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NEWS RELEASE

Agenus Presents Data at ASCO GI Demonstrating Impact of BOT/BAL in Colorectal Cancer Across Neoadjuvant and Advanced Disease

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- Results from two independent neoadjuvant studies in the U.S. and Europe, enrolling more than 80 patients, underscore BOT/BAL's potential to enable chemo-free and non-operative approaches in colorectal cancer (CRC).
- New randomized Phase 2 results in over 230 patients with refractory MSS mCRC, consistent with Phase 1 data, demonstrate durable responses and a favorable safety profile.
- Strong activity demonstrated with BOT/BAL in first-line and rechallenged MSS mCRC in combination with chemotherapy and targeted therapies shows synergy and tolerability in a large patient population.

LEXINGTON, Mass.--(BUSINESS WIRE)-- Agenus Inc. (Nasdaq: AGEN), a leader in immuno-oncology, today shared new data on botensilimab (BOT) and balstilimab (BAL) at the American Society of Clinical Oncology Gastrointestinal Cancers Symposium (ASCO GI) in San Francisco. Data from five presentations underscore the transformative potential of BOT/BAL across multiple lines of therapy in colorectal cancer, including neoadjuvant, first-line, and refractory settings. Data presented also highlight BOT/BAL's potential in treating microsatellite stable (MSS) CRC tumors, which account for 85-95%[1] of patients living with CRC that historically have been unresponsive to immuno-oncology (I/O) therapies. To date, BOT/BAL has been evaluated in approximately 1,100 patients across more than 60 centers worldwide.

"Data presented at ASCO GI highlight botensilimab and balstilimab's potential to redefine colorectal cancer treatment, delivering remarkable outcomes in neoadjuvant MSS CRC," said Dr. Steven O'Day, Chief Medical Officer of Agenus . "These findings set the stage for pivotal studies intended to create a new standard of care for colon and rectal cancer patients by reducing reliance on chemotherapy, radiation, and surgery, while improving survival."

Key Data Highlights

Neoadjuvant CRC: A Potential Path to Chemo-Free Treatment

Data presented from two independent studies, UNICORN and NEST, collectively include more than 80 patients treated with BOT/BAL:

- UNICORN: Phase 2 Trial of Pre-Operative BOT/BAL Combination Treatment in Resectable Colon Cancer (Abstract 158):
    - This multicenter Phase 2 study enrolled 56 patients across 10 centers in Italy and France.
    - Pathological complete responses (pCR) and pathological major responses (pMR) were observed in both the pMMR/MSS and dMMR/MSI-H patient populations.
    - BOT/BAL achieved a 93% pCR rate and 100% pMR in dMMR/MSI-H tumors and 29% pCR rate and 36% pMR rate in pMMR/MSS tumors, highlighting the opportunity for a non-operative, organ sparing, approach in this disease setting.
    - Serious adverse events (AEs) occurred in 9 pts (16%) and were treatment-related in 3 pts (5%). Only 1 of 56 surgeries were delayed due to an AE.
- NEST: Phase 2 Trial of Neoadjuvant Combination Treatment of BOT/BAL in Patients with Resectable Colon Cancer (Abstract 207):
    - This trial has currently enrolled 24 patients.
    - After median follow-up of 18 months (NEST-1 arm) and 9 months (NEST-2 arm), all patients (100%) remained ctDNA negative and no clinical recurrences were observed. The pMR improved in NEST-2 to 47% (7/15) in MSS tumors when the median time to surgery was extended.
    - The combination was well tolerated with no grade 4 events and no unresolved immune-mediated adverse events (imAEs). No delays in surgery occurred due to imAEs.

Dr. Filippo Pietrantonio, Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori Milan comments on the UNICORN study stating, " These results further validate the transformative potential of botensilimab and balstilimab in colorectal cancer. The remarkable pathological response rates observed in both pMMR and dMMR tumors highlight the unique strength of this combination in addressing a critical unmet need and pave the way for non-operative management strategies.”

