



Clinical Activity of AGEN1181 Demonstrated Across Nine Treatment-Resistant Cancers at SITC

November 12, 2021

- Seventeen objective responses reported across nine cancers
- Evidence of monotherapy activity, with four cases of confirmed objective response
- Objective responses noted in treatment refractory, poorly immunogenic tumors including microsatellite stable (MSS) colorectal cancer, ovarian cancer, MSS endometrial cancer, and melanoma; as well as responses in tumors not previously reported including pancreatic cancer, cervical cancer, visceral angiosarcoma, non-small cell lung cancer, and leiomyosarcoma
- No cases of hypophysitis, pneumonitis, or high-grade hepatitis
- Phase 2/3 trials to be initiated in colorectal and gynecological cancers

LEXINGTON, Mass., Nov. 12, 2021 (GLOBE NEWSWIRE) -- Agenus (NASDAQ: AGEN), an immuno-oncology company with an extensive pipeline of checkpoint antibodies, adjuvants, and vaccines designed to activate immune response to cancers and infections, today announced the presentation of new clinical data for AGEN1181 (Fc-enhanced anti-CTLA-4) as monotherapy and in combination with balstilimab (anti-PD-1) at the Society for Immunotherapy of Cancer (SITC) 36th Annual Meeting.

"AGEN1181 as monotherapy and in combination with balstilimab has shown durable responses in heavily pre-treated, poorly immunogenic 'cold' cancers, as well as those who have failed to respond to prior PD-1 inhibition," said Steven O'Day, MD, Chief Medical Officer of Agenus. "This regimen is well tolerated, with no hypophysitis, pneumonitis, or high-grade hepatitis observed to date. The clinical performance of AGEN1181 is consistent with its Fc-enhanced design, safely expanding the benefit of immunotherapy to a broader patient population."

Evidence of single agent activity

As of the data cut-off date of September 17, 2021, one hundred and sixteen patients received AGEN1181 in a dose escalation study to determine the optimal monotherapy dose and combination dose with balstilimab. Of note, this population was heavily pre-treated, with over half of these patients receiving at least 3 prior lines of therapy and nearly a third of patients receiving prior anti-PD-1 therapy. There were four cases of confirmed objective responses to AGEN1181 monotherapy. These include a complete response (CR) in MSS endometrial cancer, and partial responses (PR) in pancreatic cancer, as well as PD-1 refractory cervical cancer. These are the first reported responses to CTLA-4 monotherapy in these disease settings. The fourth response was in a patient with PD-1 refractory melanoma. Of note, three of the monotherapy responders expressed the low affinity FcγRIIIA receptor, which is associated with lack of response to first-generation CTLA-4 inhibitors¹.

Balstilimab combination benefits >60% of patients

Significant benefit was also observed with the combination of AGEN1181 and balstilimab across multiple "cold" cancers studied, with >60% of evaluable patients receiving at least 1 mg/kg AGEN1181 experiencing disease control. Among 20 evaluable patients with microsatellite stable colorectal cancer (MSS-CRC), where PD-1 inhibitors have historically shown limited to no activity²⁻⁵, there were three confirmed PRs and one unconfirmed PR. In addition, ten cases of stable disease (SD) were observed, with one patient's tumor burden reduced by 27%. The disease control rate (DCR) among these MSS CRC patients was 70%.

Among 9 evaluable ovarian cancer patients receiving at least 1 mg/kg of AGEN1181 in combination with balstilimab, there were three confirmed PRs and two cases of SD (one of the patients with SD had a 28% reduction of tumor burden). Compelling clinical activity was also seen in MSS-endometrial cancer as both patients treated with combination therapy demonstrated PRs; all three patients with MSS endometrial cancer treated with AGEN1181 (one with monotherapy, two in combination with balstilimab) had objective responses. Additional responders to combination therapy include 1 confirmed PR in a NSCLC patient who failed prior PD-1 therapy, 2 confirmed PRs in visceral angiosarcoma, and 1 unconfirmed PR in leiomyosarcoma.

Responses in this Phase 1 trial have been durable, with half lasting at least 24 weeks and the majority ongoing.

"AGEN1181 as monotherapy and in combination with balstilimab has shown promising activity in patients with poorly immunogenic tumors such as MSS-CRC, endometrial and ovarian cancers; these are tumor types that do not traditionally respond well to single agent anti PD-1/PD-L1 therapy," said Anthony El-Khoueiry, MD, Phase I Program Director and Associate Professor of Clinical Medicine at Keck School of Medicine of University of Southern California (USC). Dr. El-Khoueiry is also an oncologist at the USC Norris Comprehensive Cancer Center, part of Keck Medicine of USC. "Importantly, multiple responders expressed the low affinity FcγRIIIA receptor, a feature that makes them less likely to respond to first-generation CTLA-4 antibodies. Together, this highlights the potential of AGEN1181 to fulfill unmet medical needs in the current treatment landscape by overcoming limitations of approved immunotherapies."

