agenus

NEWS RELEASE

Agenus Announces Updated NEST Phase 2 Publication Reporting Deep Pathologic Responses and No Observed Recurrences with Neoadjuvant BOT+BAL in Resectable Colon Cancer

2026-08-26

- No colorectal cancer recurrences observed at updated median follow-up of 32.2 months in NEST-1 and 23.5 months in NEST-2
- In pMMR/MSS tumors, neoadjuvant BOT+BAL achieved 59% pathologic response, including 41% major pathologic response and 32% pathologic complete response
- 88% of evaluable patients cleared ctDNA before surgery, with no delays to planned surgical resection
- Longer follow-up and immune analysis provide clinical and biological support for Agenus' planned global Phase 3 ROBBIN trial in curative-intent MSS/pMMR colon cancer

LEXINGTON, Mass.--(BUSINESS WIRE)-- **Agenus** Inc. (Nasdaq: AGEN), a leader in immuno-oncology innovation, today announced the peer-reviewed publication of updated results from the investigator-sponsored Phase 2 NEST trial evaluating neoadjuvant botensilimab (BOT), Agenus' multifunctional, Fc-enhanced anti-CTLA-4 antibody, and balstilimab (BAL), Agenus' anti-PD-1 antibody, in patients with resectable colon cancer. The manuscript, titled "Neoadjuvant botensilimab/balstilimab for localized mismatch repair proficient and deficient colon cancer: Results of the NEST phase 2 clinical trial," was published in Clinical Cancer Research and is available **here**.

Earlier findings from NEST were presented at the 2025 ASCO Gastrointestinal Cancers Symposium. The publication provides longer follow-up and a fuller peer-reviewed analysis of tumor responses, circulating tumor DNA (ctDNA) dynamics, disease-free follow-up and immune changes in the tumor microenvironment.

At the March 31, 2026 data cutoff, no colorectal cancer recurrences had been observed, with median follow-up of

32.2 months in NEST-1 and 23.5 months in NEST-2. Among 22 mismatch repair proficient/microsatellite stable (pMMR/MSS) tumors, 59% achieved a pathologic response, including 41% with a major pathologic response and 32% with a pathologic complete response.

MSS/pMMR tumors represent approximately 85% of early-stage colorectal cancers and have historically derived limited benefit from conventional immunotherapy treatment, particularly in metastatic disease.[i,ii] In localized colon cancer, treatment remains centered on surgery and chemotherapy, creating a need for approaches that may deepen response and reduce recurrence risk. Administering immunotherapy before surgery offers a distinct biological opportunity to activate the immune system while the primary tumor, tumor-draining lymph nodes and surrounding immune microenvironment remain intact.

The publication adds peer-reviewed clinical and biological support for Agenus' previously announced decision to prioritize BOT+BAL in earlier-stage, curative-intent MSS colon cancer. Agenus is advancing ROBBIN, a planned global randomized Phase 3 trial evaluating neoadjuvant BOT+BAL followed by standard of care versus standard of care alone in previously untreated patients with high-risk Stage II or Stage III MSS colon cancer, with event-free survival as the primary endpoint. NEST's deep tumor regression, pre-surgical ctDNA clearance, preserved surgical timing and no observed recurrences at longer follow-up supports the clinical hypothesis ROBBIN is designed to test.

"NEST provides important context for Agenus' strategic focus on neoadjuvant BOT+BAL in MSS colon cancer," said Steven O'Day, M.D., Chief Medical Officer of Agenus. "With longer follow-up now extending beyond two years across both NEST cohorts, the findings show BOT+BAL can generate deep tumor responses and immune activation before surgery, without delaying surgery. These results strengthen the rationale for our phase 3 ROBBIN trial and for evaluating BOT+BAL in a curative-intent setting, where the goal is to reduce the risk of recurrence and improve long-term outcomes."

