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NEWS RELEASE

# Agenus Presents Phase 2 BOT+BAL Melanoma Data Showing Durable Responses and Meaningful Survival in Advanced Checkpoint-Refractory Melanoma at ASCO 2026

2026-05-21

- First presentation of BOT+BAL melanoma data in heavily pretreated patients whose disease had resisted prior checkpoint therapy and who had poor-risk disease features
- In the overall BOT+BAL treated population, median overall survival was 16.6 months and 42% of patients were alive at two years
- Responses were durable with median duration of response not reached and 86% of responders remaining in response at 12 months

LEXINGTON, Mass.--(BUSINESS WIRE)-- **Agenus** Inc. (Nasdaq: AGEN), a leader in immuno-oncology innovation, today announced the first disclosure of Phase 2 data from the C-800-23 study evaluating botensilimab (BOT), Agenus' multifunctional Fc-enhanced anti-CTLA-4 antibody, with balstilimab (BAL), an anti-PD-1 antibody, in patients with advanced cutaneous melanoma refractory or resistant to prior anti-PD-(L)1 therapy, including patients previously treated with anti-CTLA-4 therapy. The full dataset will be presented by Dr. Michael Atkins on May 31, 2026 at the American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago.

The BOT+BAL combination arm included 36 heavily pretreated patients with advanced cutaneous melanoma. Most had disease that had resisted prior checkpoint therapy, and many had poor-risk features, including visceral disease and elevated LDH. In this setting, where patients have often exhausted the benefit of currently available checkpoint approaches, the most meaningful signals were the durability of benefit and survival outcomes observed with BOT+BAL.

In the overall BOT+BAL population, median overall survival was 16.6 months, 42% of patients were alive at two years, and median duration of response was not reached. Among responders, 86% remained in response at 12 months. Confirmed objective response rate was 22%, providing evidence of antitumor activity in a population where durable disease control is difficult to achieve.

Survival and durability were particularly notable in the subgroup of patients whose disease was refractory or resistant to both prior anti-PD-(L)1 and anti-CTLA-4 therapy. Published benchmarks show median overall survival of approximately 13 to 14 months among patients refractory or resistant to both anti-PD-(L)1 and anti-CTLA-4 therapy[i,ii]. In this dual checkpoint-exposed subgroup, median overall survival was not reached and 64% of patients were alive at two years. Median duration of response was also not reached, with all responders remaining in response at 12 months.

“Patients with advanced melanoma whose disease has progressed after PD-1-based therapy, particularly those also exposed to CTLA-4 therapy, remain difficult to treat. For those without a BRAF mutation, who lack an effective targeted option, the choices after checkpoint therapy are especially limited,” said Michael B. Atkins, M.D., Deputy Director, Georgetown Lombardi Comprehensive Cancer Center, and lead author of the presentation. “In that setting, the survival and the durability of response seen with BOT plus BAL stand out, because sustained disease control is exactly what these patients rarely achieve.”

“Melanoma has been one of the clearest examples of the transformative potential of immunotherapy, but patients whose disease progresses after PD-1 and CTLA-4 therapy continue to face limited options,” said Steven O’Day, M.D., Chief Medical Officer of Agenus. “These findings add to the growing body of evidence supporting BOT plus BAL’s potential to drive meaningful and durable immune responses in tumors that have resisted prior checkpoint approaches. Importantly, the melanoma data are consistent with the durable activity previously reported with BOT plus BAL across other difficult-to-treat and historically immunotherapy-resistant solid tumors, including recent HCC data in a heavily prior IO-treated population.”

Safety findings were consistent with the known safety profile of CTLA-4 and PD-1 checkpoint inhibition. In the BOT+BAL combination arm, grade 3 or higher treatment-related adverse events occurred in 36% of patients, with no treatment-related deaths reported. No new safety signals were observed.

The melanoma findings add to previously reported BOT+BAL activity across difficult-to-treat and historically immunotherapy-resistant solid tumors, including recently published data in Liver Cancer evaluating BOT+BAL in heavily immunotherapy-pretreated hepatocellular carcinoma.

