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NEWS RELEASE

Agenus Reports Impact of Key Immuno-Oncology Data Presented at Leading Medical Conferences and Peer-Reviewed Publications

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LEXINGTON, Mass.--(BUSINESS WIRE)-- Agenus Inc. (Nasdaq: AGEN), a leader in immuno-oncology innovation, today highlights key scientific contributions in 2024-2025 that are shaping the future of cancer immunotherapy.

Agenus is advancing a robust clinical pipeline targeting complementary mechanisms to fight cancer, including checkpoint inhibitors, immune activators, tumor microenvironment conditioning agents and cell therapies (via MiNK Therapeutics). Our most advanced antibody candidates, botensilimab (BOT) an Fc-enhanced CTLA-4 blocking antibody, and balstilimab (BAL), a novel, PD-1 inhibitor, are central to our efforts.

Driving Innovation of Cancer Immunotherapy

- BOT has demonstrated differentiated mechanisms to enhance T cell priming, activation, and memory to drive a more effective immune response and was intentionally designed to mitigate toxicities associated with first-generation anti-CTLA-4 therapies.
- BOT is currently being investigated as a monotherapy and in combination with widely used standard of care anti-PD-1, chemotherapy, and allogeneic cell therapy across multiple indications:
    - MSS colorectal cancer (CRC), pancreatic cancer (in combination with chemotherapy), and gastroesophageal (in combination with BAL and agent-797).
- To date, BOT, either alone or in combination with BAL, has been evaluated in approximately 1,100 patients across more than 60 centers worldwide.
- The combination targets complementary pathways and has demonstrated clinical responses across nine tumor types, including those historically considered immuno-oncology (IO) "cold" tumors or resistant to prior

IO treatments.

Recent data presented at leading international conferences (ASCO, ESMO, ASCO GI, AACR IO) and featured in prestigious journals (Nature Medicine, Journal of Clinical Oncology, Cancer Discovery), showcase Agenus' pivotal role in advancing IO research and expanding the reach of IO therapies to new patient populations.

Agenus' Commitment to Advancing Immuno-Oncology Therapies

"The breadth and consistency of data we have presented over the past year reinforce the transformative potential of botensilimab and balstilimab in redefining treatment paradigms for patients battling historically treatment-resistance cancers. Decades of immuno-oncology research have set the stage for next-generation breakthroughs, and these latest findings with botensilimab and balstilimab represent a major advancement," said Dr. Steven O'Day, Chief Medical Officer, Agenus.

Dr. O'Day continues, "By leveraging our deep expertise in immune activation, we are unlocking responses in tumors previously resistant to immunotherapy. The results are even more promising as we move from treatment refractory metastatic disease to the neoadjuvant setting where we have the potential to reduce the need for adjuvant chemotherapy, preserve organs, and improve long-term survival. These results highlight an opportunity to reshape treatment paradigms and address the greatest unmet needs in oncology."

Breakthrough Findings Across Multiple Cancers

1. Colorectal Cancer:

Neoadjuvant Botensilimab Plus Balstilimab in Resectable Mismatch Repair Proficient (pMMR) and Deficient (dMMR) Colorectal Cancer (CRC) – NEST Study[1] **link**

Conference: ASCO GI 2025
Lead Author: Dr. Erika Hissong, Weill Cornell Medicine
Key Findings: This investigator-initiated Phase 2 trial assessed BOT/BAL as neoadjuvant therapy in localized pMMR/MSS and dMMR/MSI-H CRC patients. The combination achieved high major pathological response (MPR) rates, and after median follow-up of 18 months (NEST-1) and 9 months (NEST-2) no recurrences were observed. Extended time to surgery correlated with improved pathological response. The study underscores the potential of dual checkpoint inhibition in neoadjuvant settings for CRC and the potential for non-surgical approaches for some patients.

Neoadjuvant Botensilimab Plus Balstilimab in Resectable Mismatch Repair Proficient (pMMR)

and Deficient (dMMR) Colorectal Cancer (NEST-1 Trial)[2] **link**

Conference: ESMO GI 2024
Lead Author: Dr. Pashtoon Kasi (presented by Dr. Mehraneh Jafari), Weill Cornell Medicine
Key Findings: This investigator-initiated Phase 2 trial assessed BOT/BAL as neoadjuvant therapy in resectable pMMR and dMMR colorectal cancer (CRC). A major pathological response (MPR) rate was observed across both cohorts, with no recurrences reported to date. Notably, extended time to surgery was associated with improved responses. Updated data was presented in 2025.

