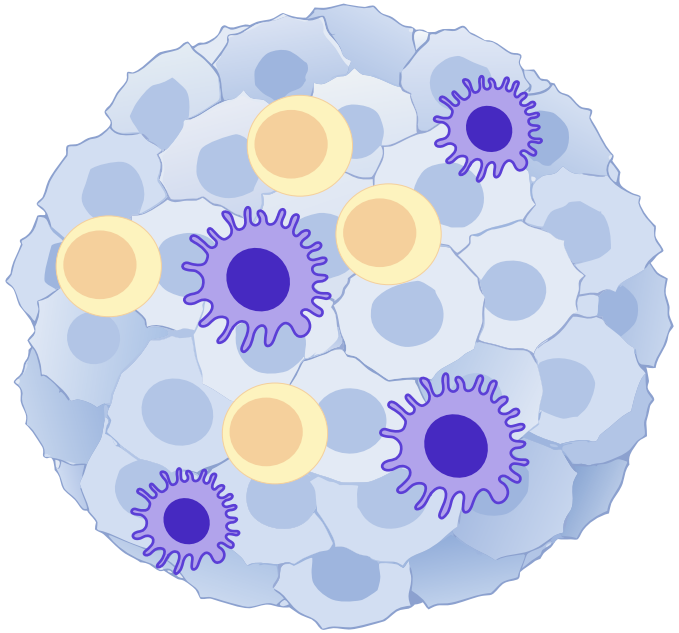
BOT+BAL Is Uniquely Effective in Driving Durable Anti-Cancer Immunity and Converting Tumors from "Cold" (Immune Evading) to "Hot" (Immune Activated)

"Cold" Tumors[1]

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

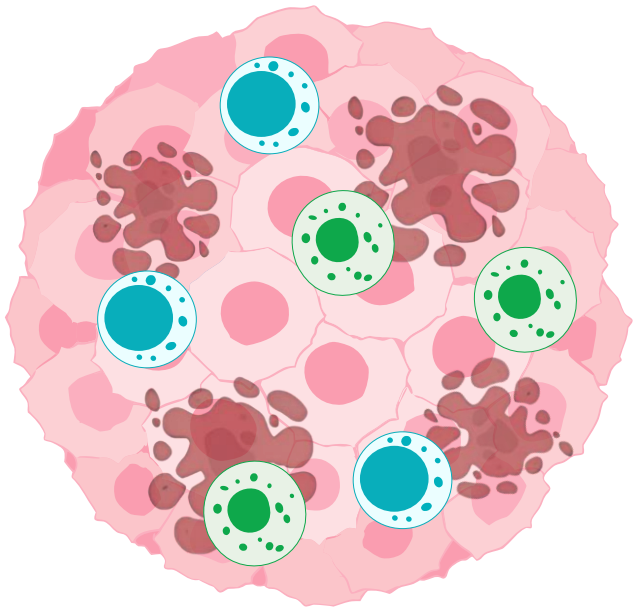
"HOT" Tumors[2]

- Detectable by the immune system
- Sensitive to immunotherapy



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

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



Immunosuppressive cells: Treg, Myeloid cell

Tumor-killing immune cells: CD8 T cell, NK cell

Dying tumor cell

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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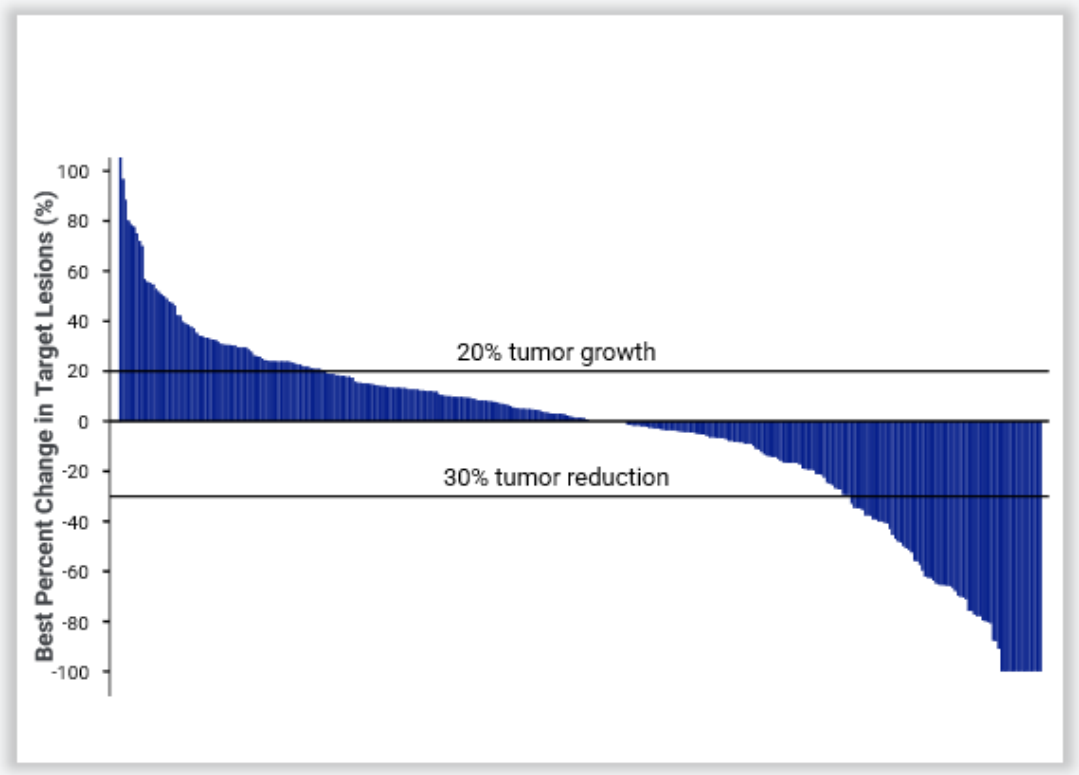
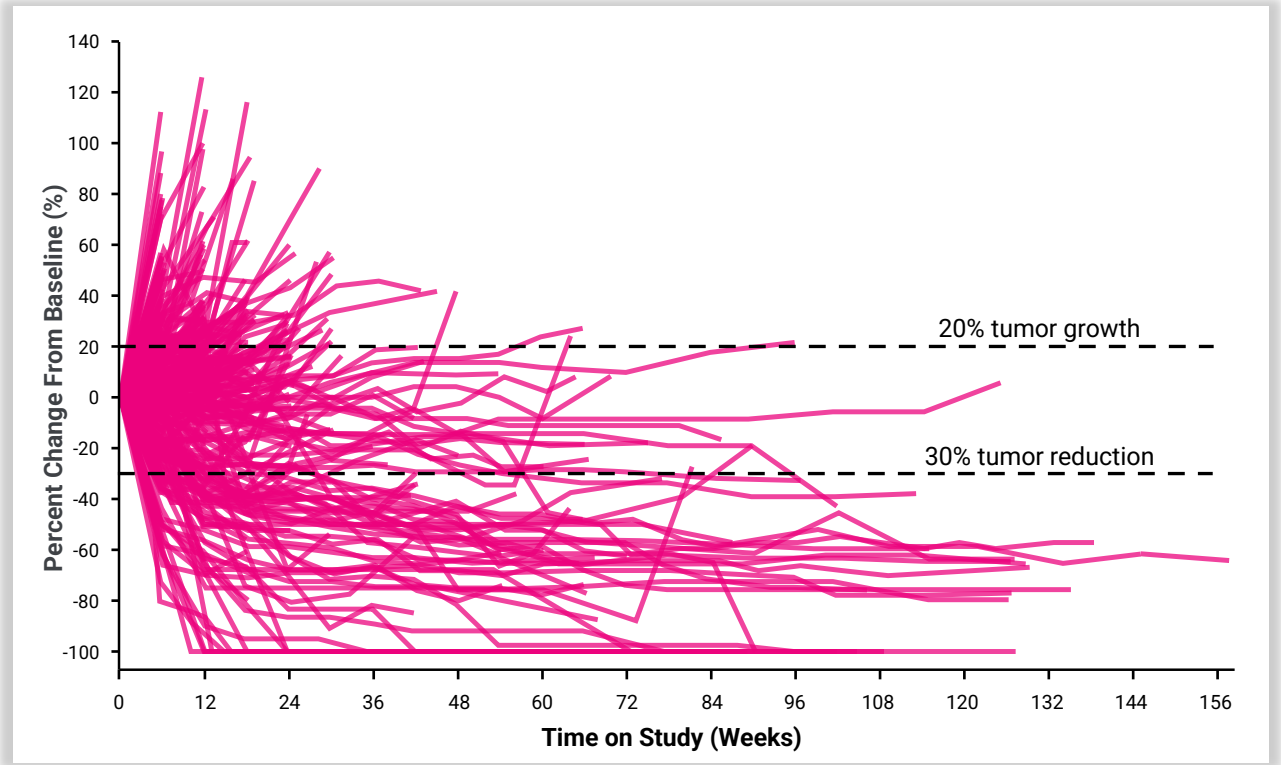
BOT+BAL Phase 1b: Clinical Activity Observed Across 339 Efficacy-Evaluable Patients and Multiple Metastatic Solid Tumor Settings[1]





