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ASCO 2020 Highlights

TIGIT: The Next Wave of Effective Immuno-Oncology Combinations
CTLA-4 + PD-1 Combination: Benefiting More Patients and More Cancers
AGEN1181 (Next-gen CTLA-4 antibody): A Potential Breakthrough in Cancer Treatment

ASCO 2020 substantially changed the dynamics of the immuno-oncology (I-O) combination therapy landscape. Before the conference, CTLA-4 + PD-1, currently indicated in six settings, was the only validated I-O + I-O combination therapy, as no other I-O target had demonstrated meaningful incremental benefit when combined with PD-1. What ASCO 2020 showed was that the addition of anti-TIGIT to PD-(L)1 blockade nearly doubled efficacy without additional toxicity when compared to PD-(L)1 monotherapy (see table). These conclusions were drawn from a single randomized study which compared the contribution of TIGIT + PD-L1 vs. PD-L1 alone. TIGIT is now a target of high interest in I-O, validated by the launch of multiple late-stage clinical trials by biopharma (i.e., Roche and Merck) as well as recent strategic transactions involving TIGIT programs.

	PD-L1 Monotherapy (n = 68)	TIGIT + PD-L1 (n = 67)
ORR (≥1% PD-L1)	21%	37%
mPFS (≥1% PD-L1)	3.9 months	5.6 months
ORR (≥50% PD-L1)	24%	66%
mPFS (≥50% PD-L1)	4.1 months	Not reached
Grade 3-5 AEs	44%	48%
AEs leading to treatment withdrawal	9%	10%

Source: Rodriguez-Abreu et al., ASCO 2020

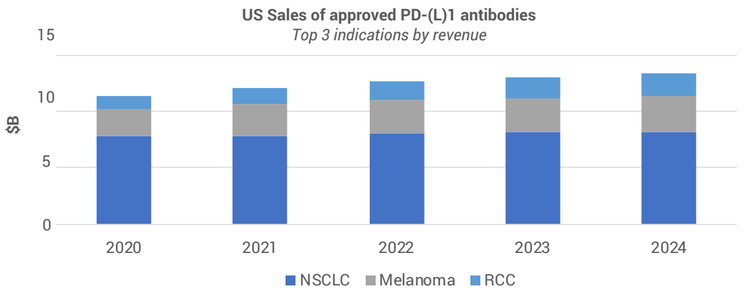
The data at ASCO were generated using tiragolumab, a TIGIT antibody which uses a standard Fc backbone. In contrast, our TIGIT monospecific, AGEN1327, is Fc enhanced. Due to its unique design, AGEN1327 has shown superior tumor killing in preclinical models compared to its first generation counterparts; Fc enhancement can expand benefit to an additional 40% of patients who may not respond to current TIGIT therapies. AGEN1327 is designed to be an optimal pairing agent for PD-1. We are also advancing a first-in-class TIGIT bispecific, AGEN1777, which targets another (undisclosed) inhibitory receptor, also expressed on T cells and NK cells. AGEN1777 is designed to be used as monotherapy in PD-1 relapsed/refractory tumors.

Additional data from a dose escalation study of anti-TIGIT as monotherapy or in combination with PD-(L)1 is expected to be presented at the upcoming AACR Virtual Meeting to be held from June 22-24. Agenus will be presenting data evaluating rational combinations of AGEN1181, including with anti-TIGIT, vaccines, and cell therapies at the same conference. Notably, our data demonstrates efficacy in models that are refractory to PD-1 blockade.

CTLA-4 + PD-1 combos show long-term benefit in additional tumor types, including NSCLC

ASCO 2020 also disclosed more data supporting durable benefit of CTLA-4 + PD-1 combinations. In 1L NSCLC, ~33% of patients were still alive after a minimum follow-up of 3 years when treated with the combination, **regardless of PD-L1 status**. Duration of response was >3X longer than noted with chemotherapy alone. This is the longest follow up data for any Phase 3 study of an immunotherapy combination in 1L NSCLC. Additionally, triple combination with a limited chemotherapy regimen also significantly increased overall survival vs. chemotherapy alone. Based on these data, both the CTLA-4 + PD-1 doublet as well as triple combination with chemotherapy were approved in 1L NSCLC last month.

Agenus will explore the broader use of balstilimab (anti-PD-1) +/- zalifrelimab (anti-CTLA-4) in melanoma, NSCLC, and RCC via inclusion in NCCN guidelines. This strategy is based on expanding use into the top 3 indications by revenue for currently-approved PD-(L)1 antibodies, with US sales expected to exceed $13B in 2024. Since CTLA-4 + PD-1 combinations are now approved in each of these indications, we have the potential to unlock a $1B+ opportunity by pursuing this path.



Indication	2024 US Sales Estimate	5% Share	10% Share
Non-small cell lung cancer (NSCLC)	$8.2B	$410M	$820M
Melanoma	$3.2B	$160M	$320M
Renal cell carcinoma (RCC)	$1.9B	$95M	$190M
Total	**$13.3B**	**$0.7B**	**$1.3B**

Source: Evaluate Pharma, based on projected sales of Keytruda®, Opdivo®, Tecentriq®, Imfinzi®, Libtayo®

Our Fc-enhanced, multipurpose CTLA-4 antibody (AGEN1181) has shown compelling early clinical data beyond first generation agents, as monotherapy and in combination with balstilimab. We intend to advance it in indications supporting accelerated development with large markets and no active treatments, such as PD-1 refractory melanoma, NSCLC and MSS cancers.

ASCO 2020 highlighted the exciting evolutions of today's dynamic I-O landscape. Our pipeline of first and best-in-class therapies, especially CTLA-4, TIGIT and PD-1 antibodies, has the potential to unlock significant value in that landscape.

Forward-Looking Statements: This Agenus Newsletter includes forward-looking statements that are made pursuant to the safe harbor provisions of the federal securities laws, including statements regarding the future of the I-O landscape, the therapeutic potential of Agenus' antibodies, additional indications that Agenus plans to explore with balstilimab (anti-PD-1) +/- zalifrelimab (anti-CTLA-4), and potential commercial market opportunities. These statements are subject to risks and uncertainties, including those described in our SEC filings.