“These data reinforce our conviction in BOT+BAL as a mechanistically differentiated CTLA-4-based combination designed to extend the benefit of immunotherapy to patients and tumor types not adequately served by current

checkpoint approaches," said Garo Armen, Ph.D., Chairman and Chief Executive Officer of Agenus. "Across melanoma, colorectal cancer and other difficult-to-treat solid tumors, we continue to see a consistent pattern: durable responses and encouraging long-term survival in settings where available options remain limited. That is the foundation of our development strategy and the reason we remain focused on advancing BOT+BAL with urgency."

## Key Phase 2 BOT+BAL Melanoma Findings

The Phase 2 C-800-23 study (NCT05529316) evaluated BOT+BAL in patients with advanced cutaneous melanoma refractory or resistant to prior anti-PD-(L)1 therapy, including patients previously treated with anti-CTLA-4 therapy. The intent-to-treat population included 36 patients treated with BOT 75 mg plus BAL 450 mg every three weeks.

### Overall BOT+BAL population, N=36:

- Median overall survival: 16.6 months
- 2-year overall survival rate: 42%
- Median duration of response: not reached
- 12-month duration of response rate: 86%
- Confirmed objective response rate: 22%
- Clinical benefit rate at 24 weeks: 33%

### Prior anti-PD-(L)1 plus anti-CTLA-4 refractory/resistant cohort, n=14:

- Median overall survival: not reached
- 2-year overall survival rate: 64%
- Median duration of response: not reached
- 12-month duration of response rate: 100%
- Confirmed objective response rate: 29%
- Clinical benefit rate at 24 weeks: 36%

Following the poster session on May 31, 2026, the full poster will be available on the Publications page of the Agenus website.

Presentation Details

Abstract Title: Botensilimab (BOT) ± balstilimab (BAL) in patients (pts) with advanced cutaneous melanoma (cMEL) refractory/resistant (R/R) to anti–PD-(L)1 ± CTLA-4: A phase 2 trial
Abstract No.: 9543

- Presenter: Michael B. Atkins M.D.; Georgetown Lombardi Comprehensive Cancer Center, Georgetown University Medical Center
- Session Title: Poster Session – Melanoma/Skin Cancers
- Location: Hall A – Posters and Exhibits
- Poster Board: 259
- Date/Time: May 31, 2026, 9:00 AM–12:00 PM CDT

## About the C-800-23 Phase 2 Melanoma Study

C-800-23 (NCT05529316) is an open-label, global Phase 2 trial evaluating botensilimab with or without balstilimab in patients with advanced cutaneous melanoma refractory or resistant to prior anti-PD-(L)1 therapy, with or without prior anti-CTLA-4 therapy.

The primary endpoint is confirmed objective response rate by RECIST 1.1. Secondary endpoints include duration of response, progression-free survival, overall survival, safety and tolerability. Clinical benefit rate, defined as complete response, partial response or stable disease at 24 weeks or later, was evaluated as an exploratory endpoint.

## About Agenus

Agenus is a clinical-stage immuno-oncology company advancing a pipeline of antibody-based programs designed to activate innate and adaptive immunity, overcome tumor immune evasion, and expand the population of patients who may benefit from immunotherapy. Founded in 1994, Agenus' lead program is botensilimab plus balstilimab (BOT+BAL), a next-generation Fc-enhanced CTLA-4 plus PD-1 combination. BOT alone or in combination with BAL has been evaluated in approximately 1,300 patients across more than nine tumor types. The global Phase 3 BATTMAN trial, conducted with the Canadian Cancer Trials Group, is evaluating BOT+BAL in refractory MSS/pMMR metastatic colorectal cancer. BOT/BAL is also available to eligible patients through regulatory-authorized access pathways in select countries, including France's national Autorisation d'Accès Compassionnel framework. Agenus also holds an equity investment in MiNK Therapeutics, Inc. (Nasdaq: INKT), a clinical-stage developer of allogeneic invariant natural killer T cell therapies, and a majority interest in SaponiQx, Inc., a vaccine adjuvant business. Agenus is headquartered in Lexington, Massachusetts. For more information, visit **www.agenusbio.com** or @agenus_bio. Information that may be important to investors will be routinely posted on the Company's website and social media channels.

## 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 1,300 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.

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References

[i] Medina T, et al. J Clin Oncol. 2025;43(33):3565–3572.

[ii] Wong MK, et al. J Clin Oncol. 2025;43(33):3589–3599.

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