Objective Response Rate
17%

Median Overall Survival
17.2 months

2-yr Overall Survival
39%

3-yr Overall Survival, MSS CRC Cohort[2]
33%

1.Gordon MS, et al. Oral Presentation at ESMO Annual Meeting. Berlin, Germany. 2025. #1517MO. Data cutoff: 13-MAR-2025.
2. Schlechter B, et al. Poster Presentation at ESMO GI Annual Meeting, Munich, Germany. 2026. #91P. Data cutoff: 13-DEC-2025.

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

Equals Selected ROBBIN Dose (75mg)

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.

Rationale for Strategic Pivot From Metastatic CRC to Neoadjuvant MSS Colon Cancer

FROM

Late-line, refractory metastatic CRC

BOT provides a significant benefit, but in a smaller and more competitive indication.

TO

High-risk Stage II/Stage III MSS colon cancer

No advances in treatment of this patient population in over 20 years since the approval of oxaliplatin.

Why Now

1

Large Market with No Immunotherapy Options

High risk-stage II/III MSS Colon Cancer has ~38,000 treated patients annually in the US[1]

2

Deeper Patient Benefit & Improved Potential Economics with BOT+BAL

Improving outcomes in the curative-intent population supports strong pharmacoeconomic position for BOT pricing

3

Unprecedented Neoadjuvant Responses with BOT+BAL

52 patients in CRC treated with BOT + BAL show deep pathologic responses, continued ctDNA clearance, and no reported recurrences support high likelihood of success in the ROBBIN trial

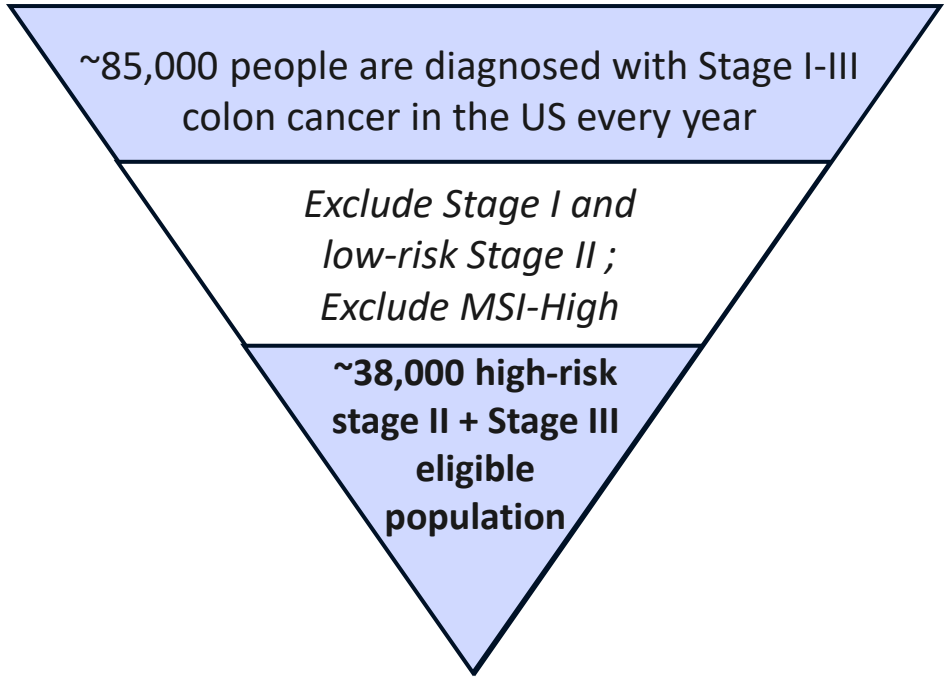
4

Regulatory Alignment, Financing to Approval

ROBBIN Ph3 design aligned with FDA feedback; $340M funds company through projected Full Approval in Neoadjuvant MSS Colon Cancer

1. Epidemiology analysis based on data from SEER, CDC, and Clarivate

Significant Market Opportunity for BOT+BAL in Locally Advanced MSS Colon Cancer



Total US Addressable Market Opportunity for High-Risk Stage II/III MSS Colon Cancer:

>$7 Billion*

- Stage I colon cancer is excluded from ROBBIN
- 15-20% of Stage I and II Patients are MSI-H, and 8-12% of Stage III patients are MSI-H (excluded from ROBBIN study)

- *Expected Target Product Profile for ROBBIN with HR = 0.65:*
- Short neoadjuvant treatment with low adverse event rate
- 3-year EFS improvement from 75% to 82%
- Reduction in oxaliplatin-induced neuropathy

1. Epidemiology analysis based on data from SEER, CDC, and Clarivate; assumes 38,000 eligible patient population annually * $200K for a course of neoadjuvant treatment.

Understanding the Value of Cure in the Context of Early-Stage Colon Cancer

Current oncology therapies in the metastatic setting often deliver 2-6 months of incremental mOS

Conventional Targeted (Non-IO) Oncolytics	Incremental Improvement in Median Overall Survival in Metastatic Settings	Total Life Years Gained per 100 Patients
Major benefit	+ 6 months	**50 years**
Modest benefit	+ 2 months	**< 17 years**

An incremental Event Free Survival of +10% at 3 years in early-stage disease delivers a very different value proposition

Immune Activation, Memory, and Surveillance	Incremental Improvement in Event Free Survival at 3 Years	Incremental Gain in Survival for Those Cured	Total Life Years Gained per 100 Patients
Benefit of **CTLA-4** activated IO-surveillance	**+ 10%**	**+ 20 years**	**+ 200 years**

ILLUSTRATIVE

Measuring the value of immune activation, memory, and surveillance in immunotherapy

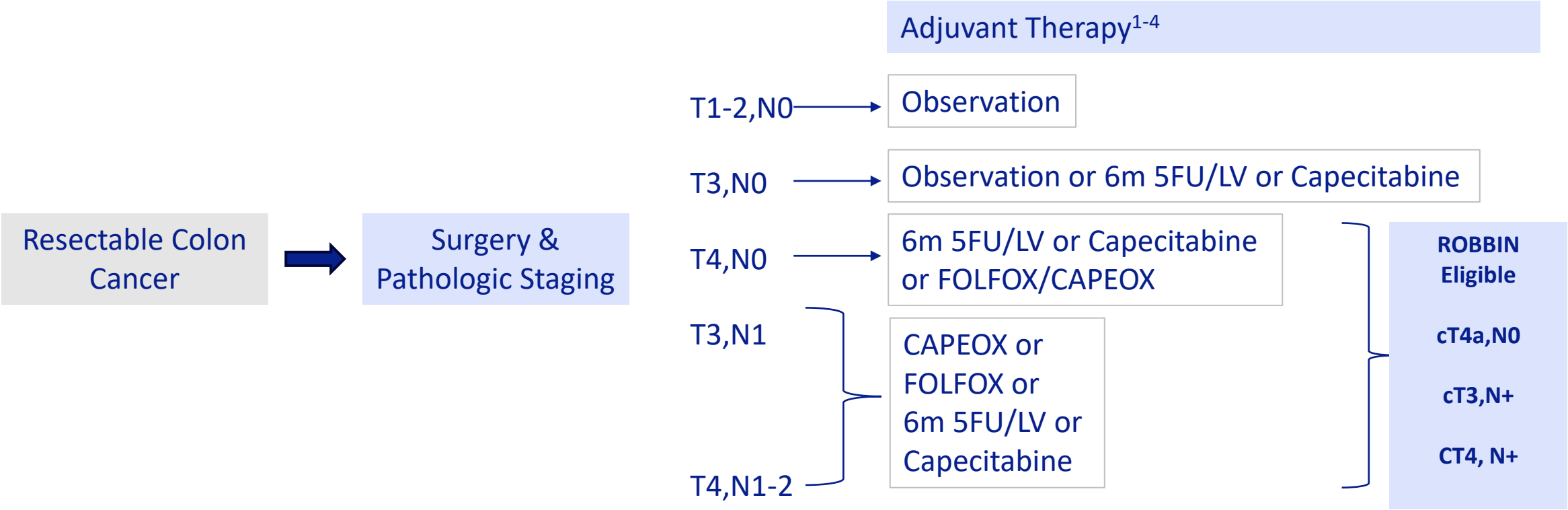
When measuring value in terms of absolute years of incremental human life gained, immune activation, memory, and surveillance in the neoadjuvant setting may deliver **4 to 10-fold greater value** than major conventional oncology breakthroughs in the metastatic setting

