TPS337

AGEN1181, a Clinical Stage Fc-engineered anti-CTLA-4 Antibody With Improved Therapeutic Potential for the Treatment of Patients With Advanced Malignancies *(NCT03860272)* C-800-01

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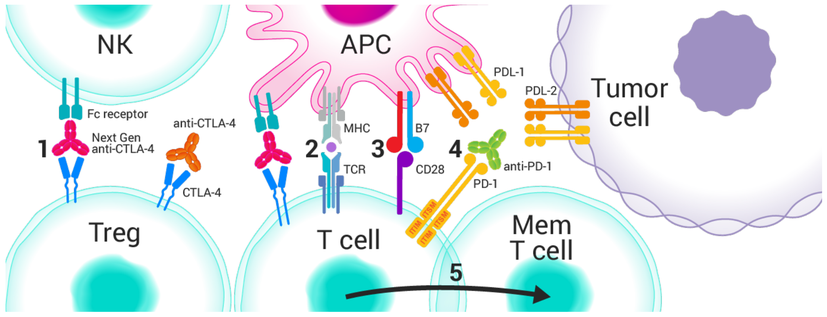
Background

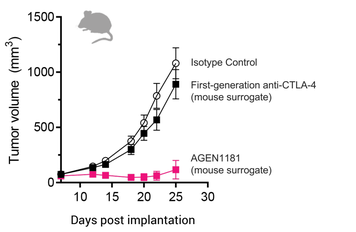
AGEN1181 is a clinical stage novel Fc–enhanced anti-CTLA4 therapy developed to deliver:

- Superior efficacy: Via novel Fc-mechanism that promotes enhanced T cell priming and Treg depletion
- Improved safety: Avoid complement mediated toxicity associated with many current immune checkpoint inhibitors
- Expand therapeutic reach: by improved binding to CD16 (FcγRIIIA) for both low and high affinity allele patients

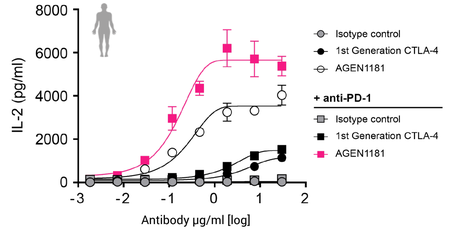


1. Optimized Fc to enhance Treg depletion
2. Optimized Fc to enhance Immune Synapse quality and T cell Priming
3. Enhance T cell Activation
4. Reverse T cell dysfunction and restore tumor targeting T cell responses
5. Enhance T cell memory responses & improve durability of response

Murine Colon Adenocarcinoma (MC38)



T cell: APC Stimulation Assay



Legend: C57BL/6J mice were injected with $2x10^5$ MC38 colon cancer cells. Eight days after tumor implantation (50-75 mm^3) tumor-bearing mice were treated intraperitoneally with 10 µg of anti-CTLA-4 variants (clone 9D9) or isotype control antibody. Tumor volume was measured by electronic caliper every 2-3 days and was calculated by the formula: (length)x(width^2)x0.52 for 4 weeks.

Waight et al., Cancer Cell 2018; Arce-Vargas et al., Cancer Cell 2018

Anti-CTLA4; anti-cytotoxic T-cell lymphocyte-4, Treg; T-regulatory cells, NK; Natural Killer Cells, APC; Antigen Presenting Cells; Mem T cell; Memory T cells, T cells; Cytotoxic T cells

Acknowledgment: We thank the patients and their families in this study and the clinical caregivers for the dedication to improve their patient's lives.

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Objectives

Primary

- Assess safety, tolerability, and DLT of AGEN1181 as monotherapy and in combination with AGEN2034 (anti-PD-1) in subjects with advanced solid tumors
- Determine the RP2D

Secondary

- Characterize the pharmacokinetic profile & immunogenicity of AGEN1181 monotherapy & combination with AGEN2034 (anti-PD1 antibody)
- To assess ORR, DOR, DCR, and PFS per RECIST 1.1

Exploratory

- Pharmacodynamic of AGEN1181 alone and in combination with AGEN2034
- Explore the correlation of polymorphism of fragment crystallizable gamma receptor (FcγR) expression with clinical responses and/or toxicity

