



## **Agenus To Advance Three Checkpoint Modulator Antibodies Into Development**

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**Novel checkpoint modulator antibodies include two GITR agonists and a CTLA-4 antagonist**

**Selections made in strategic collaboration with Ludwig Cancer Research**

Ludwig Cancer Research and Agenus Inc. (NASDAQ: AGEN) today announced the selection of three monoclonal antibody checkpoint modulators (CPMs) that Agenus is advancing into preclinical development. These product candidates—two GITR agonists and a CTLA-4 antagonist—target cell-surface checkpoint proteins that control immune responses. They are part of Agenus' recent acquisition of 4-Antibody AG and the result of several years of intensive collaborative efforts between 4-Antibody and Ludwig Cancer Research. The parties also have ongoing programs to discover and develop other immune checkpoint modulator antibodies, including OX40 agonists and antagonists of LAG-3, TIM-3 and PD-1.

"GITR, a checkpoint protein on T-lymphocytes, plays an important role in amplifying specific cellular immune responses, including those against tumors. We are encouraged to have identified high-quality agonist antibodies for this very competitive target, something that has proven difficult for many other companies," said Robert B. Stein, MD, PhD, Chief Scientific Officer of Agenus. "Furthermore, it is rational to combine CPMs such as CTLA-4 and PD-1 antagonists with anti-cancer vaccines, and we are collaborating on an on-going Phase 2 trial exploring Provenge and Yervoy® (CTLA-4 antagonist) in patients with metastatic melanoma. Intelligently designed translational studies may improve the odds of success for our CPMs and accelerate their clinical development."

In collaboration with its translational research partner Ludwig Cancer Research, Agenus and 4-Antibody plan to advance the emerging portfolio of CPMs as single agents and in optimized combinations, including potential combinations with the company's anti-cancer vaccine and other agents.

"The Retrocyte Display®1 technology developed by 4-Antibody over the last decade has allowed us to create attractive CPM antibodies directed against key checkpoint targets," said Robert Burns, PhD, CEO of 4-Antibody. "By combining our know-how with Agenus' immunotherapy development expertise, we expect to propel these candidates through preclinical and clinical development."

"The collaboration with 4-Antibody allowed us to rapidly advance antibodies into development," said Jonathan Skipper, Ludwig's Executive Director of Technology Development. "We are now planning clinical studies to evaluate novel combinations of these antibodies. Ludwig has been at the forefront of translational research in immuno-oncology for several decades. Our ongoing relationship with Agenus is a good example of our broader strategy to advance cancer therapy."

CPMs like CTLA-4 and PD-1 antagonists make cancer more vulnerable to immune attack by releasing the brakes on the anti-cancer immune response and neutralizing the defenses cancer cells use to fend off that attack. Cancer vaccines, meanwhile, are designed to enhance the immune system's recognition of cancer cells as abnormal based on mutant proteins that they display. Scientists reason that, together, these strategies should deliver a one-two punch against cancer that could have a durable therapeutic impact.

### **About Checkpoint Modulators**

Promising clinical data from studies employing monoclonal antibodies that bind to checkpoint molecules, such as cytotoxic T lymphocyte antigen-4 (CTLA-4) and programmed death receptor-1 (PD-1), have generated considerable excitement in the field of cancer immunotherapy. These molecules serve as checks employed by the body to prevent a runaway immune response, which can be debilitating, and even deadly. Unfortunately, these necessary mechanisms of control can hinder the anti-cancer immune response. They can be harnessed by cancer cells as a defense against immune attack. Antibodies that bind PD-1 and CTLA-4 and antagonize their activities are designed to override these control mechanisms, disengaging the immune system's brakes or helping immune cells to overcome the molecular defenses of cancer cells. Notably, combinations of antibodies against CTLA-4 and PD-1 have shown impressive clinical responses in recent clinical trials.

Other checkpoint proteins, such as GITR and OX40, are receptors found on T cells that stimulate immune function.

Agenus and Ludwig are driving leading-edge programs to discover and develop fully human monoclonal antibodies that bind to key checkpoint proteins and activate or block their activities for use in cancer therapy.

### **About Ludwig Cancer Research**

Ludwig Cancer Research is an international collaborative network of acclaimed scientists with a 40-year legacy of pioneering cancer discoveries. Ludwig combines basic research with the ability to translate its discoveries and conduct clinical trials to accelerate the development of new cancer diagnostics and therapies. Founded by American shipping magnate, Daniel K. Ludwig, Ludwig Cancer Research has invested \$2.5 billion in research to date. Today, the scientific efforts endowed through his resources encompass the Ludwig Institute for Cancer Research and the Ludwig Centers at six U.S. institutions, all pursuing breakthroughs that will alter the course of cancer. For more information about Ludwig Cancer Research, visit [www.ludwigcancerresearch.org](http://www.ludwigcancerresearch.org). Follow Ludwig Cancer Research on Twitter at @Ludwig\_Cancer.

### **About Agenus**

Agenus is a biopharmaceutical company developing a portfolio of immuno-oncology candidates, including checkpoint modulators (CPMs), heat shock protein vaccines and adjuvants. The company's proprietary discovery engine Retrocyte Display® is designed to rapidly generate high quality therapeutic antibody drug candidates using a high-throughput approach incorporating full-length IgG format human antibody libraries expressed in mammalian B-lineage cells. A portfolio of checkpoint modulator programs is advancing in preclinical development. The company's heat shock protein vaccines for cancer and infectious disease are in Phase 2 studies. Agenus' QS-21 Stimulon adjuvant platform is extensively partnered with GlaxoSmithKline and Janssen and includes several candidates in Phase 3 trials. Among Agenus and its partners, 23 programs are in clinical

development. For more information, please visit [www.agenusbio.com](http://www.agenusbio.com), or connect with the company on Facebook, LinkedIn, Twitter and Google+.

### **Forward-Looking Statement**

*This press release contains forward-looking statements, including without limitation, statements regarding research and development program activities the ability of 4-Antibody platform to generate product candidates and their potential application in the prevention and treatment of diseases. These forward-looking statements are subject to risks and uncertainties that could cause actual results to differ materially. These risks and uncertainties include, among others, the factors described under the Risk Factors section of our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission for the period ended September 30, 2013 and in our periodic reports on Form 8K. Agenus cautions investors not to place considerable reliance on the forward-looking statements contained in this release. These statements speak only as of the date of this document, and Agenus undertakes no obligation to update or revise the statements. All forward-looking statements are expressly qualified in their entirety by this cautionary statement. Agenus' business is subject to substantial risks and uncertainties, including those identified above. When evaluating Agenus' business and securities, investors should give careful consideration to these risks and uncertainties.*

1. E. Breous-Nystrom et al., Methods 2014, <http://dx.doi.org/10.1016/j.ymeth.2013.09.003>

Yervoy is a registered trademark of Bristol-Myers Squibb. Retrocyte Display is a registered trademark of 4-Antibody AG.

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