4x to 10x

Total years of life gained per 100 patients due to durable clinical benefit driven by immune activation, memory, and surveillance

Source: Agenus analysis

Current Treatment Paradigm for Stage I to Stage III MSS Colon Cancer



1. André T, et al. *J Clin Oncol.* 2009;27(19):3109-3116. **2.** Yothers G, et al. *J Clin Oncol.* 2011;29(28):3768-3774. **3.** Schmoll HJ, et al. *J Clin Oncol.* 2015;33(32):3733-3740. **4.** Grothey A, et al. *N Engl J Med.* 2018;378(13):1177-1188.

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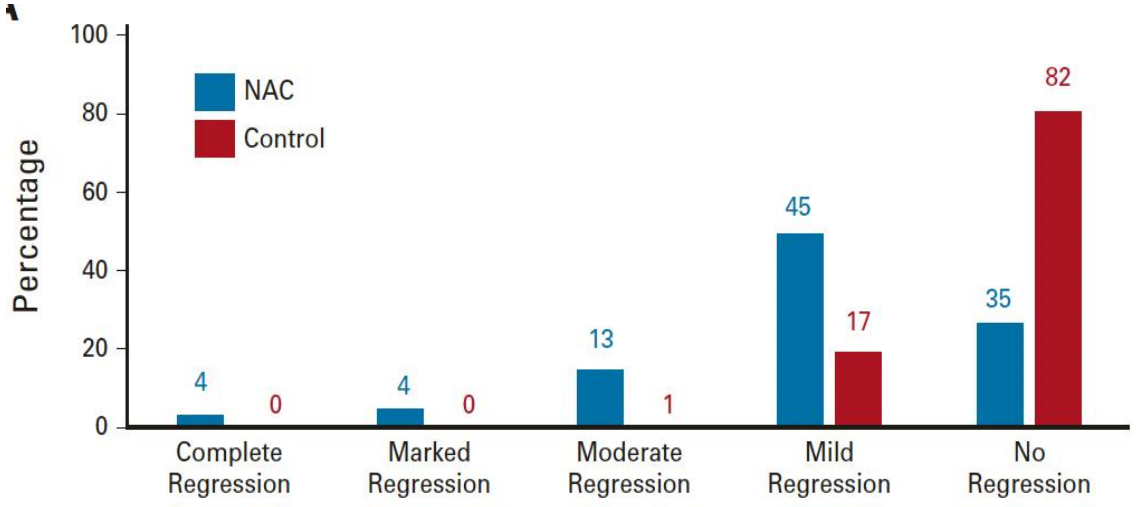
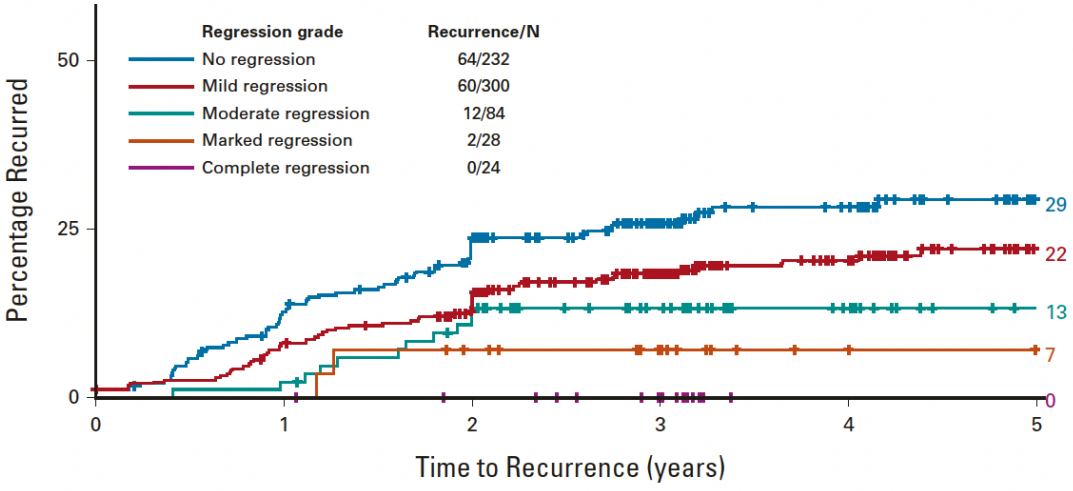
Precedent for Pathologic Response Correlating with Event-Free Survival (EFS) in Stage II/III MSS Colon Cancer: FOxTROT Neoadjuvant Chemotherapy Study

- FOxTROT (N=1,053) established that the depth of pathologic regression is associated with improved recurrence rates (notably no recurrences in patients with complete tumor regression in colon cancer)[1]
- However, the modest depth of regression achieved with neoadjuvant chemotherapy translated into only modest long-term benefit and was insufficient to change the global standard of care

Pathologic Response Assessment



Recurrence Rate by Pathologic Response



1. Morton D, et al. *J Clin Oncol.* 2023;41(8):1541-1552.

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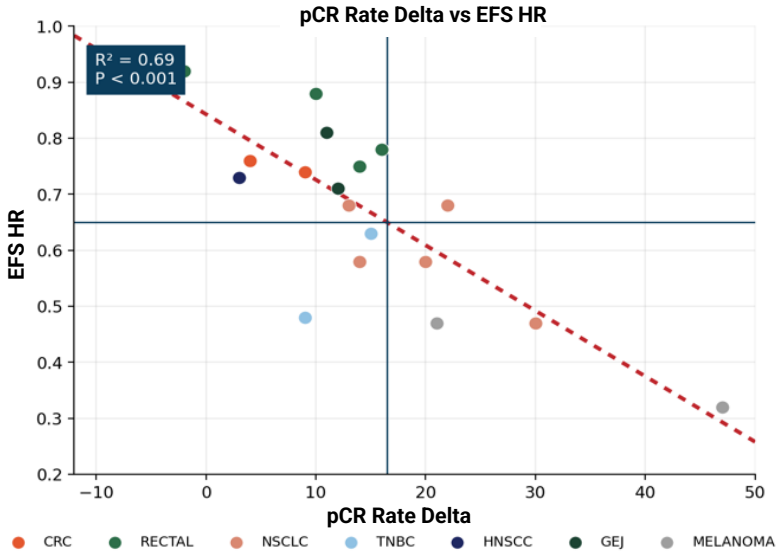
Pathologic Complete Response Rates (pCR) Correlate with EFS: pCR Rates with BOT+BAL in NEST & UNICORN Provide a Strong Signal for Success in ROBBIN

METHODOLOGY:

- 21 neoadjuvant/perioperative trials evaluated using linear regression analysis[1]
- Objective: To examine the relationship between pCR rate delta[2] and EFS hazard ratio (HR) across solid tumors

RESULTS:

- Regression shows that magnitude of pCR rate predicts EFS HR.



pCR Rate Delta	Projected EFS Hazard Ratio
0.0%	0.84
5.0%	0.78
10.0%	0.73
15.0%	**0.67**
20.0%	**0.61**
25.0%	0.55
30.0%	**0.49**
35.0%	0.43
40.0%	0.38
45.0%	0.32
50.0%	0.26

