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NEWS RELEASE

Agenus Presents Biomarker Data Demonstrating Survival Stratification in MSS mCRC and Other Immunologically Cold Tumors Treated with BOT+BAL

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- Integrated analysis of systemic inflammation and tumor immune features identifies biologically distinct patient subgroups with differential survival outcomes, outperforming conventional biomarkers

LEXINGTON, Mass.--(BUSINESS WIRE)-- **Agenus Inc**. (Nasdaq: AGEN), a leader in immuno-oncology, today announced new translational and clinical biomarker data from its Phase 1b C-800-01 trial (NCT03860272) evaluating botensilimab (BOT), an Fc-enhanced anti–CTLA-4 antibody, in combination with balstilimab (BAL), an anti–PD-1 antibody. The data were presented today at the American Association for Cancer Research Immuno-Oncology (AACR-IO) Conference in Los Angeles.

The retrospective analyses demonstrate that survival with BOT+BAL is associated with the balance of two opposing biological factors: systemic inflammation in the blood (associated with poorer outcomes) and tumor immune activity within the tumor microenvironment (TME) (associated with more favorable outcomes). Notably, BOT+BAL enabled clinical benefit even at levels of immune infiltration typically considered insufficient for conventional checkpoint inhibitors, suggesting the Fc-enhanced mechanism lowers the threshold of baseline immunity required for activity. Integrating blood-based inflammatory markers with tumor immune features improved overall survival stratification in microsatellite-stable metastatic colorectal cancer (MSS mCRC), a population historically resistant to conventional checkpoint inhibitors.

Traditional biomarkers such as PD-L1 expression and tumor mutational burden have shown limited predictive value in MSS mCRC. These findings suggest that a broader view of inflammatory and immune biology may better define patients most likely to benefit from next-generation immunotherapy.

Durable Clinical Activity Across Historically “Cold” Tumor Types

In 341 efficacy-evaluable patients with advanced, treatment-refractory cancers and available biomarker data (data cutoff December 13, 2025):

- Objective response rate (ORR): 17%
- Clinical benefit rate (CBR): 26%
- Median overall survival (OS): 17.2 months
- 24-month overall survival rate: 38%

Clinical activity was observed across tumor types commonly considered immunologically “cold,” including MSS mCRC, ovarian cancer, sarcoma, and PD-1 relapsed or refractory non-small cell lung cancer. Notably, durable benefit was observed in patients both naïve to and resistant/refractory to prior anti–PD-(L)1/CTLA-4 therapies.

To better understand the biological drivers of these outcomes, integrated translational analyses evaluated both systemic inflammation and tumor microenvironment immune features.

Biomarker Insights Identify Patient Subgroups in Immunologically “Cold” Cancers

- Systemic Inflammation Negatively Impacts Survival
  Baseline indicators of systemic inflammation were significantly associated with shorter OS, including elevated neutrophil-to-lymphocyte ratio, C-reactive protein and other markers reflective of inflammatory and organ stress.

- Even Low Immune-Infiltration of TME Associated with Longer Survival
  Survival benefit was observed across immunologically “cold” tumors, including at low levels of tumor-infiltrating lymphocytes (≥34 cells/mm^2), demonstrating activity beyond conventional checkpoint biomarker thresholds.

- Integrated Blood and Tumor Biomarkers Improve Survival Stratification in MSS mCRC
  Combining blood and tumor features distinguished biologically distinct MSS mCRC subgroups with markedly different survival outcomes (C-index up to 0.73).

- Early Immune Activation Correlates with Benefit
  Patients who experienced immune-mediated adverse events (imAEs) within the first 12 weeks of treatment demonstrated longer median OS (22.4 months vs. 13.7 months), consistent with distinct baseline immune features.

“These data show that outcomes with BOT+BAL are shaped by the interplay between systemic inflammation and tumor immune biology,” said Dhan Chand, PhD, Vice President of Research and Development at Agenus. “By integrating blood- and tumor-based features, we are establishing a biologically grounded approach to patient stratification in immunologically ‘cold’ cancers such as MSS colorectal cancer, where conventional biomarkers provide limited guidance. Notably, the activity observed at low levels of immune infiltration further underscores the differentiated immune-modulating profile of botensilimab.”

The poster (No. B036), titled “Systemic and Tumor-Microenvironment Inflammation Shape Outcomes in Patients with Immunologically Cold, Treatment-Refractory Tumors Treated with Fc-Enhanced Anti–CTLA-4 Botensilimab,” was presented during the General Poster Session and is available in the Publications section of the Company’s website at **www.agenusbio.com/publications**

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 Phase 1b Study

C-800-01 (NCT03860272) is a multicenter Phase 1b clinical trial evaluating botensilimab in combination with balstilimab across advanced solid tumors. The trial enrolled over 400 patients with refractory disease and included tumor types with limited or no responsiveness to prior checkpoint inhibitors. Endpoints included objective response rate (ORR), duration of response (DOR), disease control rate (DCR), progression-free survival (PFS), and overall survival (OS).

About Botensilimab (BOT)

Botensilimab (BOT) is a human Fc enhanced multifunctional 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, downregulating intratumoral regulatory T cells, activating myeloid cells and inducing long-term memory responses.

Approximately 1,200 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 2024, 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.

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