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NEWS RELEASE

Agenus Announces End-of-Phase-2 Meeting Outcomes and Topline Interim Phase 2 Data for BOT/BAL in MSS Colorectal Cancer

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- Agreement reached with the FDA on Phase 3 dose for the BOT/BAL combination
- Accelerated approval pathway discouraged by FDA
- Preliminary Phase 2 data tracks with Phase 1 BOT/BAL clinical activity in MSS mCRC (ORR ~19.4% and 90% alive at 6 months)
- Strategic meeting with the European agency scheduled for Q3 2024 to explore additional regulatory opportunities

LEXINGTON, Mass.--(BUSINESS WIRE)-- Agenus Inc. (NASDAQ: AGEN), a leader in developing novel immunological agents to treat various cancers, today announced the results of its end-of-Phase 2 (EOP2) meeting with the U.S. Food and Drug Administration (FDA), for the advancement of its immunotherapy combination, botensilimab (BOT) and balstilimab (BAL), for the treatment of adult patients with relapsed/refractory microsatellite stable colorectal cancer (r/r MSS CRC) with no active liver metastases (NLM).

Key Outcomes of the EOP2 Meeting:

- Dosing Regimen: Agenus gained agreement on the proposed BOT/BAL combination dosing regimen of 75mg BOT once every 6 weeks for up to 4 doses in combination with 240mg BAL once every 2 weeks for up to 2 years.
- Randomized Phase 2 Interim Data: Topline interim data suggest best activity seen at 75 mg BOT/240mg BAL combination (ORR 19.4%; 6-month survival rate of 90%; data continues to mature).
- Accelerated Approval: FDA advised against submission of these results in support of an Accelerated Approval based on their view that objective response rates may not translate to survival benefit.

- Phase 3 Protocol Design: The FDA recommended the inclusion of a BOT monotherapy arm at Agenus' discretion in the Phase 3 study.

Dr. Steven O'Day, Agenus' Chief Medical Officer, stated, "Based on the high level of enthusiasm from significant numbers of global clinical experts and the promising clinical activity we have seen in the Phase 1 and 2 studies, our commitment to seek all possible pathways to make BOT/BAL available to patients is unwavering. This includes exploring opportunities to partner in the U.S. to accomplish a successful Phase 3 trial."

Agenus previously **disclosed** data from the Phase 1 trial, which showed an overall response rate (ORR) of 23% in the 77 MSS mCRC patients without active liver metastases, with a median follow up of 13.6 months. The estimated 6-month, 12-month and 18-month overall survival (OS) rates were 86%, 71%, and 62%, respectively. The estimated median OS was 21.2 months.

Topline interim data (below) from the Phase 2 trial are showing trends consistent with the Phase 1 study, including an ORR of 19.4% and 6-month survival rate of 90% for the BOT 75mg/BAL combination. The safety profile was manageable and no new signals were observed. Agenus plans to continue future discussions with FDA as the Phase 2 data mature and will present these data in totality at an upcoming medical conference.

Topline Interim Phase 2 Data

	BOT + BAL 75 mg (n= 62)	BOT+BAL 150 mg (n=61)	BOT 75 mg (n=38)	BOT 150 mg (n=40)	SOC (n=33)
ORR % (95% CI) n/nn	19.4* (10.4, 31.4) 12/62	8.2 (2.7, 18.1) 5/61	0 (0.0, 9.3) 0/38	7.5 (1.6, 20.4) 3/40	0 (0.0, 10.6) 0/33
Follow-Up (m) Mean (SD) Range	9.5 (2.77) 1.2, 15.7	9.1 (3.25) 0.1, 16.6	7.8 (4.37) 0.2, 14.8	8.2 (4.53) 0.7, 17.1	5.5 (5.30) 0.0, 13.0

*Pending confirmation of two additional responses in 75mg BOT + BAL arm. No responses are pending confirmation in other arms.

These results are particularly meaningful, as the landscape of MSS colorectal cancer treatment has seen little advancement leaving a significant gap in effective therapies for patients.

"MSS colorectal cancer, representing approximately 95% of colorectal cancer cases, remains a disease setting with substantial unmet need and is considered to be one of the most challenging types of cancer due to its high incidence and mortality rates," said Michael Sapienza, Chief Executive Officer of Colorectal Cancer Alliance. "The rapidly growing number of diagnoses in younger individuals is particularly alarming. There is an urgent need for new treatment options that can transform the trajectory of MSS colorectal cancer and provide lasting benefits for patients."

In addition to the progress in the U.S., Agenus is advancing its efforts to bring BOT/BAL to patients in Europe.

Engagements with the European Regulatory Authority to explore registration paths are scheduled for later this summer. These discussions aim to align on the regulatory path for approval of the BOT/BAL combination in Europe.

Other areas of BOT/BAL clinical development:

Agenus continues to pursue opportunities for BOT/BAL development in earlier lines of CRC and other tumor types where BOT/BAL has demonstrated clinical activity, such as lung, melanoma, and pancreatic cancers. The company expects to present data from some of these programs at future medical congresses, including BOT/BAL in sarcoma at European Society for Medical Oncology (ESMO) in September 2024.

About Botensilimab

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 1100 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 Colorectal Cancer

Colorectal cancer (CRC) is the second leading cause of cancer death in the United States, and is estimated to be the number one killer of men aged 50 and above and second leading killer of women in the same age category. Microsatellite stable (MSS) colorectal cancer is the most prevalent form of the disease, representing approximately 95% of patients with colorectal cancer. Survival remains poor for advanced disease, and the burden is shifting to a younger population. Alarmingly, from 1995 to 2019, the number of patients under the age of 55 who were diagnosed with CRC in the United States nearly doubled.

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 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 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 2023, 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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