Expected pCR rate in Control arm for ROBBIN = 0% based on FOxTROT, NeoCol, and OPTICAL control arms

A pCR rate of ~17% correlates with a ~0.65 Hazard Ratio (target HR for ROBBIN trial)

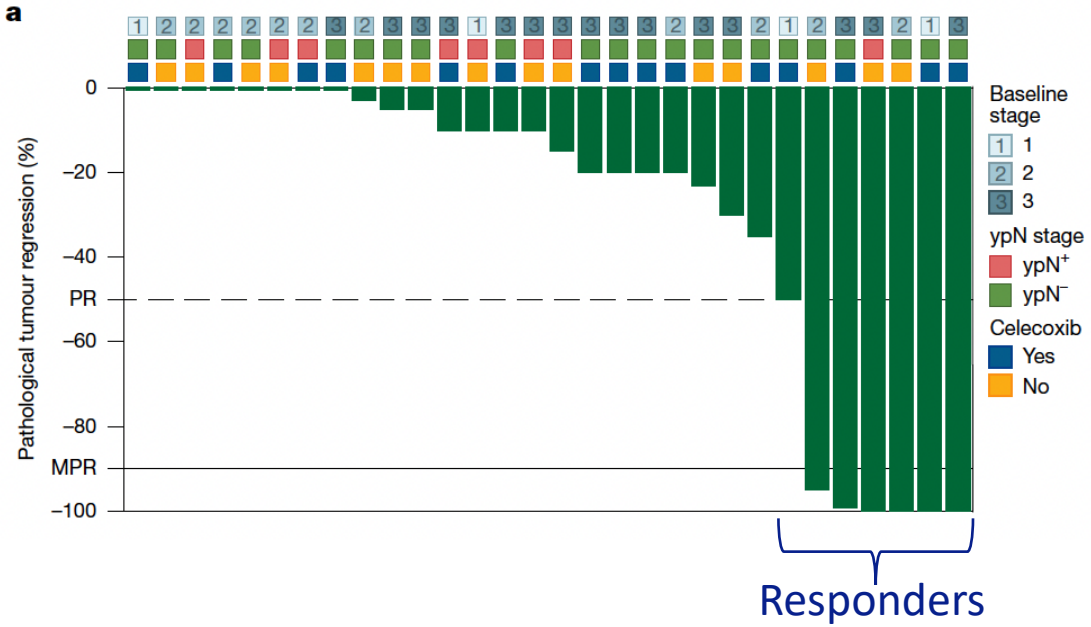
If interim readout of pCR rate in ROBBIN reaches same level as observed in NEST and UNICORN (~30%), this would predict a HR of ~0.50

1. Analysis based on 21 neoadjuvant trials with paired pCR/MPR and EFS or DFS data: Checkmate-816, KEYNOTE-522, Checkmate-77T, KEYNOTE-671, AEGEAN, KEYNOTE-689, MATTERHORN, KEYNOTE-585, NADIM3, GeparNuevo, SWOG S1801, NADINA, FoxTROT, OPTICAL, NeoCol, TORCH, RAPIDO, PRODIGE 23, STELLAR, PROSPECT, and CAO/ARO/AIO-12. **2.** pCR rate delta defined as the difference in pathologic complete response rate between the Experimental and Control arms in each of the 21 analyzed neoadjuvant trials. Note some HRs are estimated based on study results.

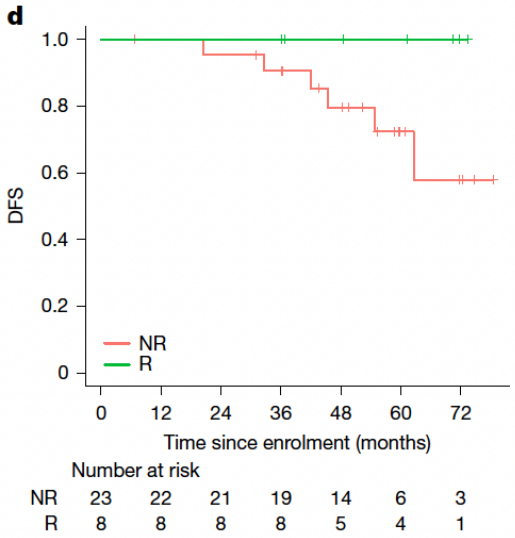
Precedent for I/O-Driven Pathologic Response and EFS: Ipilimumab + Nivolumab Neoadjuvant Treatment in MSS Colon Cancer (NICHE Study)

- The NICHE study evaluated neoadjuvant ipilimumab + nivolumab ± celecoxib in 31 patients with MSS Colon Cancer
- 30 patients underwent surgery and were assessable for pathologic response[1]
- 10% of patients had a pCR (0% residual tumor), and 23% had a Pathologic Response (≤50% residual tumor)

Pathologic Response Assessment



Recurrence over time for Non-Responders (n=23) vs Responders (n=8)



Event-free survival at 3 years was 93%. No recurrences in patients who had a response (≥50% tumor regression)

1. Tan P. et al. Nature 2025;648:726-735.

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Neoadjuvant CRC: BOT±BAL Evaluated Across Multiple Pre-Surgical Treatment Schedules

NEST (N=24)[1]

NEST 1 (*~4 weeks to surgery*)

BOT (75mg)

BAL *BAL*

Surgery

0 2

WEEKS

NEST 2 (*~8 weeks to surgery*)

BOT (75mg)

BAL *BAL* *BAL* *BAL*

Surgery

0 2 4 6

WEEKS

UNICORN (N=56)[2]

~5 weeks to surgery

BOT (75mg)

Surgery

0 2

WEEKS

~5 weeks to surgery

BOT (75mg)

BAL *BAL*

Surgery

0 2

WEEKS

1. Shah M et al. Neoadjuvant Botensilimab/Bals⍰limab for localized mismatch repair proficient and deficient colon cancer: Results of the NEST phase 2 clinical trial. Clin Canc Res Aug 2026 ePub.
2. **2.** Ghelardi F, et al. Neoadjuvant botensilimab and balstilimab in colorectal cancer. Poster presented at the ASCO Gastrointestinal Cancers Symposium. January 23-25, 2025. San Francisco, CA. Poster F20

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Neoadjuvant CRC: Patient Populations Reflect Clinically Advanced Stage II and Stage III Disease Across MSS and MSI-H Settings

NEST[1]

Characteristic	NEST-1 (n=10)	NEST-2 (n=14)
Age, median, years (Q1, Q3)	57 (35, 69)	69 (59, 75)
Male : female ratio	5:5	8:6
Clinical stage, n (%)		
Early (T1/T2)	1 (10)	10 (71)
Advanced (T3+)	9 (90)	4 (29)

UNICORN[2]

Characteristic	pMMR BOT (n=14)	pMMR BOT + BAL (n=14)
Age, median, years (IQR)	69 (56–75)	65 (57–70)
Male, n (%)	6 (43)	6 (43)
Primary tumor sidedness, n (%)		
Left colon	8 (57)	6 (43)
Right colon	6 (43)	8 (57)
Adjuvant chemotherapy, n (%)		
Yes	10 (71)	8 (57)
Fluoropyrimidine-based	4 (29)	1 (7)
Oxaliplatin + fluoropyrimidine	6 (42)	7 (50)
No	4 (29)	6 (43)

1. Shah M et al. Neoadjuvant Botensilimab/Balstilimab for localized mismatch repair proficient and deficient colon cancer: Results of the NEST phase 2 clinical trial. Clin Canc Res Aug 2026 ePub.
2. 2. Ghelardi F, et al. Neoadjuvant botensilimab and balstilimab in colorectal cancer. Poster presented at the ASCO Gastrointestinal Cancers Symposium. January 23-25, 2025. San Francisco, CA. Poster F20