NEST was a single-center, open-label, single-arm Phase 2 study that enrolled 24 eligible patients with 26 resectable colorectal tumors, including 22 pMMR/MSS tumors and four dMMR/MSI-H tumors. The study evaluated two pre-surgical treatment intervals; approximately four weeks in NEST-1 and approximately eight weeks in NEST-2. Patients in both cohorts proceeded to planned surgical resection without treatment-related delays.

NEST Results

Tumor responses in pMMR/MSS disease

Among 22 pMMR/MSS tumors, neoadjuvant BOT+BAL achieved:

- 59% pathologic response rate (pOR): defined as pathologic complete response, major pathologic response or

partial response

- 41% major pathologic response rate (MPR): 10% or less viable tumor remaining
- 32% pathologic complete response rate (pCR): no viable tumor or adjacent lymph nodes found at surgery

The manuscript cites previously reported MPR rates of approximately 19% to 20%, including pCR of approximately 10%, with first-generation CTLA-4/PD-1 combination therapy in pMMR colon cancer. Cross-trial comparisons should be interpreted cautiously because of differences in study design, patient population and follow-up.

Tumor responses in dMMR/MSI-H disease

All four dMMR/MSI-H tumors achieved an MPR, including two pCR and two additional tumors with near-complete tumor regression of 98% and 99%.

ctDNA clearance before surgery

Among patients with detectable circulating tumor DNA (ctDNA) at baseline and available pre-surgical samples, 88% cleared ctDNA prior to surgery. ctDNA remained undetectable following resection in all patients evaluated.

No observed recurrences at longer follow-up

At the March 31, 2026 data cutoff, no colorectal cancer recurrences had been observed. Median follow-up was 32.2 months in NEST-1 and 23.5 months in NEST-2. For external context, the FOxTROT study of neoadjuvant chemotherapy reported a two-year recurrence rate of 16.9%. Cross-trial comparisons should be interpreted cautiously.

Immune remodeling and activation in the tumor microenvironment

Analyses of paired tumor samples showed coordinated remodeling of the tumor immune microenvironment in responding tumors, characterized by increased CD8+ T-cell infiltration, reduced FOXP3+ regulatory T cells, increased CD8+/Treg ratios and spatial reorganization of immune cells within the tumor.

These findings provide biological support for BOT's multifunctional, Fc-enhanced mechanism, which extends beyond conventional checkpoint blockade to actively remodel the immunosuppressive tumor microenvironment, and establishes a mechanistic basis for activity in historically immunotherapy-resistant pMMR/MSS tumors.

Surgical feasibility and safety

Patients proceeded to planned surgery without treatment-related delays. No Grade 4 treatment-related adverse

events, treatment-related deaths or study discontinuations were observed.

“The NEST results reinforce a major opportunity in colorectal cancer to use immunotherapy earlier, before surgery, when the primary tumor and immune system are still positioned to generate a coordinated anti-tumor response,” said Pashtoon M. Kasi, M.D., M.S., Medical Director of GI Medical Oncology at City of Hope Orange County, Rad Family Chair in Gastrointestinal Oncology, and originator of the NEST study. “For pMMR/MSS disease, where immunotherapy has historically had limited impact, the combination of pathologic responses, ctDNA clearance, no observed colorectal cancer recurrences at longer follow-up and immune remodeling is highly encouraging, particularly when viewed against historical benchmarks. These findings provide a strong foundation for continued study of neoadjuvant BOT+BAL, including NEST3, our enrolling multicenter Phase 2 investigator-sponsored study.”

About the NEST and NEST 3 Studies

NEST (NCT05571293) was an investigator-initiated, single-center, open-label Phase 2 study evaluating neoadjuvant BOT+BAL in patients with resectable colorectal cancer. The study enrolled 24 eligible patients with 26 resectable colorectal tumors, including 22 with mismatch repair proficient/microsatellite stable and four mismatch repair deficient/microsatellite instability-high tumors. Patients received neoadjuvant BOT+BAL before planned surgical resection. The primary objectives were to assess safety, feasibility and anti-tumor activity, with exploratory analyses evaluating treatment-associated changes in the tumor immune microenvironment. Agenus supported the study and provided BOT and BAL.

