**Phase 1, Open-Label, Multiple-Ascending-Dose Trial of AGEN1884, an Anti–CTLA-4 Monoclonal Antibody, in Solid Malignancies**

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**BACKGROUND**

Cytotoxic T-lymphocyte-associated protein-4 (CTLA-4) is an immune checkpoint molecule that, when expressed on the surface of activated effector T cells, downregulates the immune response and limits the ability of the immune system to combat tumors. 

**METHODS**

The 0.1 mg/kg study is an open-label, phase 1, multicohort study. This phase 1 study involved two dose-escalation phases: Cohort 1 consisting of escalating doses of AGEN1884 from 0.1 mg/kg to 3.0 mg/kg in subjects with advanced or refractory cancer. The study consisted of a 3+3 dose-escalation design starting at a near minimally toxic dose (MTD) level. 

**RESULTS**

- The overall response rate of patients treated with AGEN1884 at 0.1 mg/kg was 55.6% (95% confidence interval: 24.9%–78.3%), with an overall reduction in NK cells. At Week 7, there was an increase in the levels of both CD4 and CD8 T cells for patients in the 0.1 mg/kg dose cohort. 

- **Clinical Trial**
  - AGEN1884 was developed under a Collaborative Research and Development Agreement with Agenus Inc.

**DISCUSSION**

This interim analysis of a phase 1 study demonstrated an acceptable safety profile of AGEN1884 in subjects with advanced solid tumors of the 1, 2, 3, and 2.3 mg/kg dose levels. 

- The average area under the curve increased with each increasing dose level, from 1.6 to 7.1 to 17.0 to 170.7 µg/mL at 0.1, 0.3, 1.0, and 3.0 mg/kg, respectively.

- **Table 3: Summary of overall response by treatment**

- **Figure 5: Absolute cell counts of patients in cohort 1 treated with AGEN1884 at 0.1 mg/kg**

- **Table 1: Patient demographics**

- **Figure 3: Study design**

- **Figure 1: Overview of pathways affected by CTLA-4**

- **Table 2: Summary of treatment-emergent adverse events (TEAEs)**

- **Table 4: Safety and Tolerability**

- **Figure 2: AGEN1884 blocks binding of CTLA-4 to CD80/CD86 and is pharmacologically active in vitro**

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**REFERENCES**