Preoperative Botensilimab (BOT) with or without Balstilimab (BAL) in Resectable, Locally Advanced pMMR or dMMR Colon Cancer – UNICORN Trial[3] **link**

Conference: ASCO GI 2025
Lead Author: Dr. Filippo Ghelardi, Fondazione IRCCS Istituto Nazionale dei Tumori Milan
Key Findings: The Investigator-initiated Phase 2 UNICORN trial, explored short-course neoadjuvant BOT ± BAL in non-metastatic CRC patients. Results showed that the addition of BAL significantly enhanced response rates compared to BOT monotherapy, particularly in pMMR tumors. The pCR rate for the combination was 29% and 93% for pMMR and dMMR status, respectively, supporting the potential for non-operative management strategies in CRC.

Phase 2 Botensilimab Plus Balstilimab in Refractory Microsatellite Stable (MSS) Metastatic Colorectal Cancer with No Liver Metastases[4] **link**

Conference: ASCO GI 2025
Lead Author: Dr. Marwan G. Fakih, City of Hope Comprehensive Cancer Center
Key Findings: A Phase 2 study demonstrated deep and durable responses in MSS mCRC patients, demonstrating reproducible response rates (19%) and disease control rate (DCR) of 55% in this refractory metastatic CRC patient population; the standard of care arm had no responses. Notably, some patients treated with BOT/BAL exhibited no active disease over two years after starting the trial.

Phase 1 Study of Botensilimab Plus Balstilimab in Relapsed/Refractory Microsatellite Stable (MSS) Metastatic Colorectal Cancer[5] **link**

Publication: Nature Medicine (September 2024)
Lead Author: Dr. Andrea J. Bullock, Beth Israel Deaconess Medical Center
Key Findings: This study evaluated BOT/BAL in heavily pretreated MSS mCRC patients, a historically checkpoint

inhibitor-resistant tumor type. The ORR was 17%, and DCR reached 61%. The combination demonstrated durable responses with a manageable safety profile. In patients with non-active liver metastases (NLM) (n = 77), the ORR was 22% and the DCR was 73% with a 12-month OS rate of 69%. Conversely, in patients with active LM (n=24), ORR was 0% and the DCR was 25% with a 12-month OS rate of 30%. Learnings from this study helped define the P2 study population in MSS mCRC NLM.

A Phase I Trial of FOLFOX-3B: A Combination of Chemotherapy, VEGF(R) Inhibitors, and Checkpoint Blockade in MSS Metastatic Colorectal Cancer[6] **link**

Conference: ASCO GI 2025
Lead Author: Dr. Marwan G. Fakih, City of Hope Comprehensive Cancer Center
Key Findings: This Phase I study evaluated the combination of BOT, BAL, FOLFOX chemotherapy, and bevacizumab in MSS metastatic CRC. Preliminary findings showed activity of the combination independent of liver metastases. The regimen demonstrated a 71% objective response rate (ORR) overall. 12/14 patients were pre-treated (FOLFOX “rechallenge”). The combination was well tolerated with only 1/14 patients having immune mediated diarrhea/colitis. Findings suggest that checkpoint blockade plus chemotherapy may enhance immunogenicity in MSS CRC and extend benefit to patients with liver metastases, warranting further investigation in the first line metastatic setting.

2. Gastroesophageal Cancer:

Biomarker Analysis from Phase 2 Study of agenT-797, Botensilimab Plus Balstilimab in PD-1 Refractory Gastroesophageal Cancer **link**

Conference: AACR IO 2025
Lead Author: Dr. Samuel L. Cytryn, Memorial Sloan Kettering Cancer Center
Key Findings: This investigator-initiated Phase 2 trial demonstrated significant immune modulation, including robust tumor T-cell infiltration and increased activation of effector-memory T cells, suggesting the potential for overcoming PD-1 resistance.[7]

3. Sarcoma:

Botensilimab Plus Balstilimab in Relapsed/Refractory (R/R) Metastatic Sarcomas[8] **link**

Publication: Journal of Clinical Oncology (January 2025)
Lead Author: Dr. Breelyn A. Wilky, University of Colorado Cancer Center
Key Findings: This Phase 1 study demonstrated promising efficacy of BOT in combination with BAL, in heavily

pretreated sarcoma patients, including soft tissue sarcoma subtypes considered immunologically "cold". Notably, the overall response rate (ORR) was 19.2%, with a 27.8% ORR among angiosarcoma patients. The disease control rate (DCR) reached 65.4%, with a median progression-free survival (PFS) of 4.4 months and a 12-month overall survival (OS) rate of 69%.

