agenus news

Vol. 3 Issue 11 · June 02, 2020

AGEN1181 Presented at ASCO by Dr. Steven O'Day

Objective Clinical Responses in Patients Who Have Failed Other Available Treatments

Dr. Steven O'Day, Executive Director of the John Wayne Cancer Institute, presented data on AGEN1181, Agenus' multipurpose CTLA-4 engager. Dr. O'Day elaborated on data of two confirmed responses: i) a complete response (CR) in a refractory endometrial cancer patient treated with AGEN1181 monotherapy at 1 mg/kg and ii) a partial response (PR) with more than 70% tumor reduction, also in an advanced endometrial cancer patient treated with low-dose AGEN1181 + Balstilimab (anti-PD-1). The trial will continue through dose escalation and expansion with accelerated development in indications with limited/no effective treatment options such as PD-1-refractory NSCLC, melanoma and MSS tumors such as colorectal and endometrial cancers.

Efficacy Data

The complete response was in a patient with refractory, microsatellite stable (MSS) endometrial cancer that is PD-L1 negative. These markers generally suggest that such a patient would not be responsive to immunotherapies. An early and durable response to AGEN1181 in this patient suggests that AGEN1181 may be performing as designed.

The partial response was in a 72-year-old patient with metastatic endometrial cancer. This patient was also PD-L1 negative and MSS stable. She had prior therapies, including carboplatin and paclitaxel. The patient was dosed with 0.3mg/kg AGEN1181 and 3 mg/kg of Balstilimab. The patient's scans revealed a significant partial response in 3 large peritoneal lesions and a complete response in another lesion, with an overall tumor reduction of 70%. This patient will be monitored for the possibility of a CR with further follow-up.

A third patient with refractory ovarian cancer treated with the lowest dose of AGEN1181 has had disease stabilization for over one year. We may be at an optimal dose for our combo strategy at 1 mg/kg AGEN1181 and 3 mg/kg Balstilimab, but our trial will continue to evaluate higher doses of AGEN1181 as we have not yet reached a dose limiting toxicity.

As we contemplate next steps for the clinical development of AGEN1181, we will be targeting potential major registration opportunities such as PD-1 refractory NSCLC, melanoma, and MSS tumors such as endometrial and colorectal cancers.

It is important to note that in addition to the PD-L1 levels and MSS status, we have analyzed the genetic polymorphisms of responding patients. Once again, responses were noted in patients who are unlikely candidates to respond to CTLA-4 therapies such as Yervoy® due to their genetic polymorphism. AGEN1181 is Fc-enhanced to expand the benefit of CTLA-4 therapy to these patients and therefore, these responses are an early validation of AGEN1181's intended activity. As a reminder, we have also engineered the Fc region of our TIGIT monospecific (AGEN1327) and bispecifc (AGEN1777), which have demonstrated preclinical superiority to the current competitor TIGIT molecules.

Safety Data

AGEN1181 was designed to avoid complement mediated toxicities which are typically associated with the current CTLA-4 class. In more than 27 patients enrolled in the trial across 4 monotherapy and two combination cohorts, no neurotoxicity or hypophysitis has been observed so far.

Hear from the Experts About AGEN1181 in the I-O Landscape

Date: June 2, 2020 • Time: 05:30 pm ET • Dial-in details: Investor access: 800.267.2845/973.413.6102 (Passcode: 842069)

A replay will be available shortly after the completion of the call with the following dial in: 800.332.6854/973.528.0005 (Passcode: 842069)

Dr. Chuck Drake, MD

Co-Director, Cancer Immunotherapy Program, Columbia University Herbert Irving Comprehensive Cancer Center

Dr. Steven O'Day, MD

Executive Director of the John Wayne Cancer Institute and Cancer Clinic

Jennifer Buell, PhD

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At ASCO 2020, data was presented from several other CTLA-4 antibodies. This ranged from only safety data in >80 patients treated with a conditionally active version of Yervoy® (BMS's Probody) to partial responses upon treatment with a CTLA-4 x PD-L1 bispecific (Alphamab Oncology, China) in patients with NSCLC and nasopharyngeal who failed prior therapy with a checkpoint inhibitor.

However, the Fc-enhanced design of AGEN1181 distinguishes it from peers: this design enhances T cell responses, Treg depletion and extends its benefit to a broader population (3X more than 1st gen CTLA-4). These outcomes are outside the reach of known CTLA-4 bispecifics or conditionally active CTLA-4 agents (see Table). For example: the activity of bispecifics may be limited because they only target immune cells co-expressing CTLA-4 and a second target. On the other hand, AGEN1181 is designed to achieve superior immune modulation by targeting a majority of CTLA-4-expressing cells in the tumor microenvironment. Further, dosing of AGEN1181 is flexible. On the contrary, bispecifics may be handicapped from potential incompatibility between dosing requirements of CTLA-4 and that of the paired target (e.g. PD-(L)1).

Based on the efficacy demonstrated at low doses of AGEN1181 coupled with a safety profile that continues to stand apart from first-generation CTLA-4 antibodies, AGEN1181 appears to demonstrate superior performance versus other molecules.

AGEN1181 Competitive Advantages

	AGEN1181	1st generation molecules (*e.g.* Yervoy®)	Conditionally active molecules (*e.g.* Probody)	Afucosylated (*e.g.* BMS)	Bispecific
EFFICACY Novel Fc-mechanism promotes better **T cell priming** and **Treg depletion**	✓	X	X	✓	X
SAFETY Expected to **avoid complement-dependent irAEs** (*e.g.* hypophysitis)	✓	X	✓	X	✓
PATIENT REACH Improved binding to CD16 (FcγRIIIA) for both **low and high affinity allele patients**	✓	X	X	✓	X