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NEWS RELEASE

Agenus Announces Peer-Reviewed Publication Linking BOT+BAL's Durable Survival in MSS Metastatic Colorectal Cancer to Its Distinct Immune-Priming Mechanism

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- Mature 123 patient analysis reports 21.2-month median overall survival and 33% three-year overall survival in heavily pretreated MSS mCRC without active liver metastases
- Responses observed in tumors with low tumor mutational burden and no PD-L1 expression, reinforcing BOT's Fc-enhanced immune priming mechanism in immunologically "cold" tumors
- Durable clinical activity and biomarker findings add biological rationale for evaluating BOT+BAL earlier in the disease course, including curative-intent neoadjuvant colon cancer

LEXINGTON, Mass.--(BUSINESS WIRE)-- **Agenus** Inc. (Nasdaq: AGEN), a leader in immuno-oncology innovation, today announced the peer-reviewed publication of mature Phase 1b results from the fully enrolled C-800-01 cohort evaluating botensilimab (BOT), a multifunctional Fc-enhanced anti–CTLA-4 antibody, plus balstilimab (BAL), an anti–PD-1 antibody, in 123 heavily pre-treated patients with microsatellite-stable (MSS) metastatic colorectal cancer (mCRC) without active liver metastases.

The manuscript, titled "Extended Follow-Up of Botensilimab Plus Balstilimab in an Expanded Cohort of Microsatellite-Stable Metastatic Colorectal Cancer Without Active Liver Metastases," was published in **Clinical Cancer Research**. The publication builds on three-year efficacy data presented at the European Society for Medical Oncology Gastrointestinal Cancers **(ESMO GI) Congress 2026** and provides additional biomarker analyses offering insight into the biology underlying BOT+BAL activity.

MSS tumors account for the vast majority of mCRC cases and have historically derived little or no benefit from

conventional checkpoint immunotherapy. In this fully enrolled cohort, patients received a median of three prior lines of therapy. BOT+BAL demonstrated a median overall survival of 21.2 months and a three-year overall survival rate of 33%. In this treatment setting, available later-line standard treatments have reported median overall survival of approximately 10-14 months in patients with refractory MSS, without active liver metastases.[i]

Durable clinical activity was observed in the context of limited drug exposure, with patients receiving a median of two BOT doses and six BAL doses. In exploratory analyses, responses were observed in tumors lacking the conventional markers of checkpoint sensitivity including low tumor mutational burden (TMB) and no detectable PD-L1 expression, and neither biomarker was associated with response. These findings are consistent with BOT's Fc-enhanced design, intended role in promoting immune priming in immunologically "cold" tumors.

“These mature results are important because they show a pattern of durable activity in MSS colorectal cancer that is not limited to tumors with the conventional features associated with checkpoint sensitivity,” said Benjamin L. Schlechter, M.D., of Dana-Farber Cancer Institute and lead author of the publication. “In a heavily pretreated setting where patients have few remaining options, BOT+BAL compares favorably with what is typically expected from available later-line standard therapies in terms of tolerability, depth of response and duration of response. That is a meaningful clinical difference and provides important evidence that antitumor immunity can be generated even in tumors traditionally considered immunologically cold.”

"BOT was specifically engineered to add Fc-mediated immune engagement to CTLA-4 blockade, with the goal of priming antitumor immunity in cancers that have historically been resistant to conventional checkpoint inhibition," said Steven O'Day, M.D., Chief Medical Officer of Agenus. “This peer-reviewed publication connects the durable clinical activity observed in refractory MSS colorectal cancer with biomarker findings consistent with that biology. When considered alongside our emerging neoadjuvant data, these findings strengthen the rationale for evaluating BOT+BAL earlier in the disease course, where immune priming before surgery may offer the greatest opportunity to alter the trajectory of MSS colorectal cancer.”

Mature Clinical Outcomes

The Phase 1b cohort included 123 patients with MSS mCRC without active liver metastases who had received a median of three prior lines of therapy.