Differentiated safety profile versus first generation CTLA-4 inhibitors

AGEN1181 was well tolerated with no hypophysitis, pneumonitis, or high-grade hepatitis. Rates of gastrointestinal and skin toxicities were comparable to those observed with first-generation CTLA-4 inhibitors.

Phase 2/3 trials to be initiated in colorectal and gynecological cancers

Based on these data, multi-arm, randomized phase 2/3 trials investigating AGEN1181 as monotherapy and in combination with balstilimab in MSS-CRC and gynecological cancers (ovarian and MSS-endometrial cancer) are being initiated. The design of these trials may support a potential filing for full and/or accelerated approval based on the magnitude of benefit demonstrated in the studies. Combination studies of AGEN1181 with AGEN2373, a conditionally active CD137 agonist, are expected to begin later this year in PD-1 refractory melanoma.

Presentation Details:

Abstract Title: AGEN1181, an Fc-enhanced anti-CTLA-4 antibody, alone and in combination with balstilimab (anti-PD-1) in patients with advanced solid tumors: Initial phase I results (NCT03860272)

Abstract Number: 479

Presenting Author: Dr. Anthony El-Khoueiry

The poster presentation can be accessed in the investor section of our website at <https://investor.agenusbio.com/events-and-presentations>.

In addition, Dr. Steven O'Day, Chief Medical Officer at Agenus and Dr. Manuel Hidalgo, Chief of the Division of Hematology and Medical Oncology at Weill Cornell Medicine and NewYork-Presbyterian/Weill Cornell Medical Center, will participate in a webcast hosted by Dr. Matt Phipps, biotechnology analyst at William Blair on Friday, November 12, 2021 at 12:00 p.m. ET.

Registration for the webinar can be done in advance at https://williamblair.zoom.us/webinar/register/WN_WzxcgiO1MRw6dKIWm3nAg-w

A replay will be available after the call for 30 days on the Events & Presentations page of the Agenus website at <https://investor.agenusbio.com/events-and-presentations>.

References:

- 1 [F Arce Vargas et al. Cancer Cell. 2018 Apr 9;33\(4\):649-663.e4](#)
- 2 [J Brahmer et al. N Engl J Med 2012; 366:2455-2465](#)
- 3 [S Topalian et al. N Engl J Med 2012; 366:2443-2454](#)
- 4 [D Le et al. Journal of Clinical Oncology 34, no. 15 suppl \(May 20, 2016\) 103-103](#)
- 5 [C Eng et al. Lancet Oncol 2019; 20: 849-61](#)

Disclosures:

Dr. El-Khoueiry has served as a consultant for Agenus.

About AGEN1181

AGEN1181 is a next-generation, Fc-enhanced, immunoglobulin G1 (IgG1) antibody designed to block CTLA-4 (cytotoxic T-lymphocyte associated antigen 4) from interacting with its ligands CD80 and CD86. The Fc region of the antibody was engineered to enhance potency, improve safety, and benefit a broader patient population versus first-generation anti CTLA-4 antibodies. CTLA-4 is a negative regulator of immune activation that is considered a foundational target within the immuno-oncology market.

About Balstilimab

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. PD-1 is a negative regulator of immune activation that is considered a foundational target within the immuno-oncology market.

About Agenus

Agenus is a clinical-stage immuno-oncology company focused on the discovery and development of therapies that engage the body's immune system to fight cancer. The Company's vision is to expand the patient populations benefiting from cancer immunotherapy by pursuing combination approaches that leverage a broad repertoire of antibody therapeutics, adoptive cell therapies (through its affiliate MiNK Therapeutics), adjuvants, and proprietary cancer vaccine platforms. The Company is equipped with a suite of antibody discovery platforms and a state-of-the-art GMP manufacturing facility with the capacity to support clinical programs. Agenus is headquartered in Lexington, MA. For more information, please visit www.agenusbio.com and our Twitter handle @agenus_bio. Information that may be important to investors will be routinely posted on our website and Twitter.

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 therapeutic candidates AGEN1181, balstilimab, and AGEN2373, for instance, statements regarding therapeutic benefit and efficacy, mechanism of action, potency, durability, and safety profile of the therapeutic candidates, both alone and in combination with each other and/or other agents, and the accuracy of top line or interim data; statements regarding future clinical and regulatory development plans for AGEN1181 alone and in combination with other agents, including balstilimab and AGEN2373; our ability to obtain regulatory approval for AGEN1181, alone and in combination with other agents, including balstilimab, including the timing (including the possibility of accelerated review) and scope of any such regulatory approval; future commercial plans, alone and in combination with other agents; and any other statements containing the words "may," "believes," "expects," "anticipates," "hopes," "intends," "plans," "forecasts," "estimates," "will" 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.

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