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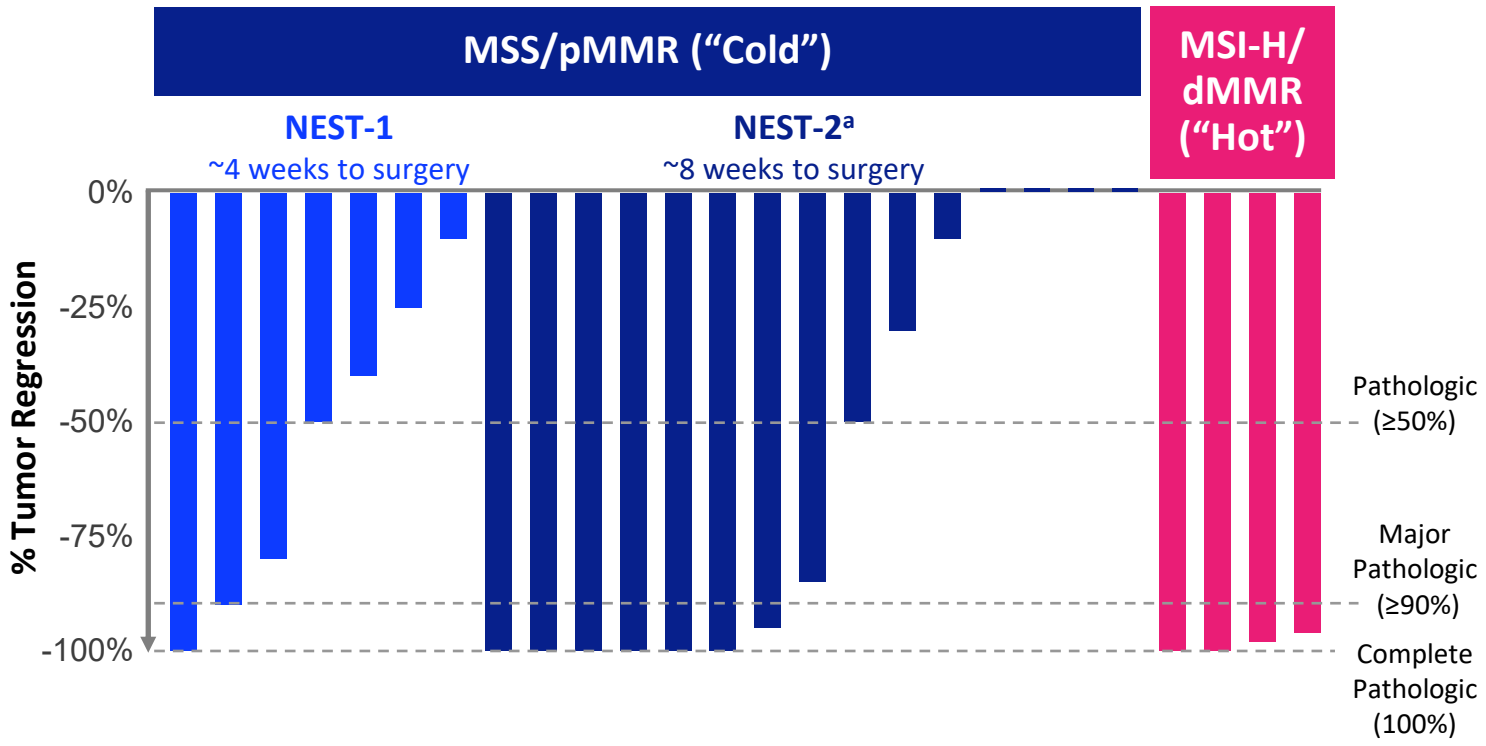
NEST Trial: Marked Tumor Reductions with 1 BOT Dose + 2-4 BAL Doses

Stage II/III (Pre-Surgery and/or Chemo or "Neoadjuvant") Patients Treated with BOT+BAL



No recurrences reported with BOT+BAL
(median follow-up 23–32 months)

Topline Results

(1 dose BOT + 2-4 doses BAL)

MSS CRC (n=22 tumors)

59% Pathologic Response
(*Ipi+Nivo: 23%*)[b,2]

41% Major Pathologic Response
(*Ipi+Nivo: 20%*)[b,2]

32% Complete Pathologic Response
(*Ipi+Nivo: 10%*)[b,2]

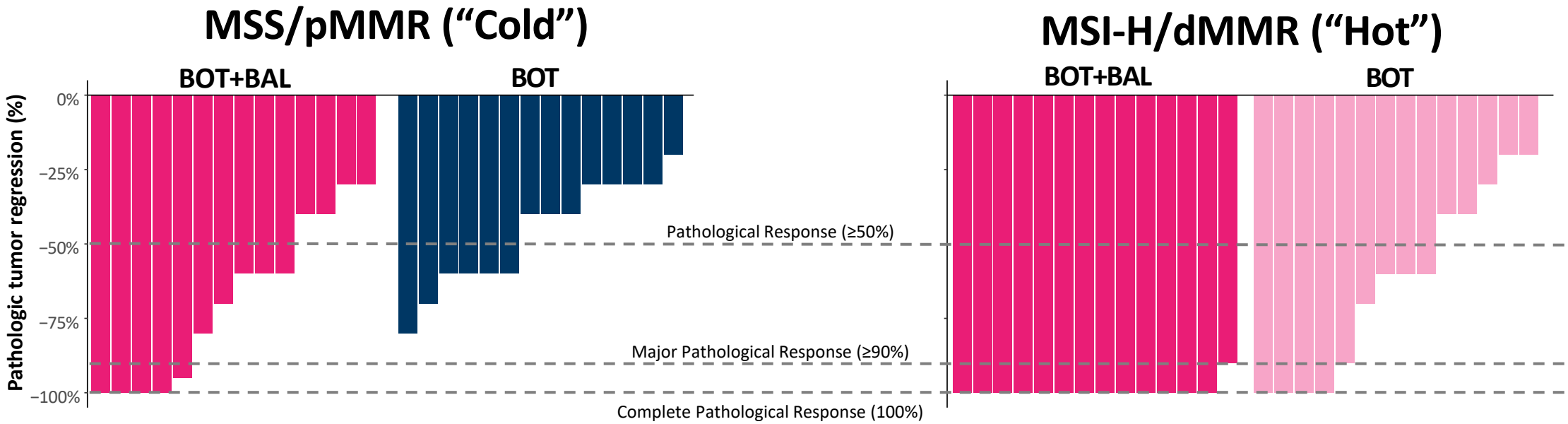
MSI-H/dMMR CRC (n=4 tumors)

100% Major Pathologic Response
(*Ipi+Nivo: 95%*)[b,3]

ClinicalTrials.gov Identifier: NCT05571293. [a]Two patients in NEST-2 each had synchronous primary tumors (each tumor was analyzed separately for percent tumor regression). [b]Cross-trial comparisons are descriptive; differences in eligibility, assessments, and data cutoffs may confound comparisons; 1. Shah M et al. Neoadjuvant Botensilimab/Balsilimab for localized mismatch repair proficient and deficient colon cancer: Results of the NEST phase 2 clinical trial. Clin Canc Res Aug 2026 ePub. 2. Tan P. et al. Nature 2025;648:726-735. 3. Chalabi M, et al. *N Engl J Med.* 2024;390(21):1949-1958.

UNICORN Trial: Consistent Demonstration of Benefit with BOT+BAL

56 Patients Treated with BOT Mono (n=28) and BOT+BAL Combo (n=28) ; Further Support for Contribution of Components



Response	BOT+BAL (n=14)	BOT (n=14)
Pathologic	71%	43%
Major Pathologic	36%	0
Complete Pathologic	29%	0

Response	BOT+BAL (n=14)	BOT (n=14)
Pathologic	100%	64%
Major Pathologic	100%	36%
Complete Pathologic	93%	29%

No recurrences reported with BOT+BAL (median follow-up 6-9 months)

Ghelardi F, et al. Neoadjuvant botensilimab and balstilimab in colorectal cancer. Poster presented at the ASCO Gastrointestinal Cancers Symposium. January 23-25, 2025. San Francisco, CA. Poster F20 .

