TIGIT: Breakthrough Potential in Immuno-oncology
Two Agenus TIGIT antibodies on track to enter clinic in 1H 2021

Blocking TIGIT is synergistic with existing I-O antibodies

TIGIT is shaping up as a powerful combination partner with PD-1 antibodies; especially in tumors expressing TIGIT. Agenus’ portfolio of TIGIT targeting antibodies includes an Fc enhanced TIGIT monospecific (AGEN1327) and our TIGIT bispecific (AGEN1777). We believe both molecules have unique advantages over other TIGIT antibodies that are in clinical development.

Our Fc enhanced TIGIT monospecific antibody has outperformed all tested competitor antibodies and showed superior T cell activation when combined with PD-1 or LAG-3 antagonists - we presented this data at AACR 2019.

TIGIT has also been implicated to be an important target for overcoming resistance to anti-PD-1 therapy. In this regard, our TIGIT bispecific has demonstrated potent tumor killing as monotherapy in a difficult to treat colon cancer model where PD-1 antibodies alone are ineffective. The reason: We have demonstrated that AGEN1777 has unique advantages in targeting key inhibitory receptors expressed on T and NK cells to improve anti-tumor activity.

There is growing conviction that targeting TIGIT will provide a breakthrough in I-O, and we are uniquely positioned with two distinct molecules on track to be launched into clinical development as early as the first half of 2021.

What is TIGIT?

TIGIT is a receptor primarily expressed on T cells and NK cells. TIGIT tunes down innate and adaptive immune responses by inhibiting the actions of T cells and NK cells. In addition, it increases the immune suppressive activity of regulatory T cells. The result: cancers thrive.

Blocking TIGIT allows T cells and NK cells to kill many types of cancer (see Figure 1).

Our Fc-enhanced TIGIT monospecific antibody (AGEN1327): An ideal PD-1 partner

Our Fc-enhanced TIGIT antibody has outperformed all competitor TIGIT antibodies that we have tested. In fact, Agenus was the first to discover and report that TIGIT antibodies require Fc enhancement to promote optimal T cell activity against tumors. Hence, AGEN1327 is differentiated by virtue of its Fc enhancement as a highly potent TIGIT antagonist among its peers which are already in clinical development.

What are the potential advantages of AGEN1327?

• Maximizing anti-tumor activity, as with AGEN1181, our multipurpose NextGen CTLA-4 antibody that has already shown remarkable activity in early clinical trials. We expect that AGEN1327 will also show superior tumor killing compared to its first-generation counterparts (See Figure 2)

• Pairing as an optimal combination partner for anti-PD-1 antibodies for more potent tumor killing; particularly for TIGIT expressing tumors, including, non-small cell lung cancer (NSCLC)

• Expanding the population of cancer patients by an additional 40%, as compared to currently evaluated TIGIT therapies by targeting a genetic polymorphism.

We are accelerating entry to the clinic and expect to file an IND in 1H 2021.

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 expectation that TIGIT antibodies will provide the next breakthrough in I-O, Agenus’ development and regulatory plans and timelines for its TIGIT antibodies, including the potential to initiate clinical trials in 1H 2021, and the expectation that Agenus’ TIGIT antibodies are superior to competitor antibodies. These statements are subject to risks and uncertainties, including those described in our SEC filings.
Our Bispecific TIGIT Antibody (AGEN1777) - Designed to be used as monotherapy for tumors which are unresponsive to PD-1 antibodies

AGEN1777 is a first-in-class TIGIT bispecific which targets another inhibitory receptor (not yet disclosed), also expressed on T cells and NK cells. AGEN1777 when used alone, has potent tumor killing activity in a colon cancer model where PD-1 monotherapy is ineffective (see Figure 3). Therefore, AGEN1777 can be an important therapy in PD-1 relapsed/refractory tumors.

While PD-(L)1 antibodies have been a spectacular commercial success, only a small proportion of patients have had sustainable long term benefit. Therefore, there is substantial need for therapies in patients who relapse or do not respond to PD-1 monotherapy. We expect to file an IND by the end of 2020.

References
1. Chauvin et al., J Clin Invest. 2015 May;125(5):2046-58
3. Waight et al., Cancer Cell. 2018; 33(6):1033-1047

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 expectation that TIGIT antibodies will provide the next breakthrough in I-O, Agenus’ development and regulatory plans and timelines for its TIGIT antibodies, including the potential to initiate clinical trials in 1H 2021, and the expectation that Agenus’ TIGIT antibodies are superior to competitor antibodies. These statements are subject to risks and uncertainties, including those described in our SEC filings.