What do AZ’s negative MYSTIC trial results mean for other anti-CTLA-4 antibody developers?

AZ’s Tremelimumab is an IgG2 antibody which has a different mechanism of action than IgG1 anti-CTLA-4 antibodies.

The only approved anti-CTLA-4 antibody is BMS’s Yervoy®, which is an IgG1.

Agenus’ anti-CTLA-4 antibody, which is currently in clinical development is also an IgG1.

We see the MYSTIC trial negative result as a positive for Agenus for the following reasons:

- Other than Yervoy, AGEN1884 is the most clinically advanced anti-CTLA-4 antibody that has a differentiated mechanism of action as compared to Tremelimumab.

- It has been shown that an IgG1 anti-CTLA-4 antibody provides more than just blockade of the CTLA-4 receptor. In addition to blocking CTLA-4, AGEN1884 promotes FcyR-dependent anti-tumor mechanisms which is expected to provide superior therapeutic benefit to IgG2 antibodies.

- In BMS’ checkmate trial, the combination of Opdivo™ (anti-PD-1) and Yervoy (anti-CTLA-4) in advanced non–small cell lung cancer (NSCLC) resulted in a PFS that was double that observed with Opdivo alone. If the follow-up Checkmate 227 trial confirms these results, it would further confirm the superior efficacy of the IgG1 format. Again, supporting the rationale for AGEN1884 value in combinations.

Agenus' IgG1 anti-CTLA-4 antibody (AGEN1884) clinical development plan is advancing, with increased potential to be second to market.

- Agenus’ anti-CTLA-4/PD-1 combination dosing schedule will be consistent with what has been used in previous successful clinical trials.

- The potential for targeting CTLA-4 remains unrealized, including to enable future immuno-oncology combinations, when paired with the right molecule, including vaccines.

CTLA-4 remains attractive for future Agenus I-O combinations

In summary, we believe that the value of our anti-CTLA-4 antibody is supported by underlying scientific rationale – importantly, biological advantages of an IgG1 vs IgG2 backbone and prior clinical validation remains intact.
We will be providing an update on Agenus at our Q2 earnings call on August 3, 2017, and invite you to join for information on the company and a Q&A. You can access information about the Q2 call and webcast here.

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