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NEWS RELEASE

Agenus Presents New Data at ASCO Highlighting Botensilimab's Immune Activation in MSS Colorectal Cancer

2025-05-30

Study shows botensilimab "switches on" the body's own T-cells to attack a common, treatment-resistant form of colorectal cancer

LEXINGTON, Mass.--(BUSINESS WIRE)-- Agenus Inc. (Nasdaq: AGEN), a leader in immuno-oncology, today presented new translational data at the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting. The study demonstrates that botensilimab-based therapy induces a robust and persistent T cell immune response in microsatellite stable (MSS), or mismatch repair proficient (pMMR), metastatic colorectal cancer (mCRC)—a tumor type traditionally resistant to immunotherapy and representing approximately 85-95% of all colorectal cancers. T cells are key immune cells capable of recognizing and attacking cancer cells. Activating these typically 'cold' tumors and driving a strong T cell response suggests that botensilimab has the potential to overcome resistance and improve patient outcomes.

The research was led by Dr. Gertjan Rasschaert of Leuven University Hospitals in collaboration with Agenus, KU Leuven, and Omniscope. This joint effort brings together global leaders in immuno-oncology and advanced immune profiling technologies.

"These data provide clinical evidence of botensilimab's unique ability to enhance T-cell priming, activation, and diversity—key mechanisms that help render 'cold,' poorly immunogenic MSS colorectal tumors visible to the immune system," said Dr. Dhan Chand, PhD, Vice President of Research at Agenus. "Our findings offer new insight into how patients with immunotherapy-resistant colorectal cancer are responding at the immune level and highlight botensilimab's potential to activate immune responses in tumors that have historically been

unresponsive."

Data Highlights:

- Fast T cell priming and activation: T-cells begin activating within two weeks of starting botensilimab.
- Robustly expands and sustains T cell activity: Newly primed T cells persist and expand across treatment cycles, correlating with improved clinical responses.
- Immune activity detected before scans: Immune-profiling tests detect this activity even when standard imaging hasn't yet caught a response.
- Blood signals predict benefit: A quick blood draw can reveal early immune markers that help doctors identify who is most likely to respond and live longer.

"We're seeing — at the immune level — how botensilimab can help the body recognize and attack pMMR colorectal cancer, a form of the disease that has historically resisted immunotherapy and represents the vast majority of colorectal cancer cases," said Dr. Steven O'Day, Chief Medical Officer at Agenus. "By activating T cells and making these typically 'cold' tumors visible to the immune system, botensilimab is showing real promise in overcoming resistance and opening the door to better outcomes for patients who previously had limited options."

Presentation Details:

The presentation will be available on the publications section of the Agenus website at **https://agenusbio.com/publications/** on the date of the poster session.

Presentation Title: Monitoring botensilimab and balstilimab induced T cell dynamics in refractory mismatch repair proficient metastatic colorectal cancer.
Presenting Author: Dr. Gertjan Rasschaert
Poster Session: Gastrointestinal Cancer—Colorectal and Anal
Session Date and Time: May 31st, 2025; 9:00 AM-12:00 PM CDT
Abstract Number: 3527
Poster Number: 196

About Botensilimab (BOT)

Botensilimab is a human Fc enhanced CTLA-4 blocking 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 1,100 patients have been treated with botensilimab 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 >900 patients to date and has demonstrated clinical activity and a favorable tolerability profile in several tumor types.

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 (through SaponiQx). 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.

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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