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Curing cancers with innovation and speed

Agenus is developing next-generation immunotherapeutics from its discovery platforms, providing the company with a deliberate balance between its wholly owned and partnered pipeline of novel therapies specifically designed to expand the benefit of immuno-oncology for patients with cancer.

Agenus is an immuno-oncology company with an extensive portfolio and technology platforms to drive speedy innovation and development. The company and its partners are positioned to treat cancers with optimal combinations from its broad portfolio of immunomodulatory antibodies, neoantigen vaccines, allogeneic cell therapies and adjuvants. With proprietary agents across key therapeutic approaches, Agenus is uniquely positioned to deliver innovative as well as personalized combinations that address the shortcomings of first-generation therapies with faster, more focused trials.

Importantly, Agenus's novel technology platforms and end-to-end capabilities, from target discovery to good manufacturing practice (GMP) manufacturing, have enabled the advancement of new therapeutics with speed and efficiency. Vertical integration has enabled the rapid design, evaluation and development of new candidates, allowing Agenus to dramatically shrink industry timelines from target to investigational new drug (IND) in as little as two years.

"Through our innovation engine and strategic acquisitions, we have developed an unparalleled suite of proprietary technologies and capabilities," said Agenus's COO Jennifer Buell. "The integration of our discovery, development and manufacturing capabilities provides Agenus with unique advantages in an era when quality, efficiencies and speed of development and commercialization are paramount to successfully developing a new generation of immuno-oncology therapies."

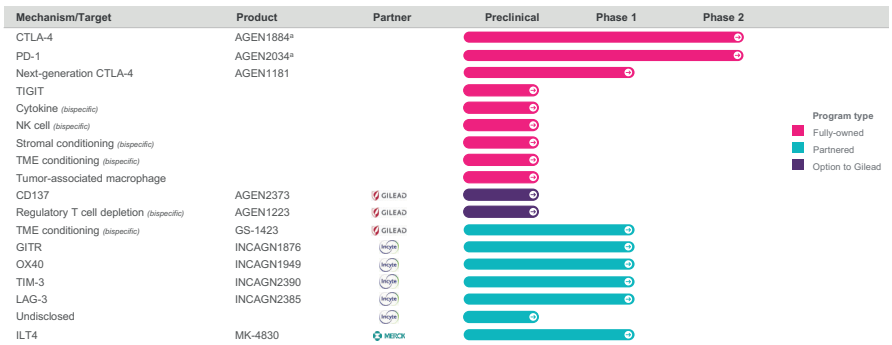

Fig. 1 | Agenus's immunomodulatory antibody pipeline. CTLA-4, cytotoxic T lymphocyte protein 4; ILT4, immunoglobulin-like transcript 4; LAG-3, lymphocyte activation gene 3 protein; NK, natural killer; PD-1, programmed cell death 1; TIGIT, T cell immunoreceptor with immunoglobulin and ITIM domains; TIM-3, T cell immunoglobulin mucin receptor 3; TME, tumor microenvironment. [a]AGEN1884 and AGEN2034 are being evaluated as second-line cervical cancer treatments and for undisclosed tumors. Recepta Biopharma S.A. has exclusive rights to AGEN1884 and AGEN2034 in Brazil and five other South American countries.

Clinical pipeline designed for combinations

Agenus is building a pipeline of first-in-class or best-in-class therapeutics from its antibody libraries and discovery platforms (**Fig. 1**). Over 12 antibody and vaccine discoveries are in the clinic as monotherapies or in combination, including fully-owned agents as well as products partnered with Gilead, Merck, Incyte and GlaxoSmithKline.

Agenus's first-generation cytotoxic T lymphocyte protein 4 (CTLA-4) (AGEN1884) and programmed cell death 1 (PD-1) (AGEN2034) antagonists are in clinical studies as monotherapies and in combination for patients with metastatic and locally advanced solid tumors. Agenus is on track for its first biologics license application (BLA) filing in second-line cervical cancer in 2020.

Agenus's second-generation CTLA-4 (AGEN1181) antibody entered the clinic in early 2019. This unique molecule is expected to benefit patients who do not respond to first-generation CTLA-4 antagonists, while also offering an improved potency and therapeutic index. Agenus scientists leveraged an internal discovery to modify a part of the antibody known as the Fc region, which improves the crosstalk between antigen-presenting cells and T cells and is designed to enhance antitumor immunity[1]. This Fc-engineered antibody has the potential to become a best-in-class CTLA-4 antibody and a next-generation breakthrough in immuno-oncology.

Agenus's extensive pipeline of antibodies advancing in clinical studies through partnerships with Gilead, Incyte and Merck, include a first-in-class tumor microenvironment-conditioning bispecific antibody, which entered the clinic with Gilead this summer. An additional bispecific antibody and a conditionally active CD137 agonist antibody, each optioned to Gilead, are expected to enter the clinic this year.

"Our diverse pipeline has the potential to deliver combination therapies that are tailored to each patient's cancer," Buell said. "We believe personalized combinations will be among the key drivers of success in substantially expanding the benefit of immunotherapies."

High-impact clinical trials

Agenus's complementary portfolio allows the company and its partners to optimally design clinical trials to achieve high and durable responses. The company uses its proprietary systems, which model the tumor–immune interface, coupled with machine learning of large datasets generated from its clinical trials, to inform combinations, biomarkers, dosing and sequencing.

"We envision adaptive, patient-centric clinical trials where we can adjust a patient's individualized therapy in real time, based on resistance mechanisms identified in their tumor-infiltrating lymphocyte transcriptional signatures that change over time and with treatment," Buell said.

Artificial intelligence-driven drug discovery

Agenus's technology platforms also enable the identification of new targets and therapeutic combinations for the development of multispecific antibodies. To rapidly progress novel candidates into development, the company leverages extensive antibody discovery tools, multi-specific and Fc platforms, and physiologically relevant assays.

Agenus is continuing to rapidly develop novel immunotherapeutics with multiple INDs planned in 2019 and beyond. These programs address mechanisms beyond T cells, including natural killer cell inhibitory pathways, myeloid populations and stromal biology, as well as cytokines.

"We are integrating advanced technologies, including AI [artificial intelligence] platforms, to fuel a new wave of innovative therapies that address resistance pathways that can significantly improve treatment of patients with cancer," Buell said. "We will continue to execute new partnerships with companies that have the shared vision to accelerate our innovations."

1. Waight, J. D. et al. *Cancer Cell* **33**, 1033–1047 (2018).

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