agenus news

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Antibodies with Multiple Benefits – Agenus' Multipecifics

Antibody-based drugs have come a long way since the first therapeutic monoclonal antibody, Orthoclone OKT3, was approved in 1986. Today, Agenus is at the forefront of antibody engineering. Our innovation engine is discovering novel therapeutic antibodies designed to unlock the immune system's ability to kill cancer cells.

Two of our monospecific antibodies, AGEN1884 (anti-CTLA4) and AGEN2034 (anti-PD-1), are advancing in the clinic. Early data from our lead trials support a possible BLA filing as early as 2020. Besides our monospecific antibodies, we have also established a robust platform to create novel bispecific (BiS) and multispecific antibodies. Unlike classic monospecific molecules, bispecific and multispecific antibodies target two or more different proteins simultaneously. Therefore, multiple pathways could be targeted simultaneously using one drug.

Agenus' potential first-in-class BiS/multispecific molecules, AGEN1223 and AGEN1423, have generated interest from Gilead Sciences, which recently acquired worldwide exclusive rights to AGEN1423 (now known as GS-1423), and an exclusive option to license AGEN1223. The FDA recently accepted the IND filing for AGEN1423. Here we focus on these two, potential best / first-in-class antibodies, AGEN1223 and AGEN1423, which were discovered at Agenus.

Agenus Has Set an Industry Record in BiS Manufacturing Speed

BiS molecules are engineered to target two distinct antigens. This provides a unique therapeutic potential in complex diseases like cancer, where more than one pathway, protein, or cell type often needs to be targeted for clinical benefits. Due to their complexity in structure and production challenges, some developers do not work on BiS molecules, despite their potential advantages. However, our antibody design experts in Cambridge, UK, and Lexington, MA, and our antibody manufacturing experts at Agenus West, have collaborated to develop BiS molecules under rapid timelines. As a matter of fact, we completed at scale manufacturing of our bispecific antibody, AGEN1223, from research cell bank in ~ 2 months.

AGEN1223 and AGEN1423 are Potentially First-in-class Multispecifics Targeting Tumor Resistance Mechanisms

AGEN1223: Regulatory T Cell Depletion

Intratumoral regulatory T cells (Tregs) block productive anti-cancer immune responses. However, elsewhere in the body these cells are essential to maintain tolerance and guard against autoimmunity. Therefore, depleting Tregs specifically within tumor microenvironment is considered an attractive strategy to enhance anti-tumor immune responses. Agenus' novel BiS antibody AGEN1223 is designed to selectively eliminate Tregs within the tumor. Preclinical data show that AGEN1223 simultaneously engages two antigens that are co-expressed specifically on tumor-infiltrating Tregs thereby prompting their depletion. These data further show that cancer-fighting effector T cells and essential peripheral Tregs, which do not sufficiently co-express these targets, are largely spared from destruction.

In addition to its Treg depleting capabilities, AGEN1223 can co-stimulate antigen-specific effector T cells that are essential for tumor killing, in preclinical assays. Overall, AGEN1223 may represent a promising combination partner for a range of other therapeutic interventions – which could include checkpoint inhibitors, vaccines, or cell therapy. Agenus is responsible for conducting the initial clinical trial with AGEN1223, which we expect to start this year.

AGEN1423: Tumor Micro-environment Conditioning

AGEN1423 is a potential first-in-class multispecific antibody designed to block two immunosuppressive pathways present in a wide range of cancers. It targets two multi-functional proteins that are expressed in highly aggressive tumors (unlike AGEN1223 which targets immune cells that block tumor killing). AGEN1423 targets proteins that support tumor growth and metastatic spread, and represent major roadblocks to anti-tumor immunity. By blocking these two pathways simultaneously in the tumor microenvironment, we believe that AGEN1423 provides a novel strategy to address therapeutic resistance to immune checkpoint blockade and other therapeutic approaches. Recently, the FDA accepted the AGEN1423 IND. Gilead has worldwide exclusive rights to GS-1423/AGEN1423 and will be leading clinical development.

AGEN1223 and AGEN1423 are the first two Agenus developed multispecific antibodies advancing to the clinic. Through our ALPS platform, we are identifying novel targets and target-combinations for other BiS antibodies, and then applying our proprietary antibody platforms and scaffolds to optimize function. These efforts reflect our commitment to advance innovative molecules that have the potential to be breakthrough in the treatment of patients with cancer.

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 and regulatory plans and timelines, including the expectation to initiate a Phase 1 trial with AGEN1223 this year, 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.