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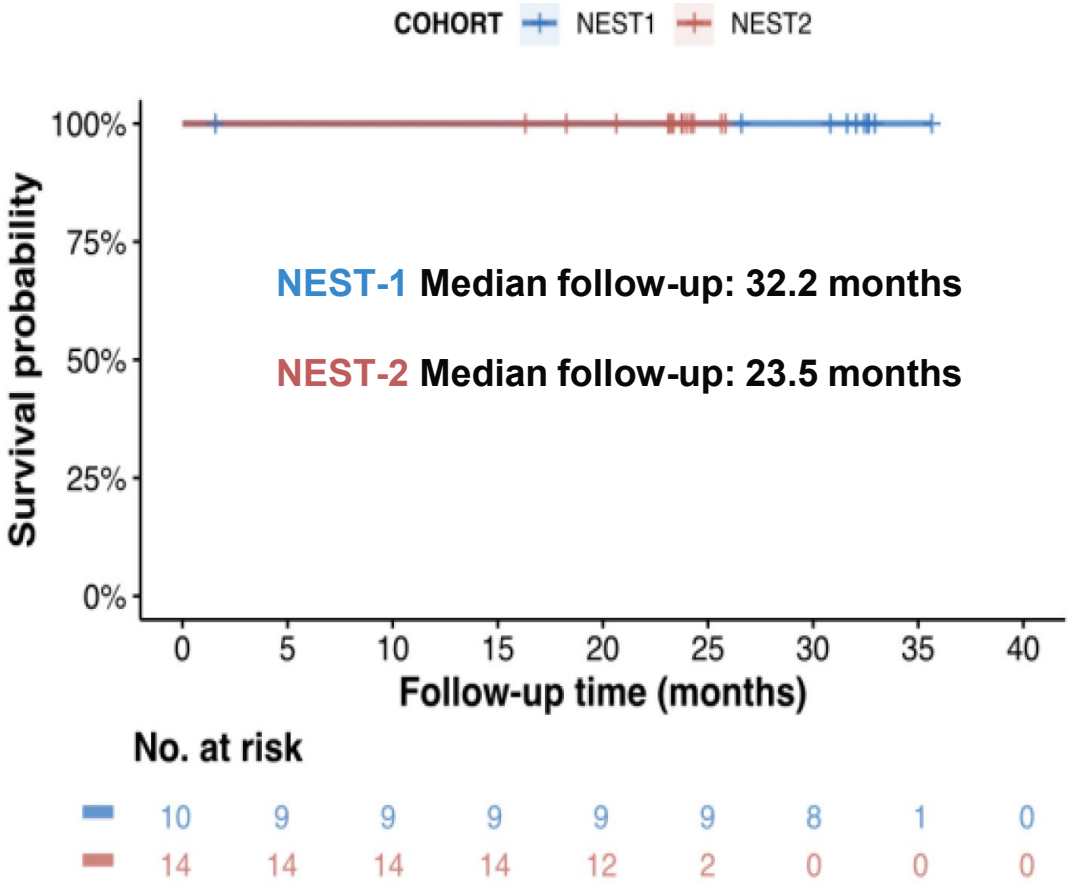
No Disease Recurrence Reported in 38 BOT+BAL Treated Patients Across NEST and UNICORN

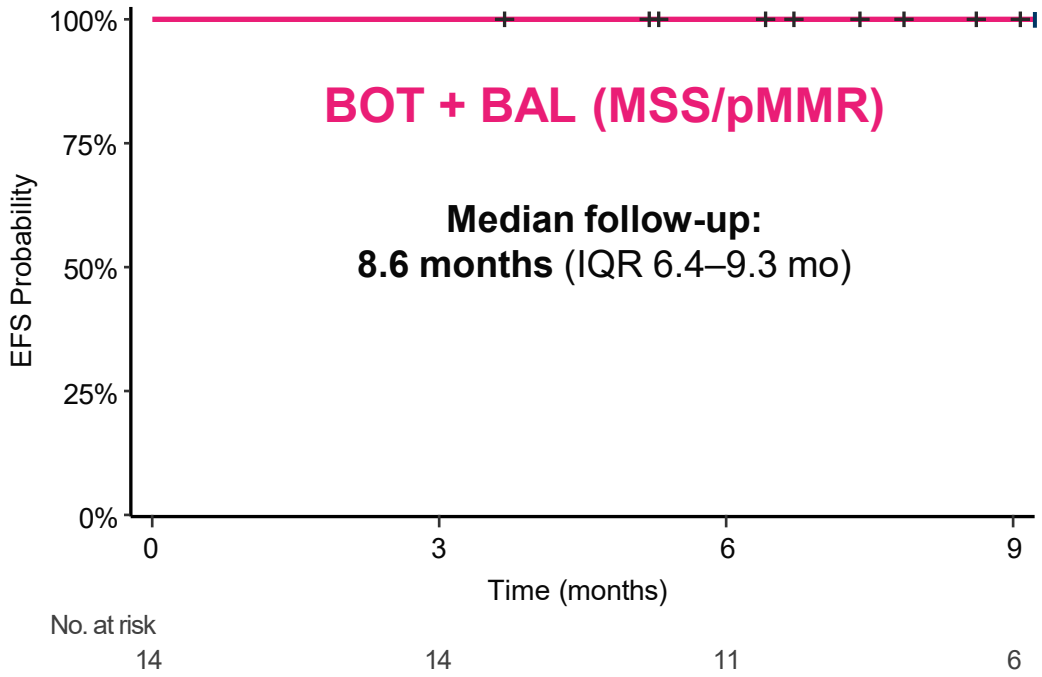
NEST[1]

Event-Free Survival (N=24)



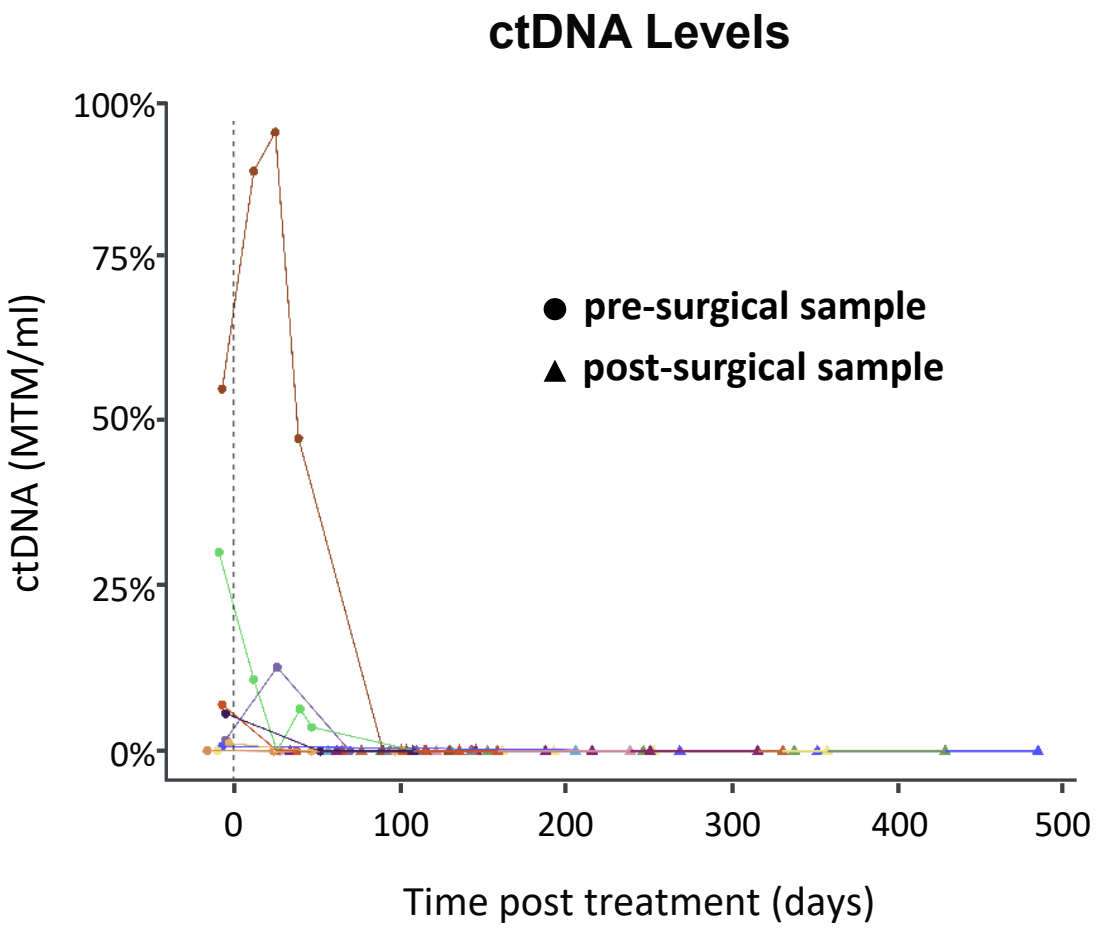
UNICORN[2]

Event-Free Survival (N=14)



1. Shah M et al. Neoadjuvant Botensilimab/Bals⍰limab for localized mismatch repair proficient and deficient colon cancer: Results of the NEST phase 2 clinical trial. Clin Canc Res Aug 2026 ePub.
2. 2. Ghelardi F, et al. Neoadjuvant botensilimab and balstilimab in colorectal cancer. Poster presented at the ASCO Gastrointestinal Cancers Symposium. January 23-25, 2025. San Francisco, CA. Poster F20

No ctDNA Recurrences Observed in NEST



 Shah M et al. Neoadjuvant Botensilimab/Balsilimab for localized mismatch repair proficient and deficient colon cancer: Results of the NEST phase 2 clinical trial. Clin Canc Res Aug 2026 ePub.

