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NEWS RELEASE

Agenus Reports Deep, Durable Responses with Botensilimab + Balstilimab in Highly Refractory Ovarian Cancer, Published in JITC

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- Deep and durable responses observed in a heavily pretreated, historically immunotherapy-resistant population
- Findings reinforce the broad, pan-tumor activity of BOT+BAL across immunologically “cold” cancers

LEXINGTON, Mass.--(BUSINESS WIRE)-- **Agenus Inc.** (Nasdaq: AGEN), a leader in immuno-oncology innovation, today announced the publication of clinical results from the ovarian cancer cohort of its Phase 1b C-800-01 trial evaluating botensilimab plus balstilimab (BOT+BAL) in The Journal for ImmunoTherapy of Cancer (JITC).

The peer-reviewed manuscript titled, “Botensilimab (Fc-enhanced anti–CTLA-4 antibody) plus balstilimab (anti–PD-1 antibody) in patients with treatment-refractory ovarian cancer,” is available online **here**.[i]

In this heavily pretreated population, BOT+BAL demonstrated clinically meaningful activity and durable benefit in women with treatment-refractory ovarian cancer, a population with few remaining options. The combination achieved a 23% overall response rate and 31% clinical benefit rate, including durable responses with a median duration of 9.7 months. Median overall survival reached 14.8 months, with an estimated of 75% of patients alive at 12 months.

These findings build on results from the broader C-800-01 dataset presented at ESMO 2025, where BOT+BAL showed activity across multiple refractory solid tumors. Collectively, these data reinforce the potential of BOT+BAL to generate meaningful immune responses in cancers historically considered unresponsive to immunotherapy.

High Unmet Need in Treatment-Refractory Ovarian Cancer

Ovarian cancer causes approximately 13,000 deaths annually in the U.S. and 200,000 globally[ii,iii], and outcomes are particularly poor once tumors become platinum-resistant or platinum-refractory. Therapy with first-generation checkpoint inhibitors has yielded modest responses, with objective response rates between 8–10% and median progression-free survival of roughly 2 months[iv,v], leaving many women with rapidly diminishing options and no approved immunotherapy combinations.

Publication Highlights

- The study enrolled 44 women with treatment-refractory ovarian cancer who had received multiple prior lines of therapy. Nearly three-quarters were platinum-resistant or platinum-refractory, and most had high-grade serous tumors.
- Activity was demonstrated in primary platinum-refractory patients—a rare and high-risk group often excluded from clinical studies.
- Responses occurred in multiple ovarian cancer subtypes including high-grade serous, clear cell, and endometrioid tumors.
- The BOT+BAL combination demonstrated a manageable and reversible safety profile, consistent with CTLA-4 and PD-1 therapy. Most common treatment-related adverse events such as diarrhea/colitis (43%; 16% grade 3), fatigue and nausea (36%) were effectively managed using established treatment guidelines. No treatment-related deaths were reported.

Steven O'Day, MD, Chief Medical Officer, Agenus, commented, "These results offer a meaningful signal of clinical activity for women with platinum-refractory ovarian cancer, a group that has seen little therapeutic progress. Botensilimab's unique immune activation profile translated into clinically significant responses in a population long considered resistant to immunotherapy. These findings strengthen our confidence in BOT+BAL's potential and support moving this combination into larger, randomized studies."

Rebecca Porter, M.D., Ph.D., Dana-Farber Cancer Institute and Lead Author added, "These women faced some of the most treatment-resistant forms of ovarian cancer, yet several achieved meaningful and durable benefit. Seeing this level of activity in such a heavily pretreated population is encouraging and provides important insights to the field regarding therapy approaches for patients with very limited remaining options."

Patient Access and Ongoing Development

BOT+BAL continues to advance through global clinical development across multiple tumor types. In parallel, eligible patients may be able to access BOT+BAL through regulatory-authorized early access mechanisms, including France's AAC program, where treatment is reimbursed, as well as paid named-patient programs in select countries

where permitted by local regulations. These programs are intended to provide access for patients with serious or life-threatening diseases who lack satisfactory therapeutic alternatives.

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). Results of the study were presented at ESMO 2025 and the full presentation is available on the publications page of the Agenus website **here**.

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] Porter R, Bockorny B, Corr BR, et al. Botensilimab (Fc-enhanced anti–CTLA-4 antibody) plus balstilimab (anti–PD-1 antibody) in patients with treatment-refractory ovarian cancer. J Immunother Cancer. 2025;13(12)e:013222. doi:10.1136/jitc-2025-013222.
[ii] Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024. CA Cancer J Clin 2024;74:12–49.
[iii] Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020:GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021;71:209–49.
[iv] Disis ML, Taylor MH, Kelly K, et al. Efficacy and Safety of Avelumab for Patients With Recurrent or Refractory Ovarian Cancer: Phase 1b Results From the JAVELIN Solid Tumor Trial. JAMA Oncol 2019;5:393–401.
[v] Matulonis UA, Shapira-Frommer R, Santin AD, et al. Antitumor activity and safety of pembrolizumab in patients with advanced recurrent ovarian cancer: results from the phase II KEYNOTE-100 study. Ann Oncol 2019;30:1080–7.

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