First-Line and FOLFOX Rechallenged MSS CRC: Powerful Combination with Standard Therapies

- Phase 1/2 Trial of BOT/BAL With FOLFOX-Bevacizumab in MSS mCRC (Abstract 180):
    - Preliminary findings showed activity of combination independent of liver metastases.
    - In the initial 14 patients, 12 which were previously treated with FOLFOX, a 71% overall response rate

(ORR) was achieved. In the 9/14 patients with liver metastases, a 67% ORR was achieved.
    - The combination was well-tolerated with limited severe imAEs, supporting the opportunity for higher doses of BOT.

Refractory MSS CRC: Consistent Results Across Phase 1 and 2 Studies

- Global Randomized Phase 2 Study of BOT/BAL in MSS mCRC NLM (Abstract 23):
    - This is a global Phase 2 trial (NCT05608044) of BOT/BAL versus standard-of-care treatments of regorafenib or trifluridine/tipiracil in patients with refractory metastatic colorectal cancer that had spread to either peritoneum, lymph nodes, lungs, bone or brain. 234 patients were enrolled across 40 centers worldwide.
    - These results reinforce the activity and safety seen in the Phase 1 study and confirm the contribution of BAL to BOT.
    - BOT75/BAL achieved a 19% ORR and 55% disease control rate (DCR) in this refractory population. Standard of care had no responses.
    - 70% of responses were ongoing at the time of data cut-off, demonstrating durability as DOR continues to mature.
    - BOT/BAL showed a superior benefit-risk profile at 75 mg compared to BOT/BAL 150mg and has been selected for Phase 3 trials.
    - No new safety signals were observed, and no treatment related deaths occurred. The most common imAEs at BOT 75mg + BAL included diarrhea/colitis (35%) and hypothyroidism (13%).

“The Phase 2 results highlight the unique and consistent activity of the botensilimab and balstilimab combination, demonstrating a compelling objective response rate in microsatellite stable metastatic colorectal cancer, a disease where responses to immunotherapy have historically been absent,” said Dr. Marwan Fakih, Department of Medical Oncology and Therapeutics Research, City of Hope Comprehensive Cancer Center. “These findings underscore the potential of botensilimab and balstilimab combination treatment in addressing this critical unmet need, paving the way for further investigation.”

Gastric Cancer

- Phase 2 BOT/BAL/AgenT-797 in Combination with Ramucirumab and Paclitaxel in Patients with Previously Treated, Unresectable or Metastatic Gastroesophageal Cancers (Abstract TPS515):
    - The Phase 2 trial (NCT06251973) is investigating a novel combination approach, which leverages cellular therapy and immune modulation to address the unmet needs in gastroesophageal cancers. Gastroesophageal cancers continue to be a growing global burden responsible for nearly 1.3 million global deaths annually[2].

- The novel approach demonstrated early signals of activity and tolerability in the second-line treatment setting, with additional efficacy data anticipated in 2H 2025.

Future Development Plans

Agenus has developed registrational enabling trials in MSS CRC across neoadjuvant, first-line, and late-line settings. These trials will launch upon completion of strategic transactions. Upon the options being considered are, partnerships, licensing, or joint ventures. These initiatives aim to accelerate global access to BOT/BOL to deliver transformative patient outcomes and drive substantial value for stakeholders.

Botensilimab, balstilimab, and agenT-797 are investigational agents and are not approved for use as therapies in any jurisdiction worldwide.

For additional data and publications, visit **agenusbio.com/publications**.

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, leveraging a unique innate immune cell type that serves as a master regulator of both innate and adaptive immunity. iNKTs combine the cytotoxic capabilities of natural killer (NK) cells with the adaptive memory of T cells, enabling them to elicit a broad range of immune responses in a pathogen-agnostic manner.

AgenT-797 is a scalable, “off-the-shelf” cell therapy product, manufactured by MiNK Therapeutics in Lexington, MA, to deliver transformative treatment solutions to patients.

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] Ros J et al. Front Oncol 2023;13:1112276; 2. André T et al. Am Soc Clin Oncol Educ Book 2022;42:1-9;
[2] e Clinical Medicine , 2022

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