agenus news

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# Headlines from Agenus Investor Day

- Balstilimab (PD-1) + Zalifrelimab (CTLA-4) combination nearly doubles response rates in advanced cervical cancer compared to standard of care therapy
- AGEN1181 achieves early complete response in first of three patients dosed (1mg/kg) in a Phase 1 trial

## The combination of balstilimab and zalifrelimab could be the most promising off-the shelf treatment option in pivotal development for the broadest proportion of the relapsed/refractory cervical cancer market

Cervical cancer affects hundreds of thousands of young women each year. There remains an urgent need for effective treatments that allow patients to live longer and better. At Agenus, we are focused on bringing these patients a safer, more effective, and convenient treatment option. Interim data from a pre-planned interim analysis of our pivotal trial reveals that our anti-CTLA-4 and anti-PD-1 nearly doubles response rates with an acceptable safety profile for these patients. Our BLA filing is planned for this year.

Agenus is advancing a well-controlled pivotal trial designed to support a BLA filing for the combination of balstilimab (anti-PD-1) and zalifrelimab (anti-CTLA-4) in patients with relapsed/refractory cervical cancer.

At our Investor Day, Dr. Brad Monk, Professor of Gynecologic Oncology and Chair Cervical Cancer Committee at the Gynecologic Cancer Intergroup presented the data from our pre-planned interim analysis. Dr. Monk reported that available anti-PD-1 antibodies, including Agenus' balstilimab, have clinical benefit (ORR) between 12-14%. Adding anti-CTLA-4, such as Agenus' zalifrelimab, to anti PD-1 significantly improves this clinical benefit by nearly doubling response rates (~20.6%) and an acceptable safety profile in a broad group of patients (non-biomarker restricted). Importantly, Agenus' interim data show that approximately *9% of patients had a complete response (CR, total elimination of detectable tumors) which is nearly three times more than those on pembrolizumab alone (Table 1).*

These data suggest that Agenus' combination (balstilimab + zalifrelimab) could be an effective and most clinically advanced off-the shelf treatment for relapsed/refractory cervical cancer patients, with a highly tolerable safety profile. See below table comparing competitive agents in the cervical cancer immuno-oncology (I/O) market *(Table 1)*.

Our goal is to deliver effective and accessible therapies to patients who need them. The market opportunity for our combination in relapsed/refractory cervical cancer patients has the potential to be significant for Agenus:

- Over 10,000 eligible relapsed/refractory cervical cancer patients in the US and Europe (~4,000 eligible patients in the US alone)
- Feedback from independent KOL interviews have suggested that Agenus' combination would have important clinical utility for the majority of cervical cancer patients
- Approved immunotherapies are priced at $120,000-$300,000 annually
- Agenus' fully integrated capabilities and efficient operations allows for rapid market launch and patient access

**Table 1: Approved and Advanced Candidates in Development for Advanced Cervical Cancer**

| Sponsor | Agent | # of Patients | Overall Response Rate | Complete Response | Partial Response | Related AEs (Grade 3+) |
|---|---|---|---|---|---|---|
| Agenus | Balstilimab* | 42 | 11.9% | 2.4% | 9.5% | 9.1% |
| Merck | Pembrolizumab*** | 98 | 12.2% | 3.1% | 9.2% | 12.2% |
| Agenus | Balstilimab + Zalifrelimab* | 34 | 20.6% | 8.8% | 11.8% | 14.6% |
| BMS | Ipilimumab + Nivolumab | 26 | 23.1% | 3.8% | 19.2% | 28.9% |
| Seattle Genetics / Genmab | Tisotumab vedotin | 55 | 22% | 2% | 20% | 56%** |
| Iovance | LN-145 | 27 | 44.4% | 11.1% | 33.3% | 96.3%** |

**Data from pre-planned interim analysis; **Sponsor reported as Treatment Emergent Adverse Events; ***Chung, HC, et al. 2019. Efficacy and Safety of Pembrolizumab in Previously Treated Advanced Cervical Cancer: Results From the Phase II KEYNOTE-158 Study. J Clin Oncol. 37(17):1470-1478. (Pembrolizumab data for full population [no biomarker restrictions for comparison]).*

**Note:** *Iovance's TIL is expected to see minimal use among our target 2L cervical cancer population, according to our KOL interviews. The autologous cell therapy treatment takes 21 days to prepare, is only appropriate for a subset of patients able to tolerate it, and it has significant toxicity and a high total cost of care.*

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# AGEN1181 achieves early complete response at a low dose early in our phase 1 trial

## What makes AGEN1181 potentially the most effective CTLA-4 antibody

Charles G. Drake, MD, PhD

*Herbert Irving Comprehensive Cancer Center*

Dr. Charles Drake, Co-Director of the Cancer Immunotherapy Program at Columbia University, profiled the case of a patient that had a complete response (total elimination of detectable tumors) after four doses (1mg/kg dose) in the AGEN1181 dose escalation study. **This patient had an advanced, difficult-to-treat form of endometrial cancer that had progressed after treatment with PD-1 therapy. Importantly, this patient exhibited** a **genetic** marker that would have made her an unlikely candidate to respond to CTLA-4. **Why is this important?** More than 40% of patients have this same marker and those patients are also unlikely to respond to CTLA-4[1,2].