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NEST Safety Summary: Favorable Safety Profile With No Surgical Delays and No Unresolved High-Grade irAEs[1,2]

Treatment-Related Adverse Events

Treatment-Related Adverse Event*	NEST-1 (n=10)		NEST-2 (n=14)	
	Grade 2	Grade 3	Grade 2	Grade 3
Fever	1 (10%)	0	2 (14%)	0
Fatigue	0	1 (10)	1 (7%)	0
Colitis/Diarrhea	0	1 (10%)	3 (21%)	2 (14%)
Anemia	0	0	1 (7%)	0
Nausea	0	0	1 (7%)	0
Myositis	0	0	1 (7%)	0

All data shown as n (%).
*Adverse events possibly, probably, or definitely related to BOT/BAL.

- There were no grade 4 irAEs, and no unresolved high-grade irAEs
- There were no delays in surgery in any patient

Shah M et al. Neoadjuvant Botensilimab/Bals□limab for localized mismatch repair proficient and deficient colon cancer: Results of the NEST phase 2 clinical trial. Clin Canc Res Aug 2026 ePub.

UNICORN Safety Summary: Manageable Safety Profile with Limited High-Grade irAEs and Minimal Impact on Surgical Timing

Immune-Mediated Adverse Events

	Botensilimab + Balstilimab (N=56)	
	Any grade N (%)	Grade ≥3 N (%)
Any IMAE	22 (39%)	1 (2%)
Flu-like syndrome	7 (13%)	0
Fatigue	3 (5%)	0
Pruritus	3 (5%)	0
Skin Rash	3 (5%)	0
Thyroiditis	3 (5%)	1 (2%)
Diarrhea	2 (4%)	0
Hepatitis	1 (2%)	0
Nephritis	1 (2%)	0
Myalgias	1 (2%)	0
Mucositis	1 (2%)	0

- Timely surgery was performed in all but 1 patient
  - 10-day delay in surgery due to treatment-related Gr 3 hyperthyroidism

Ghelardi F, et al. Neoadjuvant botensilimab and balstilimab in colorectal cancer. Poster presented at the ASCO Gastrointestinal Cancers Symposium. January 23-25, 2025. San Francisco, CA. Poster F20

NEST and UNICORN Safety Summary: Favorable Toxicity Profile with Low Incidence of High-Grade irAEs and No Significant Surgical Delays

NEST[1]

Treatment-Related Grade 3	BOT+BAL (n=24)
Fatigue	1 (4%)
Colitis/Diarrhea	3 (13%)

No delays in surgery in any patients and no Grade 4 AEs

UNICORN[2]

Immune-mediated AE Grade ≥3	BOT+BAL (N=28)
Hyperthyroidism	1 (2%)

1 surgery delay (10 days)

Among a total of 52 Patients treated with BOT + BAL:

Low rate of grade ≥3 AEs

One short surgical delay due to immune-mediated hyperthyroidism

1. Shah M et al. Neoadjuvant Botensilimab/Bals□limab for localized mismatch repair proficient and deficient colon cancer: Results of the NEST phase 2 clinical trial. Clin Canc Res Aug 2026 ePub.
2. 2. Ghelardi F, et al. Neoadjuvant botensilimab and balstilimab in colorectal cancer. Poster presented at the ASCO Gastrointestinal Cancers Symposium. January 23-25, 2025. San Francisco, CA. Poster F20

Setting the Stage for the ROBBIN Phase 3 Study: Neoadjuvant BOT+BAL Demonstrates Deep and Durable Responses in Stage II/III MSS CRC

Depth of Pathologic Response in MSS CRC

	BOT+BAL (NEST[1])	BOT+BAL (UNICORN[2])	Neoadj Chemo (FOxTROT[a])	IPI/NIVO (NICHE[b])
Complete PR (100% tumor reduction)	32%	29%	4%	10%
Major PR (≥90% tumor reduction)	41%	36%	8%	23%
Path Response (≥50% tumor reduction)	59%	71%	23%	29%

No Disease Recurrence Reported with BOT+BAL

BOT+BAL[1,2] (NEST & UNICORN)	Adjuvant Chemo (FOxTROT Control[a])
0% recurrence at 9–18-month follow-up	**25% recurrence** at 3 years

[a]Neoadjuvant FOLFOX in the FOxTROT trial; Morton D, et al. *J Clin Oncol.* 2023;41(8):1541-1552. [b]Neoadjuvant ipilimumab and nivolumab in the NICHE trial; Tan P. et al. *Nature* 2025;648:726-735.
Complete pathological regression (pCR) is defined as 100% tumor regression; major pathologic regression (mPR) as at least 90% tumor regression; and pathologic regression as at least 50% tumor regression.
1. Shah M et al. Neoadjuvant Botensilimab/Balstilimab for localized mismatch repair proficient and deficient colon cancer: Results of the NEST phase 2 clinical trial. Clin Canc Res Aug 2026 ePub. **2.** Ghelardi F, et al. Neoadjuvant botensilimab and balstilimab in colorectal cancer. Poster presented at the ASCO Gastrointestinal Cancers Symposium. January 23-25, 2025. San Francisco, CA. Poster F20

ROBBIN* Phase 3: Neoadjuvant BOT+BAL in High-Risk Stage II and Stage III MSS Colon Cancer

Trial Size
- N=850

Patient Population
- High Risk Stage II (cT4aN0M0) and Stage III (cT3-T4Na+M0) resectable MSS colon cancer
- ECOG 0 or 1
- Age ≥18 years

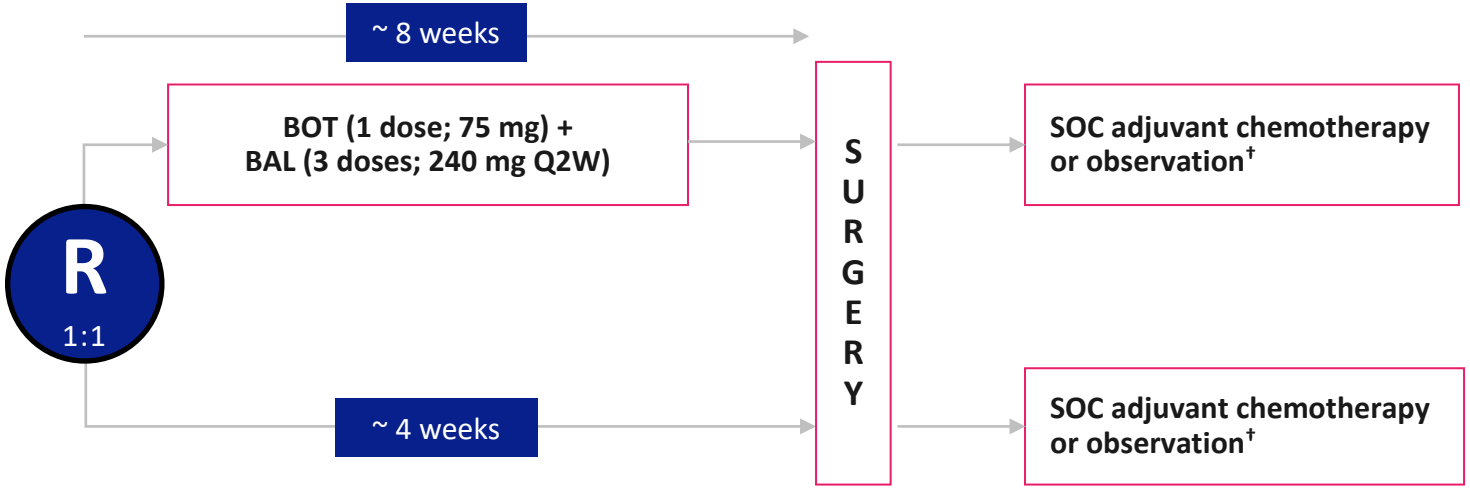
Target Endpoints

Primary: Event-free survival (EFS)

Key Secondary:
- Overall survival
- Circulating tumor DNA (ctDNA) negativity

Additional Secondary:
- HR-QoL
- Safety
- Sparse pharmacokinetic analyses

Exploratory Endpoints
- Pathologic response rate
- Pathologic response correlation with EFS and OS
- Utilization of adjuvant chemo
- Biomarkers



†Adjuvant chemotherapy or observation in both arms to be decided by investigator per standard of care based on pathologic stage and society guidelines.

