



Agenus Initiates Botensilimab Phase 2 ACTIVATE Trials in Advanced MSS Colorectal Cancer and Advanced Melanoma

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- Phase 2 ACTIVATE trials to advance globally in metastatic patients who have progressed on available therapies
- Botensilimab, alone and in combination with balstilimab (PD-1), has demonstrated [robust clinical activity](#) in nine treatment-resistant tumor types, including [microsatellite stable colorectal cancer](#)

LEXINGTON, Mass., Sept. 12, 2022 (GLOBE NEWSWIRE) -- Agenus (NASDAQ: AGEN), an immuno-oncology company with an extensive pipeline of therapeutics designed to activate the immune response to cancers and infections, today announced the initiation of a global Phase 2 program of botensilimab, an Fc-enhanced anti-CTLA-4 that activates innate and adaptive immune responses. These trials include ACTIVATE-Colorectal, a Phase 2 study designed to evaluate botensilimab as monotherapy and in combination with balstilimab (anti-PD-1) for the treatment of microsatellite stable colorectal cancer (MSS CRC), and ACTIVATE-Melanoma, a Phase 2 study designed to evaluate botensilimab as a single agent for advanced melanoma, refractory to either prior anti-PD-1 or combined anti-PD-1/anti-CTLA-4 therapy. An additional Phase 2 study in pancreatic cancer is anticipated to begin later in 2022.

"The Phase 1 botensilimab program demonstrated remarkable activity in poorly immunogenic and difficult to treat tumor types," said Steven O'Day, MD, Chief Medical Officer at Agenus. "In light of our compelling clinical data, we have received clearance from the FDA to initiate our Phase 2 development program in two indications and intend to expand to multiple additional indications as rapidly as possible with the aim of delivering a transformative new treatment option to patients in need."

ACTIVATE-Colorectal is a global, randomized, open-label, dose-optimization study evaluating the safety and efficacy of botensilimab as monotherapy and in combination with balstilimab in advanced refractory MSS CRC patients. Key elements of ACTIVATE-Colorectal include:

- Patients must have received at least one prior chemotherapy regimen
- Patients cannot have received prior PD-1, CTLA-4 or other immune checkpoint inhibitor therapy
- Primary endpoint is overall response rate (ORR); secondary endpoints include duration of response (DOR), progression-free survival (PFS) and overall survival (OS)
- Recruitment will be global, including sites in the United States and Europe

ACTIVATE-Melanoma is a global, randomized, open-label, multi-cohort, dose-optimization study evaluating the safety and efficacy of botensilimab as a single agent in advanced refractory melanoma. Key elements of ACTIVATE-Melanoma include:

- Study will enroll patients who have failed prior anti-PD-1 therapy (cohort A) or both anti-PD1 and anti-CTLA-4 therapy (cohort B)
- Primary endpoint is overall response rate (ORR); secondary endpoints include duration of response (DOR), progression-free survival (PFS) and overall survival (OS)
- Recruitment will be global, including sites in the United States and Europe

About Microsatellite Stable Colorectal Cancer

Colorectal cancer remains the third most common cancer diagnosis and second-leading cause of cancer death worldwide, affecting 1.93 million and 916,000 individuals each year¹. MSS colorectal cancer is a form of colorectal cancer where the cells' DNA repair mechanisms remain intact². It accounts for over 95% of metastatic colorectal cancer cases³ and has historically been unresponsive to immune checkpoint therapy⁴. Standard of care in pretreated metastatic MSS colorectal cancer offers limited benefit, with an approximate 1-2% response rate and a median of 6-7 months of survival^{5,6}.

About Advanced Refractory Melanoma

Melanoma is a serious skin cancer that affects approximately 132,000 individuals each year and has been growing in incidence⁷. Advanced refractory melanoma refers to cancer that has spread to other parts of the body and stopped responding to medical therapy. Recent advances in the use of targeted therapy and immunotherapy, including anti-PD-1 and anti-CTLA-4, have improved survival for patients diagnosed with advanced melanoma. However, while anti-PD-1 monotherapy can be effective as a first-line treatment for some patients with metastatic melanoma, roughly half fail to achieve an objective response and those who do often subsequently relapse^{8, 9, 10}. Those patients with non-BRAF mutated tumors who are refractory to or who relapse after having received anti-PD-1 and anti-CTLA-4 therapy have few effective treatment options.

About Botensilimab

Botensilimab is a novel innate and adaptive immune activator that binds CTLA-4. The antibody was designed to enhance FcγR effector functions while avoiding complement-related toxicities and has demonstrated activity in cancer patients for whom current immuno-oncology agents have historically been ineffective. As presented at SITC 2021, botensilimab is the first CTLA-4 inhibitor to demonstrate clinical responses across nine cold and treatment-resistant cancers. At ESMO GI 2022, botensilimab demonstrated unprecedented activity in combination with balstilimab in MSS colorectal cancer, with a 24% response rate and 73% disease control rate in heavily pre-treated patients with a median of 4 prior lines of therapy.

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 and infections. 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 subsidiary MiNK Therapeutics), and adjuvants (through its subsidiary SaponiQx). 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 our technologies, therapeutic candidates, and capabilities, for instance, statements regarding therapeutic benefit and efficacy, mechanism of action, potency, durability, and safety and tolerability profile of our therapeutic candidates, both alone and in combination with each other and/or other agents; statements regarding future plans, including research, clinical, regulatory, and commercialization plans; and any other statements containing the words "may," "believes," "expects," "anticipates," "hopes," "intends," "plans," "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 and available on our website: www.agenusbio.com. 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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¹ [World Health Organization. \(n.d.\). Cancer. Retrieved September 8, 2022](#)

² [Li, K., Luo, H., Huang, L. et al. *Cancer Cell Int* 20, 16 \(2020\)](#)

³ [Koopman et al. *Br J Cancer* 2009 Jan 27;100\(2\):266-73](#)

⁴ [Sahin et al. *American Society of Clinical Oncology Educational Book* 42 \(June 3, 2022\) 242-253](#)

⁵ [Grothey et al. *Lancet* 2013 Jan 26;381\(9863\):303-12](#)

⁶ [Mayer et al. *N Engl J Med* 2015 May 14;372\(20\):1909-19](#)

⁷ [World Health Organization. \(n.d.\). Radiation: Ultraviolet \(UV\) radiation and skin cancer. Retrieved September 8, 2022](#)

⁸ [Larkin J, Hodi FS, Wolchok JD. *N Engl J Med* 2015 Sep 24;373\(13\):1270-1](#)

⁹ [Gide TN, Wilmott JS, Scolyer RA, Long GV. *Clin Cancer Res* 2018 Mar 15;24\(6\):1260-1270](#)

¹⁰ [Kluger HM, Tawbi HA, Ascierto ML, et al. *J Immunother Cancer* 2020 Mar;8\(1\):e000398](#)