Updated Efficacy and Safety of Botensilimab Plus Balstilimab in Metastatic Sarcoma[9] **link**

Conference: ESMO 2024
Lead Author: Dr. Breelyn A. Wilky, University of Colorado Cancer Center
Key Findings: Data from an expanded Phase 1 study reaffirmed the activity of BOT/BAL across refractory metastatic sarcomas, including angiosarcoma and leiomyosarcoma. ORR reached 19.2%, with durable responses beyond 21 months in some patients.

4. Mechanistic Insights

Botensilimab, an Fc-Enhanced Anti–CTLA-4 Antibody, Is Effective against Tumors Poorly Responsive to Conventional Immunotherapy[10] **link**

Publication: Cancer Discovery (December 2024)
Lead Author: Dr. Dhan Chand, Agenus Inc.
Key Findings: This landmark study highlighted how botensilimab's unique design and Fc-enhancement overcomes the limitations of conventional checkpoint inhibitors through multiple immune-activating mechanisms. The research demonstrates that botensilimab potentiates T-cell responsiveness, reduces regulatory T cells, and enhances antigen-presenting cell activation across both preclinical models and patient samples. Clinical data showed significant efficacy in multiple treatment-refractory cancers, including those that progressed on prior immunotherapies. The findings establish a new mechanistic paradigm for expanding immunotherapy benefits to patients with traditionally immunotherapy-resistant cancers.

AGEN1721 – a first-in-class Fc-enhanced Bifunctional Antibody Targeting FAP and TGFβ, Remodels the Tumor Microenvironment to Overcome Cancer-associated Fibroblast-mediated Immune Suppression[11] **link**

Conference: SITC 2024
Lead Author: Dr. Priya Iyer, Agenus Inc.
Key Findings: AGEN1721, a novel dual-targeting agent, demonstrated the ability to modulate the tumor stroma, enhancing T-cell infiltration and antitumor responses in preclinical models. These findings provide a strong

rationale for clinical development.

Additional updates in mCRC, NSCLC, melanoma, ovarian and pancreatic cancer are anticipated in the second half of 2025.

For further details on these studies, please visit **www.agenusbio.com**, **www.minktherapeutics.com** or access the respective publications and conference presentations.

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.

About Botensilimab (BOT)

Botensilimab (BOT) 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 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 with the identifiers NCT03860272, NCT05608044, NCT05630183, and NCT05529316.

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 AgenT-797

AgenT-797 is an allogeneic invariant natural killer T (iNKT) cell therapy that harnesses the dual power of innate and adaptive immunity. iNKTs function as “master regulators,” combining the cytotoxic capabilities of NK cells with T-cell–like antigen recognition and memory. This unique biology enables a robust, pathogen-agnostic immune response that can be directed against hard-to-treat tumors.

Manufactured by MiNK Therapeutics in Lexington, MA, agenT-797 is a scalable, off-the-shelf product designed to provide accessible, transformative treatment options. In clinical trials, agenT-797 can bolster peripheral memory T-cell activation, enhance tumor infiltration, and potentially improve outcomes for patients with solid cancers (Cytryn et al. AACR IO 2024, **Oncogene. 2024**) and to combat inflammation in critically ill patients with severe respiratory pathology (**Nature Communications** . 2024).

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.

[1] JCO 42, 117-117(2024).

[2] Annals of Oncology (2024) 35 (suppl_1): S1-S74.

[3] J Clin Oncol 43, 2025 (suppl 4; abstr 158)

[4] J Clin Oncol 43, 2025 (suppl 4; abstr 23)

[5] Nat Med 30, 2558–2567 (2024).

[6] J Clin Oncol 43, 2025 (suppl 4; abstr 180)

[7] Cytryn, S. (2025, February 25) Biomarker Analysis of Phase 2 Study of agenT-797, Botensilimab Plus Balstilimab in

PD-1 Refractory Gastroesophageal Cancer. www.aacr.org/meeting/aacr-io-discovery-and-innovation-in-cancer-immunology-revolutionizing-treatment-through-immunotherapy/abstracts

[8] J Clin Oncol 0, JCO-24-02524.

[9] Annals of Oncology , Volume 35, S1034.

[10] Cancer Discov (2024) 14 (12): 2407–2429.

[11] Journal for ImmunoTherapy of Cancer (November 2024)12(Suppl 2):A1518-A1518.

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