AGEN1181 was specifically designed to expand the benefit of CTLA-4 to these patients and furthermore, to optimize the benefit of the first generation CTLA-4. This complete response is an early validation of AGEN1181's intended activity.

## PD-1 revenues are driven by combinations

AGEN1181 is designed to expand the curative benefit of first generation CTLA-4 from 20% of patients to more than 3x the patient population. This could be transformative as a monotherapy and in combination with PD-1 in a market projected to reach $50Bn in annual revenues by 2025[3].

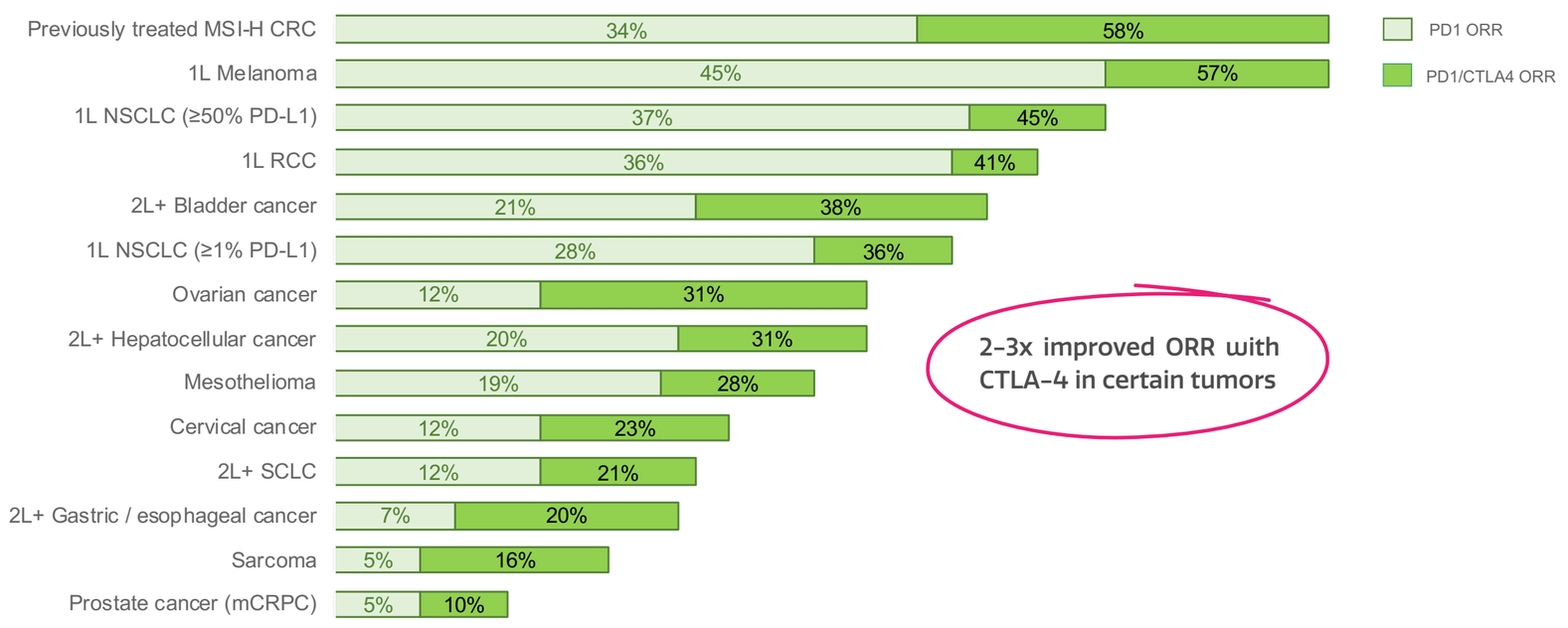
Agenus' first generation anti-CTLA-4 (zalifrelimab) is the most clinically advanced CTLA-4 antibody in development. AGEN1181+ balstilimab is the most advanced nextgeneration CTLA-4 combination in development.

AGEN1181 has shown superiority to first generation CTLA-4 as a monotherapy and in combination with anti-PD-1 in all preclinical models. Thus, AGEN1181 is being developed as monotherapy and in combination with balstilimab (AGENUS PD-1) with the objective of capturing a substantial portion of this growing PD-1 market.

## CTLA-4 and PD-1 will continue to grow as the mainstay in cancer treatment

We have seen that the addition of CTLA-4 to PD-1 has **consistently** led to significant improvements in response rates across >10 tumor types. More importantly, CTLA-4 + PD-1 significantly enhances the durability of response in multiple malignancies[4]. For example, >50% of melanoma patients reported to be alive at five years[5], which may be considered curative. More recently, results from a 42-month follow up[6] in renal cell carcinoma also revealed that over 50% of patients treated with the combination remained alive, representing the longest follow up for any immunotherapy-based regimen in this setting. Thus, the durable survival benefit of CTLA-4 combinations extends across multiple cancer types, and it represents the only chemo-free treatment option to produce such remarkable survival outcomes in the near future.

**Addition of CTLA-4 to PD-1 substantially increases response rates vs PD-1**

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