Methods

AGEN 1181 (Q3W)	0.1 mg/kg	0.3 mg/kg	1 mg/kg	2 mg/kg	4 mg/kg
AGEN 1181 (Q6W)			1 mg/kg	2 mg/kg	4 mg/kg
AGEN 1181 (Q6W) + AGEN2034 (Q2W)			0.1 mg/kg	0.3 mg/kg	1 mg/kg	2 mg/kg	4 mg/kg

Key Inclusion Criteria

1. ≥ 18 years of age
2. Histologically or cytologically confirmed diagnosis of metastatic or locally advanced solid tumor for which no standard therapy is available or standard therapy has failed
3. Measurable disease on imaging based on Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1)
4. Life expectancy of ≥ 3 months and Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1

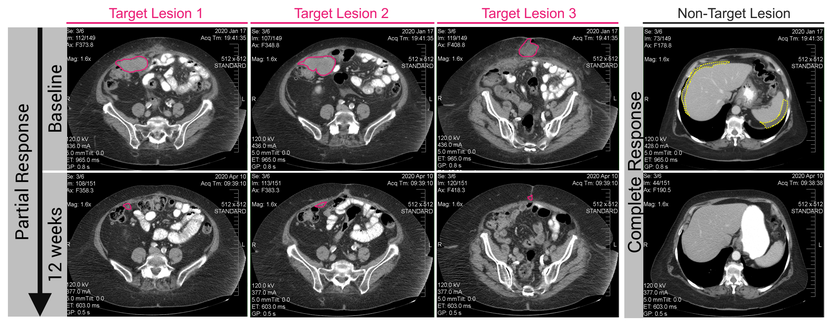
Key Exclusion Criteria

- Currently participating and receiving other investigational product
- Received prior systemic cytotoxic chemotherapy, biological therapy radiotherapy, or major surgery within 3 weeks prior to first dose
- Received prior therapy with an anti–CTLA-4 antibody or agent
- Known severe (Grade ≥ 3) hypersensitivity reactions to fully human monoclonal antibodies

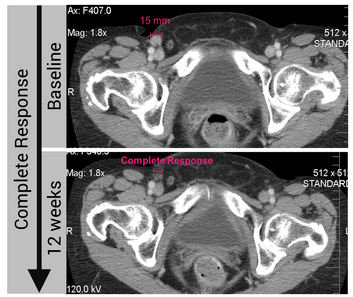
DLT; Dose Limiting Toxicity, ORR ; Objective Response Rate, DOR; Duration of Response, DCR; Disease Control Rate, PFS; Progression Free survival, RECIST 1.1; Response Evaluation Criteria 1.1, RP2D; Recommended Phase 2 dose

Clinical Trial Status**

- Clinical benefit observed in patients with poor prognosis*
- Benefit was observed in majority of patients treated with monotherapy or combination
- Prolonged disease stabilization has been observed at low doses of AGEN1181 monotherapy



**Clinical benefit is defined as presence of stable disease, partial and complete response;*
***Combination therapy with low doses of AGEN1181 and Monotherapy;*
***Previously Published Data: Corporate update 08 May 2020 http://agenusbio.com/wp-content/uploads/2020/05/Corporate-Update-2020.pdf*



Waight et al., Cancer Cell 2018; Arce-Vargas et al., Cancer Cell 2018

Accrual Information

- From April 2019 to May 12, 2020, a total of 27 patients have been enrolled in the dose escalation
- Currently, four monotherapy cohorts and 2 combination cohorts have been completed and cleared the DLT
- Study population represents a heterogenous tumor histology consistent with unselected phase 1 population
- Patients were heavily pretreated with prior cancer therapies

AGEN1181

- ✓ Benefit seen in patients unresponsive to other anti-CTLA4 molecules due to genomic correlates of response and phenotypes
- ✓ Clinical benefit has been observed in patients with multiple tumor types
- ✓ AGEN1181 is designed to avoid complement mediated toxicities
- ✓ No hypophysitis has been observed to date. The safety observations from this early phase

Summary and Next Steps

AGEN1181 was Fc-engineered and designed to: Promote superior

- T cell Priming/Activation
- Enhance Treg Depletion
- Provide safety benefits (i.e. eliminate hypophysitis)
- Broaden the patient population of responders

The AGEN1181 Ph1 trial will continue through dose escalation and expansion with accelerated development in prevalent indications with limited/no effective treatment options including but not limited to PD-1-refractory non-small-cell lung cancer and Melanoma, MSS-colorectal cancer and endometrial, and others

***Previously Published Data: Investor's Day New York City 20FEB2020; https://investor.agenusbio.com/presentation-webcasts?item=66*