Botensilimab/Balstilimab Breakthrough Data Presented at ASCO-GI Shows Unprecedented Tumor Shrinkage and Robust Biomarker Response in Prevalent Colorectal Cancer Population

- Botensilimab/Balstilimab (BOT/BAL) shows major tumor regression in 67.5% of Patients with Localized MSS Colorectal Cancer (CRC), a tumor typically unresponsive to IO therapy

- The study achieved durable elimination of ctDNA, a critical biomarker for cancer clearance and long-term disease-free survival

LEXINGTON, Mass. -- (BUSINESS WIRE) -- Jan. 22, 2024 -- Agenus Inc. (Nasdaq: AGEN), a leader in developing immunological cancer treatments, today announced results from the NEST-1 study, an investigator-sponsored trial (IST) evaluating the combination of botensilimab and balstilimab (BOT/BAL) in the neoadjuvant setting for colorectal cancer (CRC), both those with Microsatellite Stable (MSS) CRC and Microsatellite Instability High (MSI-H) CRC. Dr. Pashtoon Kasi, M.D., Director of Colon Cancer Research at Weill-Cornell Medicine, presented these findings at the ASCO-GI conference.

"BOT/BAL's potential impact on colorectal cancer is groundbreaking. The study's findings, particularly the significant tumor regression after only a single dose of BOT and two doses of BAL, and the complete elimination of ctDNA in 100% of patients tested, offer a potentially transformative treatment approach for CRC patients diagnosed with early stage and locally advanced colon and rectal cancers. These results hold great promise for patients and providers as a framework for reduced reliance on chemotherapy and/or surgical resection" said Dr. Pashtoon Kasi, M.D., Director of Colon Cancer Research at Weill-Cornell Medicine and lead investigator of the NEST-1 study.

Study Highlights:

- Treatment Protocol: Patients received a single dose of BOT and two doses of BAL between diagnosis and surgery, which was approximately a four-week period.
- Impressive Pathologic Response: Tumor shrinkage of ≥50% was observed in 67.5% of patients in the Microsatellite Stable (MSS) CRC cohort and 100% in the Microsatellite Instability-High (MSI-High) CRC cohort.
- Surgery Without Delays: Treatment with BOT/BAL did not cause any postponements in surgical procedures, with only two instances of Grade 3 Treatment-Related Adverse Events (TRAEs) observed.
- BOT/BAL Eliminates Circulating Tumor DNA (ctDNA): patients in the NEST-1 study were tested for ctDNA, a biomarker closely associated with long-term Disease-Free Survival (DFS).
- In a separate, independent observational study of 1,792 patients (NCT04264702; https://meetings.asco.org/abstracts-presentations/228848), also led by Dr. Kasi and presented at the ASCO-GI meeting on January 20th, showed a correlation between ctDNA clearance and improved disease-free survival (DFS) rates. Patients who remained ctDNA negative post-treatment exhibited better 2-year DFS as compared to ctDNA-positive patients.

Dr. Steven O'Day, Chief Medical Officer of Agenus, stated, "The NEST-1 trial results are remarkable. Neoadjuvant BOT/BAL in both MSS and MSI-H CRC resulted in marked tumor regression and robust immune cell infiltration in a very short interval. These results in MSS CRC (90% of all CRC) are particularly compelling and may lead to an unprecedented shift away from invasive and morbid standard treatments in the future."

NEST-1 data presented at the conference is available to view in the publications section of the Agenus website (https://agenusbio.com/publications).

About Botensilimab

Botensilimab is an investigational multifunctional anti-CTLA-4 immune activator (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 750 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 with the identifiers NCT03860272, NCT05608044, NCT05630183, and NCT05529316.

About Agenus

Agenus is a leading immuno-oncology company targeting cancer and infectious diseases with a comprehensive pipeline of immunological agents. The company's mission is 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 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 relating to the use of botensilimab and balstilimab, for instance, statements regarding therapeutic benefit and efficacy, mechanism of action (including validation of mechanism of action), potency, durability, and safety profile (including the absence of specific toxicities) of the Company's therapeutic candidates; 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 Quarterly Report on Form 10-Q or Annual Report on Form 10-K 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.

Investor Contact
917-362-1370
investor@agenusbio.com

Media Contact
781-674-4784
communications@agenusbio.com