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NEWS RELEASE

Agenus Reports 39% of Patients Alive at Two-Years with BOT/BAL Across Multiple Refractory Solid Tumors at ESMO 2025

2025-10-17

- Durable survival in heavily pretreated patients, including those who failed prior immunotherapy and with active liver metastases
- Signals of tumor agnostic benefit observed
- Tumor types included CRC, sarcoma, ovarian, NSCLC, and liver

LEXINGTON, Mass.--(BUSINESS WIRE)-- **Agenus** Inc. (Nasdaq: AGEN), a leader in immuno-oncology innovation, today announced new data from its botensilimab (BOT), a multifunctional, Fc-enhanced CTLA-4 antibody and balstilimab (BAL), a PD-1 inhibitor, combination demonstrating durable survival across multiple cancer types in late-stage patients who have limited treatment options. The results, featured in an oral session at the European Society for Medical Oncology (ESMO) Congress 2025 in Berlin, Germany presented by Dr. Michael Gordon of HonorHealth Research Institute, include emerging two-year survival plateaus indicating a strong clinical signal that BOT/BAL's benefit may be agnostic to tumor type.

"With longer follow up, we're finding that approximately 40% of patients with very limited survival expectation are alive at two years," said Michael S. Gordon, MD, HonorHealth Research Institute. "These results are in patients with cancers that historically have been resistant to earlier immunotherapy approaches or have progressed following prior immunotherapy treatment, and they support advancing randomized trials like the phase 3 BATTMAN trial to create an immunotherapy option for patients who have historically had none."

Highlights from the Oral Presentation (Abstract #1517MO):

New data from expansion cohorts of 411 patients (339 evaluable for efficacy) enrolled in the Phase 1b C-800-01

study evaluating BOT/BAL in patients with advanced, refractory disease across more than 5 cancer types.

- 61% of patients enrolled received three or more prior lines of therapy
- Objective response rates (ORR): 17% across both BOT 1 mg/kg and 2 mg/kg doses
- Signals of benefit across tumor types, including those historically unresponsive to immunotherapy, had prior treatment with checkpoint inhibitors, and/or with active liver metastases.
- 2-year median overall survival (OS): 39%
- Median OS (mOS): 17.2 months
- Combination was well tolerated with most immune-related side effects were reversible and gastrointestinal in nature; no treatment-related deaths occurred
- Immune activation correlated with improved survival

These findings build on previously reported 2-year overall survival of 42% and median OS of 20.9 months with BOT/BAL in refractory MSS mCRC with non-liver metastases[i] and complement emerging data in the neoadjuvant setting, where BOT/BAL has also shown activity across multiple tumor types[ii], further underscoring the platform potential of Agenus' next-generation Fc-enhanced CTLA-4.

In a further validation of its clinical impact, the French National Authority for Health (HAS) recently authorized BOT in combination with BAL under France's Compassionate Access (AAC) early access program. This marks the first government-funded access pathway in France, for patients with refractory microsatellite-stable (MSS) metastatic colorectal cancer (mCRC) who have exhausted all available treatment options.

"BOT/BAL's immune activation profile is truly differentiated," said Steven J. O'Day, MD, Chief Medical Officer, Agenus. "We are seeing consistent signals that this combination can convert 'cold,' IO-resistant tumors into responsive ones, not only in late-line settings but potentially in earlier lines where immunotherapy may deliver even greater benefit."

Broader Presence at ESMO 2025

In addition to the pan-tumor dataset, three additional posters will be presented highlighting clinical activity across hard-to-treat cancers:

- Cervical cancer: Results from the global Phase 2 RaPiDs trial (Abstract #2952)
- MSS mCRC: A Phase 1 trial of BOT/BAL + regorafenib (Abstract #6197)
- Non-melanoma skin cancer: Data from the AGENONMELA study (Abstract #7273)

These presentations further support the breadth and versatility of Agenus' immunotherapy pipeline across diverse cancer types and clinical settings.

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 the C-800-01 Study

C-800-01 (NCT03860272) is an ongoing, 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).

Agenus' Commitment to Patient Access

Agenus is dedicated to making investigational medicines available to patients with cancer at the appropriate time and in the correct manner. For more information, visit **https://agenusbio.com/access-to-investigational-medicines-policy**

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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[i] Schlechter BM, et al. Poster presented at the ESMO Gastrointestinal Cancers Congress 2025. Barcelona, Spain. 2025. Poster #8P
[ii] Chalabi M, et al. Oral presentation at AACR 2025. Chicago, IL, USA. 2025. Abstract #CT130.

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Source: Agenus Inc.