Agenus Inc. or subsidiary thereof (current or former employee), Lexington, MA

**Background**

Agenus, an Fc-enhanced anti-CTLA-4 antibody, engages multiple mechanisms of action to promote effector and memory T-cell-mediated anti-tumor immunity.

**Hypothesis**

Optimizing Fc-Fyco co-engagement enhances the activity of anti-CTLA-4 antistatic antibodies. Fc-enhanced antibodies improve binding affinities to activating Fc receptors (CD16, -2a), or Fyco receptors (CD300f, human) enhance NK-mediated ASCO of CTLA-4 high expressing cells such as T regulatory cells (Treg) and strengthen the immune synapse between a T cell and an antigen presenting cell (APC) to amplify the breadth and depth of effector T-cell priming.

**Characteristics of studied antibodies**

<table>
<thead>
<tr>
<th>Table 1: Fc Enhanced Anti-CTLA-4 Antibodies</th>
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<tr>
<td><strong>Antibodies</strong></td>
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<tr>
<td>Agenus 1181</td>
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<td>Agenus 1181 (Fc Enhanced)</td>
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<td>Agenus 1181 (Fc Enhanced)</td>
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**Conclusion**

Agenus 1181 is an Fc-enhanced anti-CTLA-4 antibody that promotes single agent activity and broader combination ability than conventional CTLA-4 mAbs.

Agenus 1181 engages multiple mechanisms of action to promote optimal anti-tumor immunity:

- Promotes immunostimulatory T-cell depletion and T-cell infiltration
- Enhances T-cell priming and the breadth and depth of anti-tumor associated lymphocytes
- Enhances T-cell memory formation and activation to promote durable anti-tumor immunity
- Promotes tumor responses in checkpoint-resistant preclinical cancer models such as PDAC: YC-8, as single therapy and in combination with immunomodulatory adjuvant chemotherapy.

**Supplemental Information**

Combining the Therapeutic Potential of anti-PD-1 and anti-CTLA-4: Prospective Randomized Phase II Trial Assessing Combination in Patients with Metastatic NSCLC

**References**

Unpublished internal data, Agenus Inc.

**Correspondence**

Sarina Liu, Senior Member of Technical Staff, Agenus Inc.

**Poster # 1878**

**On-going Trials**

AACR 2020 Poster # 922 Therapy with Innovative Fc Engineering and Rationale Combinations of Antibody Therapies in Advanced Solid Tumors (NCT03860272)

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