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NEWS RELEASE

Agenus' BOT/BAL Achieves 42% Two-Year Survival in Refractory MSS CRC, Advances Toward Registration with FDA Alignment on Phase 3

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LEXINGTON, Mass.--(BUSINESS WIRE)-- Agenus Inc. (Nasdaq: AGEN) a leader in immuno-oncology innovation, today announced that its botensilimab and balstilimab (BOT/BAL) combination achieved a two-year survival rate of 42% along with a now more mature 21-month median overall survival (OS) in an expanded cohort of 123 patients with microsatellite-stable (MSS) metastatic colorectal cancer (mCRC) without active liver metastases (NLM). Agenus also confirmed that it has reached agreement with the U.S. Food and Drug Administration (FDA) on the design of the global BATTMAN Phase 3 trial. The FDA waived the need for a BOT monotherapy arm, allowing for a simple two-arm study design. These new BOT/BAL data were reported at the 2025 ESMO Gastrointestinal Cancers Congress (ESMO-GI) in Barcelona, Spain, along with regulatory updates from its July 1, 2025 End-of-Phase 2 (EoP2) meeting with the U.S. Food and Drug Administration (FDA).

ESMO-GI Clinical Highlights

The new data presented at ESMO-GI represent an approximate 40% increase in number of patients (n=123) compared to earlier reports published in Nature Medicine in 2024. The expanded dataset demonstrates continued durability of tumor responses and median overall survival approaching two years in an immunotherapy-resistant treatment setting. Among these 123 heavily pretreated MSS mCRC patients (third-line or later) treated with BOT/BAL, the confirmed objective response rate (ORR) was 20%, with a median duration of response (DOR) of 16.6 months. The disease control rate (DCR, responses plus stable disease) was 69%. Notably, median overall survival (OS) reached 20.9 months, with 42% of patients still alive at two years in this refractory population. Patients in fourth-line or later (n=37), having exhausted all standard therapies, saw similar benefits, with a ~19% ORR and 43% two-year survival. These findings are particularly meaningful in this refractory population for which best supportive

care has been historically limited to roughly 5-8 months median overall survival.

No new safety signals were observed. Immune-related side effects were manageable and no treatment-related deaths occurred. The combination was tolerated across dose levels.

“These results reinforce the consistency and durability of the botensilimab plus balstilimab combination in a population that has historically seen minimal benefit from immune checkpoint blockade,” said Dr. Benjamin Schlechter of Dana-Farber Cancer Institute, who presented the data. “For patients with MSS colorectal cancer who have exhausted standard therapies, this combination is showing the kind of meaningful, long-lasting benefit we rarely see in this setting. It has the potential to fundamentally shift how we treat this disease.”

“Deep, durable responses and survival plateaus emerging at two years and beyond are rarely seen in microsatellite stable refractory colorectal cancer – they are usually only seen in highly immunogenic tumors,” said Dr. Steven O’Day, Chief Medical Officer of Agenus. “These data reinforce the potential for a chemo-free option in a population with limited alternatives.”

FDA Meeting Outcomes

Official minutes from the July 1, 2025 End-of-Phase 2 (EoP2) meeting reflect a meaningful shift in FDA alignment since July 2024, establishing two new areas of agreement:

1. Contribution of components – FDA wrote that the current data “appears to support” balstilimab’s contribution to the combination’s clinical activity and therefore a registrational Phase 3 trial may proceed without a BOT monotherapy arm.
2. Phase 3 registrational trial – BATTMAN (CCTG CO.33): FDA and Agenus aligned on the core design of this global registration study for BOT/BAL. Agenus is incorporating the Agency’s feedback and will initiate BATTMAN in Q4 2025.
   During the discussion on July 1, 2025, the FDA stated that it continues to recommend Agenus conduct a randomized controlled trial to support the approval of BOT/BAL in the metastatic setting and the demonstrated magnitude of treatment effect “does not appear to meet the standard of reasonably likely to predict benefit.” Agenus and key experts in oncology and immunotherapy, including those present in the FDA meeting—strongly believe that the BOT/BAL data meets the standard of Subpart E given the magnitude, durability, and urgent unmet need in this patient population.

Jennifer Buell, Ph.D., Executive Chairwoman of Agenus, commented: “FDA’s acknowledgement of balstilimab’s role and its constructive guidance on the Phase 3 trial mark a pivotal step forward. We have incorporated the Agency’s input and are moving swiftly to launch BATTMAN, while continuing to mature our

existing dataset. Guided by Commissioner Makary's commitment to accelerate promising therapies, we intend to use every expedited pathway—Fast Track, Real-Time Oncology Review, the new Commissioner's National Priority Voucher Program, and other accelerated mechanisms—to bring this chemo-free option to patients who have exhausted all other treatments."

Clinical Urgency

"Colorectal cancer is rising fastest in people under 50 and is projected to become the leading cause of cancer death in that age group by 2030," said Richard Goldberg, M.D., Chief Development Officer, Agenus. "Given the dismal five-to-eight-month median survival with current late-line therapies, making BOT/BAL available quickly is not just prudent—it is imperative."