NEST3 (NCT07595874) is an open and actively enrolling multicenter Phase 2 investigator-sponsored study evaluating neoadjuvant BOT+BAL in advanced resectable colorectal cancer. The study is sponsored by City of Hope Medical Center, led by Pashtoon M. Kasi, M.D., M.S., as overall principal investigator, and designed to enroll approximately 100 patients across 11 U.S. sites. The first patient was dosed in July 2026. NEST3 is being conducted through City of Hope’s National Clinical Trials Model, a centralized research framework designed to expand patient access to clinical trials across multiple City of Hope locations. More information is available at **ClinicalTrials.gov**.

About Agenus

Agenus is a leading immuno-oncology company targeting cancer with a comprehensive pipeline of immunological agents. The company was founded in 1994 with a mission to expand patient populations benefiting from cancer immunotherapy through combination approaches, using a broad repertoire of antibody therapeutics, adoptive cell therapies (through MiNK Therapeutics) and adjuvants. Agenus has robust end-to-end development capabilities, across commercial, research and discovery. Agenus is headquartered in Lexington, MA. For more information, visit **www.agenusbio.com** or @agenus_bio. Information that may be important to investors will be routinely posted on

our website and social media channels.

About Botensilimab (BOT)

Botensilimab (BOT) is a human multifunctional, Fc-enhanced anti-CTLA-4 antibody designed to boost both innate and adaptive anti-tumor immune responses. Its novel design leverages mechanisms of action to extend immunotherapy benefits to “cold” tumors which generally respond poorly to standard of care or are refractory to conventional PD-1/CTLA-4 therapies and investigational therapies. Botensilimab augments immune responses across a wide range of tumor types by priming and activating T cells, reducing intratumoral regulatory T cells, activating myeloid cells and inducing durable memory responses.

Approximately 1,300 patients have been treated with botensilimab and/or balstilimab in phase 1 and phase 2 clinical trials. Botensilimab alone, or in combination with Agenus’ investigational PD-1 antibody, balstilimab, has shown clinical responses across nine metastatic, late-line cancers. For more information about botensilimab trials, visit **www.clinicaltrials.gov**.

About Balstilimab (BAL)

Balstilimab is a novel, fully human monoclonal immunoglobulin G4 (IgG4) designed to block PD-1 (programmed cell death protein 1) from interacting with its ligands PD-L1 and PD-L2. It has been evaluated in more than 900 patients to date and has demonstrated clinical activity and a favorable tolerability profile in several tumor types.

Forward-Looking Statements

This press release contains forward-looking statements that are made pursuant to the safe harbor provisions of the federal securities laws, including statements regarding its botensilimab and balstilimab programs, expected regulatory timelines and filings, and any other statements containing the words "may," "believes," "expects," "anticipates," "hopes," "intends," "plans," "forecasts," "estimates," "will," “establish,” “potential,” “superiority,” “best in class,” and similar expressions are intended to identify forward-looking statements. These forward-looking statements are subject to risks and uncertainties that could cause actual results to differ materially. These risks and uncertainties include, among others, the factors described under the Risk Factors section of our most recent Annual Report on Form 10-K for 2025, and subsequent Quarterly Reports on Form 10-Q filed with the Securities and Exchange Commission. Agenus cautions investors not to place considerable reliance on the forward-looking statements contained in this release. These statements speak only as of the date of this press release, 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.

References

[i] Buchler T. Front Oncol. 2022;12:888181.
[ii] Guven DC, et al. Oncologist. 2024;29(5):e580-e600.

Investors

917-362-1370 | **investor@agenusbio.com**

Media

781-674-4422 | **communications@agenusbio.com**

Source: Agenus Inc.