Key findings reported in the publication include:

- Overall survival: Median overall survival was 21.2 months, with 24-month and 36-month overall survival rates of 41% and 33%, respectively
- Objective response: Confirmed objective response rate was 21%, including three complete responses and 23

partial responses

- Duration of response: Median duration of response was not reached, with responses extending to at least 37.4 months
- Disease control: Disease control rate was 69% at six weeks, and clinical benefit rate was 28% at 24 weeks
- Treatment-free status: At last follow-up, 17% were alive and off all systemic anticancer therapy, including 13 responders

Activity Maintained in the Most Heavily Pretreated Patients

In an exploratory subgroup of 37 patients who had already exhausted available later-line therapies, patients had received a median of five prior lines of therapy. In this subgroup, BOT+BAL demonstrated a 22% confirmed objective response rate, median overall survival of 16.2 months, and a three-year overall survival rate of 30%. Median duration of response was 16.6 months, disease control rate was 70%, and clinical benefit rate at 24 weeks was 27%, indicating that clinical benefit was preserved even in the most refractory setting.

Biomarker Findings Support Fc-Enhanced Immune Priming Biology

Exploratory biomarker analyses showed that responses were observed among patients with low tumor mutational burden (TMB) and no detectable PD-L1–expression, and neither biomarker was associated with response in the evaluable population. These findings suggest that activity was not confined to tumors with conventional markers of checkpoint sensitivity.

These observations are consistent with BOT's Fc-enhanced design, which is intended to engage activating Fc-gamma receptors on antigen-presenting and other myeloid cells, promote T-cell priming, reduce intratumoral regulatory T cells, and reshape the immunosuppressive tumor microenvironment rather than relying solely on pre-existing tumor immunogenicity.

Extended Safety Follow-Up Supports Optimized Dosing

No new safety signals were observed with extended follow-up, and there were no treatment-related deaths. Immune-mediated diarrhea/colitis, the most common immune-mediated adverse event, resolved in 98% of affected patients, with a median time to resolution of 14 days.

Efficacy was consistent across the two BOT dose levels evaluated, with a 21% objective response rate at both 1 mg/kg and 2 mg/kg. Lower rates of immune-mediated adverse events were observed with BOT 1 mg/kg plus BAL compared with the higher BOT dose.

From Durable Metastatic Activity to Curative Intent Neoadjuvant Setting

The publication follows the recent peer-reviewed report of updated NEST Phase 2 data evaluating neoadjuvant BOT+BAL in resectable colon cancer. The NEST results provide direct clinical evidence in the neoadjuvant setting, while the C-800-01 manuscript adds metastatic durability and biomarker evidence consistent with Fc-enhanced immune priming. This body of evidence supports continued evaluation of BOT+BAL in neoadjuvant, curative-intent MSS colon cancer, including Agenus' planned Phase 3 ROBBIN trial.

About the C-800-01 Study

C-800-01 (NCT03860272) is a first-in-human Phase 1b clinical trial evaluating botensilimab with or without balstilimab in patients with advanced solid tumors. The MSS mCRC without active liver metastases cohort enrolled 123 patients who received BOT 1 mg/kg or 2 mg/kg every six weeks plus BAL 3 mg/kg every two weeks. The primary endpoint was safety and tolerability. Secondary efficacy endpoints included objective response rate, duration of response, disease control rate and progression-free survival; overall survival was an exploratory endpoint.

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 and clinical cGMP manufacturing facilities, research and discovery, and a global clinical operations footprint. 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.

[†] Available later-line standards include regorafenib, trifluridine/tipiracil with or without bevacizumab, and fruquintinib in refractory metastatic colorectal cancer, including analyses in patients without active liver metastases. Cross-trial comparisons are descriptive; differences in study design, eligibility criteria, patient populations, assessments, follow-up and data cutoffs may confound comparisons.

References: Garcia-Carbonero R, et al. Presented at ESMO 2024. Poster #520P; Tabernero J, et al. Presented at ASCO 2024. Poster #3584; Cohen R, et al. Eur J Cancer. 2024;207:114160.

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