2H2025 Catalysts

1. Launch Global Registrational Trial (BATTMAN): Initiate BATTMAN in 4Q2025; rapidly accrue trial designed to confirm OS benefit and registration.
2. Advancing Earlier-Line CRC: Ongoing data of BOT/BAL in 1L and neoadjuvant MSS CRC will inform upcoming discussions with regulatory agencies on potential pathways for expanded development.
3. Global Clinical Infrastructure: Advancing collaboration with Zydus and other strategic partners to support rapid global enrollment, high-quality data generation, and future regional access.
4. Upcoming Data Presentations: Updated data of BOT/BAL in CRC and other tumors to be presented at major oncology congresses in Q4 2025, reinforcing the combinations activity across solid cancers.
5. Regulatory Engagement & Expedited Pathways: Ongoing collaboration with Dr. Makary, the FDA, and senior U.S. government stakeholders to pursue expedited regulatory mechanisms, including Accelerated Approval, the Commissioner's National Priority Voucher Program, and Real-Time Oncology Review to address the current cancer crisis.

Agenus' Commitment to Patient Access

Agenus is committed to making our investigational medicines available to patients with cancer. Our goal is to provide access to our investigational medicines at the appropriate time and in the correct manner for patients. You can find information on access on our website at **www.agenusbio.com/medical-affairs/** and apply.

About the C-800-01 Phase 1 Study

The C-800-01 Phase 1, open-label, multicenter trial (NCT03860272) evaluated botensilimab alone or in combination with balstilimab across multiple solid tumors, including an expansion cohort in microsatellite stable metastatic colorectal cancer. In the MSS CRC cohort, patients received botensilimab (1 or 2 mg/kg every six weeks) plus

balstilimab (3 mg/kg every two weeks) for up to two years. The study enrolled heavily pretreated patients, including those with no active liver metastases, and assessed safety, objective response rate, progression-free survival, and overall survival. No maximum tolerated dose was reached, and the safety profile was manageable across dose levels. The trial also included exploratory biomarker analyses to inform potential predictors of response. Preliminary findings from this study in refractory MSS CRC were published in Nature Medicine in September 2024.

About Agenus

Agenus is a leading immuno-oncology company targeting cancer with a comprehensive pipeline of immune-driven therapies. Founded in 1994, the company's mission is to expand the patient populations benefiting from cancer immunotherapy through innovative combination approaches. Agenus' portfolio includes a broad repertoire of antibody therapeutics, adoptive cell therapies (via its affiliate MiNK Therapeutics), and adjuvants (via SaponiQx). The company has end-to-end capabilities spanning research, discovery, and GMP manufacturing, and it has a global clinical development footprint. Agenus is headquartered in Lexington, MA. For more information, visit **www.agenusbio.com** or follow @agenus_bio on social media. Important information for investors will be routinely posted on the company's website and social channels.

About Botensilimab (BOT)

Botensilimab (AGEN1181) is a novel, multifunctional, Fc-enhanced CTLA-4 antibody engineered to boost both innate and adaptive anti-tumor immune responses. Its unique design aims to overcome the limitations of first-generation CTLA-4 inhibitors (like ipilimumab) and extend immunotherapy benefits to "cold" tumors that typically respond poorly or not at all to standard immune checkpoint blockade. Botensilimab's Fc-enhanced structure allows it to robustly engage activating Fc receptors on key immune cells, thereby priming and activating T cells, depleting immunosuppressive regulatory T cells in the tumor microenvironment, activating myeloid cells, and inducing long-term immune memory. Through these mechanisms, botensilimab has demonstrated the ability to ignite immune responses across a range of solid tumors, including those resistant to conventional PD-1 or CTLA-4 therapies.

To date, approximately 1,200 patients have been treated with botensilimab and/or balstilimab in Phase 1 and 2 trials. Botensilimab alone or in combination with Agenus' investigational PD-1 antibody balstilimab has shown clinical responses in nine different metastatic cancers in late-line settings. For more information on ongoing botensilimab trials, please visit **www.clinicaltrials.gov**.

About Balstilimab (BAL)

Balstilimab (AGEN2034) is a novel, fully human monoclonal IgG4 antibody that blocks PD-1 (programmed cell death-1) from interacting with its ligands PD-L1 and PD-L2. By inhibiting the PD-1 checkpoint pathway, balstilimab aims to

restore T-cell activity against tumors. It has been evaluated in over 900 patients to date and has demonstrated clinical activity with a favorable tolerability profile in several tumor types. Balstilimab is being studied both as a monotherapy and in combination with other agents (such as botensilimab) to expand its therapeutic impact.

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 the botensilimab and balstilimab clinical programs, expected trial initiations and regulatory plans, and the potential benefits of the combination therapy. Words such as “may,” “believes,” “expects,” “anticipates,” “hopes,” “intends,” “plans,” “forecasts,” “estimates,” “will,” “potential,” “game-changing,” “curative,” and similar expressions are intended to identify forward-looking statements. These statements are subject to risks and uncertainties that could cause actual results to differ materially from current expectations. Factors that could cause actual results to differ include, but are not limited to, those described under the “Risk Factors” section of Agenus’ most recent Annual Report on Form 10-K for 2024 and subsequent Quarterly Reports on Form 10-Q filed with the SEC. Agenus cautions investors not to place undue reliance on forward-looking statements in this release, which speak only as of the date of this announcement. The company undertakes no obligation to update or revise these statements, except as required by law. All forward-looking statements are expressly qualified in their entirety by this cautionary statement.

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