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Agenus' Next-Gen Antibodies
Can they be the next breakthroughs in I-O?

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The Annual Meeting of the American Association for Cancer Research (AACR) is one of the most prominent medical conferences for new cancer therapies. The meeting covers the latest discoveries and advances in cancer research from institutions all over the world. At the recent AACR meeting, which was held in Atlanta, GA, **Agenus presented pre-clinical data on its anti-TIGIT antibody**, a molecule from our in-house antibody engineering engine.

Agenus' Antibody Engineering Capabilities Have Led to the Discovery of Multiple Novel I-O Candidates

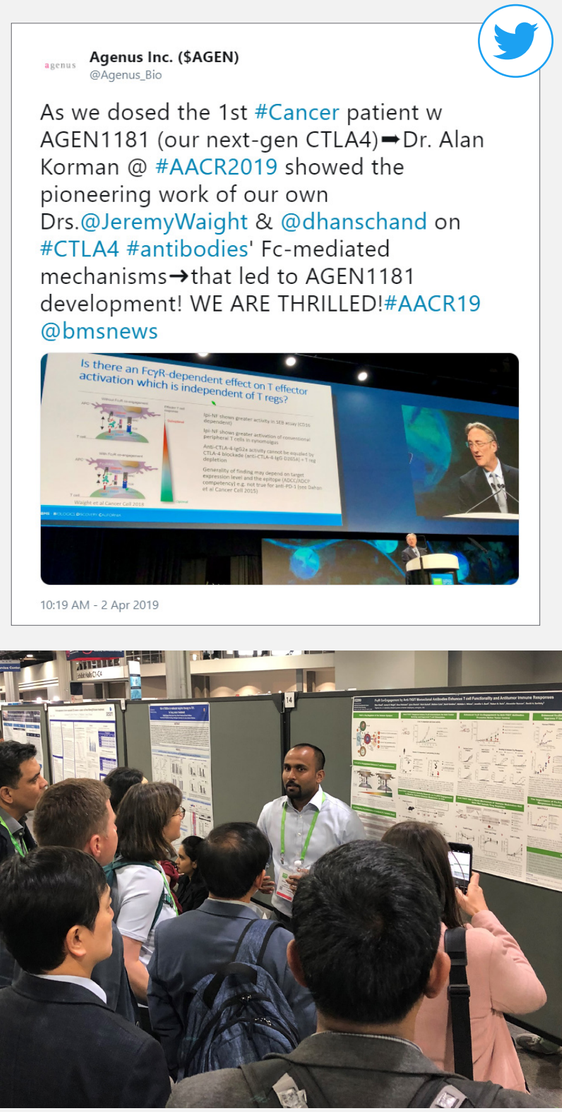
One of the key factors that influence the therapeutic activity of immuno-oncology (I-O) antibodies is their interaction with cancer-fighting immune cells such as antigen presenting cells and T cells. This interaction is accomplished, in part, by the "Fc region", an important section of the antibody. Optimizing this interaction by "engineering" the Fc-region holds a key to developing next-generation antibodies with potentially enhanced functionality, i.e., superior therapeutic potential.

Based on a **novel mechanism** of action, **discovered by Agenus scientists** (Cancer Cell 2018), we have engineered the Fc-region of antibodies. These include CTLA-4 and TIGIT antibodies, for which enhancement of their Fc-regions has been shown to improve their cancer-fighting ability in preclinical models of cancer. This phenomenon was highlighted at a plenary session at the recent AACR meeting by Dr. Alan Korman (Vice President, Immuno Oncology Discovery, BMS).

Our scientists believe these findings could expand clinical benefit in patients too. Our enhanced "Next-Gen" anti-CTLA4 (AGEN1181) is already in phase 1 clinical trials, and we expect to generate safety data in patients with cancer starting this year.

This year at AACR, we presented pre-clinical data on our **Fc-enhanced TIGIT molecule, another product of our Fc engineering engine. We showed that this molecule promotes better T cell responsiveness and tumor control in preclinical studies, compared to currently available anti-TIGIT antibodies.**

Agenus at AACR 2019



Agenus Anti-TIGIT Antibody Has Potential Best-in-Class Tumor Killing Properties in Pre-clinical Studies

The primary goal of cancer immunotherapies is to stimulate the immune system to kill cancer cells. Two key cancer-fighters of the immune system are T cells and Natural Killer (NK) cells. Therefore, it is crucial to remove any hindrances that limit the ability of these cells to fight cancers.

TIGIT (also called T cell immunoreceptor with Ig and ITIM domains) is a major immune suppressing protein receptor found on T cells and NK cells. Therefore, blocking TIGIT has emerged as a promising therapeutic strategy in cancer immunotherapy. Preclinical studies have demonstrated that antibodies that block TIGIT can enhance anti-tumor immunity driven by T cells and NK cells, even in models that respond poorly to anti-PD-1 therapy.

Using our antibody engineering capabilities, we have developed a novel, "Fc engineered" next-gen, anti-TIGIT antibody. At the recently concluded AACR meeting, we presented pre-clinical data showing that **compared to currently available anti-TIGIT antibodies, our Fc engineered molecule:**

- Significantly improved T cell responses (alone and in combination with other checkpoint modulators);
- Promoted enhanced infiltration of cancer-killing CD8 effector T cells into the tumor microenvironment; and
- Demonstrated superior tumor control in mouse tumor models. Tumor control was dependent on enhanced CD8 T cell and NK cell function.

For full presentation, please use this link.

These new data emphasize our ability to engineer novel and differentiated molecules to improve their therapeutic potential.

It is important to also emphasize that we can use our Fc engineering capabilities along with our established robust platform to create novel bispecific and multispecific antibodies. Unlike classic monospecific molecules, bispecific and multispecific antibodies target two or more different proteins simultaneously. Therefore, multiple pathways can be targeted simultaneously using one drug. Fc engineering can enhance the tumor killing potential of multispecific antibodies. For example, selecting an optimal Fc format can be critical in ensuring that our multispecifics can harness additional mechanisms that are not available to a monospecific or a combination of monospecific antibodies. This added benefit versus the combination of monospecifics allows us to tap into novel biology and pharmacology.

We are tireless in our pursuit to cure cancer; these novel molecules are specifically designed and engineered to have the potential for better efficacy and they exemplify our commitment to advancing novel potential best/first-in-class molecules into and through the clinic.

Forward-Looking Statements: This Agenus News Brief includes forward-looking statements that are made pursuant to the safe harbor provisions of the federal securities laws, including statements regarding Agenus' clinical development plans and timelines, the potential efficacy of its product candidates, and its ability to produce novel, best-in-class molecules. These statements are subject to risks and uncertainties, including those described in our SEC filings.