agenus

NEWS RELEASE

Nature Medicine Reports Agenus' Novel Immunotherapy Demonstrates Clinical Activity Against a Deadly Form of Colorectal Cancer on the Rise in Americans Under 50

6/13/2024

BOT/BAL Combination Shows Promising Results in the Most Prevalent Form of Colorectal Cancer, Affecting 95% of Diagnosed Patients

LEXINGTON, Mass.--(BUSINESS WIRE)-- Agenus has published results from a groundbreaking clinical trial in Nature Medicine, revealing the potential of a novel immunotherapy combination for treating microsatellite stable metastatic colorectal cancer (MSS mCRC), a cancer type historically resistant to immunotherapy. This pioneering research, led by an international team of oncologists, focuses on the efficacy and safety of botensilimab (BOT), an Fc-enhanced anti-CTLA-4 antibody, in combination with balstilimab (BAL), an anti-PD-1 antibody. Together, these therapies are designed to activate the immune system against a cancer type historically resistant to immunotherapy.

Colorectal cancer is the second leading cause of cancer death in the United States. While overall death from CRC has declined, survival rates for advanced disease remain poor, with an increasing burden on younger populations. For the 95% of patients diagnosed with MSS mCRC, there are no approved immunotherapies, making long-term survival exceedingly rare.

Publication Highlights:

- Patient Group: The Phase 1 trial assessed 148 heavily pretreated MSS mCRC patients treated with the combination at active doses; 101 of these with long term follow-up, and 77 of these without active liver

metastases as of the data cutoff of November 29, 2023.

- Safety and Tolerability: There were no treatment related deaths in patients treated with the combination BOT/BAL, and side effects were manageable and consistent with immunotherapies.
- Efficacy Results: In the 77 patients without active liver metastases with a median follow-up of 13 months, the Objective Response Rate (ORR) was 22% (17/77) and a majority of these responses were ongoing.
- Long-term Benefits: Noteworthy are the durable responses observed in those without active liver metastases, with a median Duration of Response (DOR) not yet reached and the majority of patients (69%) alive at one year.

In a recent **press release**, Agenus disclosed updated results as of the data cutoff of March 1, 2024. At that time, the ORR had increased to 23% in the 77 patients, with a median follow up of 13.6 months. The median duration of response in the 18 responders was still not reached. The estimated 12-month and 18-month OS rates were 71% and 62%, respectively. The median OS was 21.2 months. The most common safety observations were immune-related diarrhea or colitis, which were managed in accordance with standard therapies.

Clinical Implications:

This research highlights the potential of BOT and BAL as a significant advancement in the immunotherapy landscape, particularly for MSS mCRC, the most common type of colorectal cancer which has no approved immunotherapies.

Future Directions:

A randomized Phase 2 study to confirm the comparative safety and efficacy of the BOT and BAL combination has completed enrollment and will be included in an upcoming discussion with the U.S. Food and Drug Administration at a scheduled End-of-Phase 2 Meeting in July. A Phase 3 trial is planned to initiate later this year.

Access the Full Publication:

The full details of this study can be found **here**.

About Nature Medicine

Nature Medicine is a premier weekly scientific journal, publishing the finest peer-reviewed research across all fields of science and technology. Nature prides itself on providing cutting-edge studies that significantly advance knowledge and understanding in the scientific community. Only about 8% of the manuscripts submitted to Nature Medicine are accepted for publication, underscoring the journal's stringent selection criteria and commitment to publishing only the most pioneering and significant scientific discoveries.

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 900 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, comprising an estimated 8.3% of cancer-related deaths annually. Although overall mortality from CRC has declined, 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 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 regarding a 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.

Investors

917-362-1370

investor@agenusbio.com

Media

612-839-6748

communications@agenusbio.com

Source: Agenus