Powering Assumptions
- 80% power assuming EFS HR=0.65

Analyses
- Interim analysis for EFS at 75% Information Fraction
- Final analysis for EFS at 100% Information Fraction

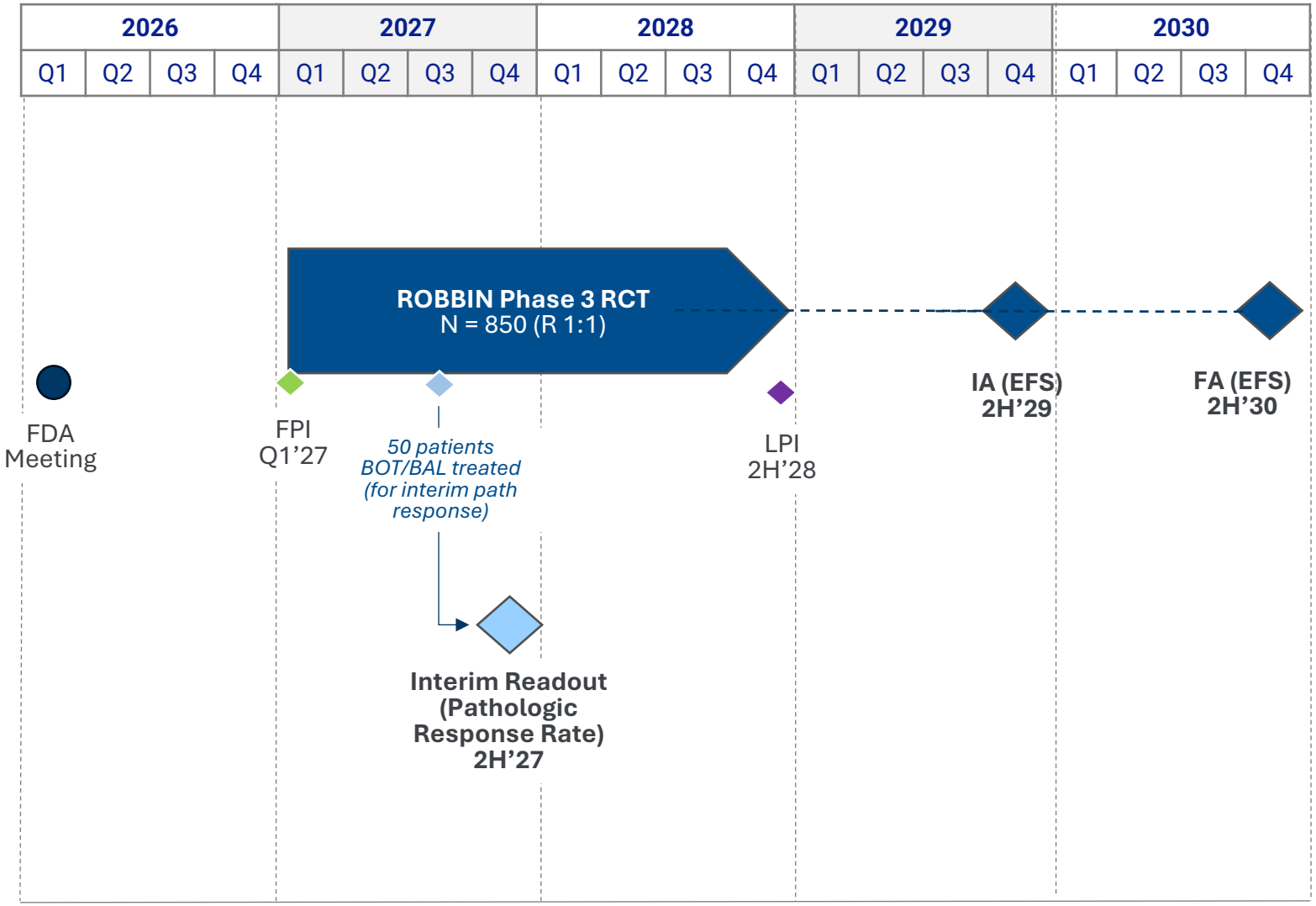
*A Phase 3 **R**andomized, **O**pen-Label Study of **B**otensilimab Plus **B**alstilimab **I**n the **N**eoadjuvant Setting followed by Standard of Care Versus Standard of Care Alone in Previously Untreated High-Risk Stage II and Stage III Non–MSI-H/dMMR Colon Cancer (**ROBBIN** Study)

ROBBIN Phase 3 Trial Design Aligned with FDA Feedback

The following key elements of the Phase 3 study are aligned with FDA feedback:

- The proposed patient population of Stage II (cT4aN0M0) and Stage III (cT3-T4Na+M0) colon cancer that is not MSI-H/dMMR
- The proposed experimental arm of neoadjuvant BOT and BAL followed by surgery and guideline-directed adjuvant chemotherapy based on pathologic staging
- The control arm based on the current standard of care of surgery followed by guideline-directed adjuvant chemotherapy based on pathologic staging
- The primary endpoint of EFS and the proposed interim analysis plan

Projected Timeline for ROBBIN Phase 3 Study



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Consistent Adoption of BOT+BAL in Paid Compassionate Access Programs (AAC & NPP)

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

Pre-Commercial Product Revenue*	
Q4’25	Q1’26
$3.2 M	$4.6 M

*Unpromoted Product Revenues - Source: Agenus 2025 Results: https://investor.agenusbio.com/news/news-details/2026/Agenus-Reports-2025-Results-BOTBAL-Advances-to-Phase-3-and-Early-Access-Programs-Expand-Globally-with-Initial-Revenues-Recognized/default.aspx
Agenus Q1 2026 Results: https://investor.agenusbio.com/news/news-details/2026/Agenus-Reports-First-Quarter-2026-Financial-Results-and-Highlights-BOTBAL-Execution-Across-Global-Access-and-Phase-3-Development/default.aspx

Fully Funded, FDA-aligned Phase 3 Trial Testing Neoadjuvant BOT+BAL in MSS Colon Cancer, a Multi Billion-Dollar Opportunity in the US

- July financing of $85M upfront and up to $340M in total, focused on BOT+BAL opportunity in high-risk Stage II and Stage III MSS Colon Cancer, >$7 Billion TAM in the US[1]

- Capital will be directed to an FDA-aligned pivotal Phase 3 study ("ROBBIN") of neoadjuvant BOT+BAL for MSS Colon Cancer (n=850, Randomized 1:1, Primary Endpoint EFS)

- To focus company resources, Agenus is discontinuing support for the ongoing BATTMAN Phase 3 study

- Key upcoming catalysts for Neoadjuvant BOT+BAL:
  - Publications for NEST & UNICORN anticipated 2H of 2026
  - NEOASIS Data Update anticipated 2H of 2026
  - ROBBIN trial initiation; First patient in anticipated Q1 of 2027
  - Interim pathologic response data: anticipated second half of 2027
  - Interim analysis of EFS: anticipated second half of 2029
  - Final analysis of EFS: anticipated second half of 2030

1. Epidemiology analysis based on data from SEER, CDC, and Clarivate; assumes 38,000 eligible patient population annually * $200K for a course of neoadjuvant treatment.

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