BIOCENTURY

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EMERGING COMPANY PROFILE

Palleon: Sweeter checkpoints

BY ELIZABETH S. EATON, STAFF WRITER

With two platforms targeting glycan ligands and their receptors, and a third to match cancer patients to a therapy, Palleon Pharmaceuticals Inc. aims to treat cancer by removing the brakes on a class of checkpoints found on both adaptive and innate immune cells.

Glyco-immune checkpoints are receptors on immune cells that turn cell activation off when they detect the presence of glycan patterns on tumors. Because glyco-immune receptors occur on both innate and adaptive immune cells, inhibiting their activity could have a broader immune effect than inhibitors of a conventional checkpoints, which occur only on adaptive immune cells like T cells.

"Tumors hijack this hardwired inhibitory pathway by evolving glycan patterns on the tumor surface to trick the immune system to turn off when it should be on," Palleon CEO Jim Broderick said.

However, inhibiting glycans is challenging because of their branched structures and the sheer complexity with which individual building blocks can be combined into a unique glycan. So instead of trying to block glycans, Palleon breaks down the molecules with an antibody-enzyme bispecific developed on its EAGLE (Enzyme Antibody Glycan Ligand Editing) platform.

One arm of the EAGLE bispecific targets conventional tumor antigens, such as HER2 or EGFR, to localize the therapy to the tumor microenvironment, where the other arm delivers an undisclosed sialidase, which cleaves the glycans' sialic acid building blocks, destroying the glycan's immunosuppressive function.

Palleon has developed several antibody-enzyme products for different indications by customizing the first arm according to the antigens found on a tumor type.

Because the mechanism of action appears to be separate from that of other checkpoint inhibitors, VP of Biotherapeutics Discovery Li Peng, who co-developed EAGLE, said Palleon has the potential to overcome the primary or acquired resistance to current immuno-oncology therapies.

PALLEON PHARMACEUTICALS INC.
Waltham, Mass.

Technology: Antibody-based therapies targeting glyco-immune checkpoint interactions

Disease focus: Cancer

Clinical status: Preclinical

Founded: 2015 by Jim Broderick, Carolyn Bertozzi and Paul Crocker

University collaborators: Stanford University, University of Dundee, Kings College London, Scripps Research Institute, The Rockefeller University, University of Basel, University of Bern and University of Chicago

Corporate partners: None

Number of employees: 25

Funds raised: $47.6 million

Investors: SR One, Pfizer Ventures, Vertex Ventures HC, Takeda Ventures, and AbbVie Ventures

CEO: Jim Broderick

Patents: 2 issued covering SIGLEC targets

In a mouse model of breast cancer, EAGLE-302, which targets HER2, led to complete responses in more animals than the anti-HER2 mAb trastuzumab. In a T cell "cold" melanoma mouse model, EAGLE-302 decreased tumor growth compared with a combination of anti-PD-1 and anti-CTLA-4 antibodies. Palleon presented the data at the American Association for Cancer Research (AACR) meeting last year.

Palleon also has an antibody platform, called Convergence, to target sialic acid binding Ig like lectins (SIGLECs), the largest family of glyco-immune checkpoint receptors. Broderick said the company is focusing on SIGLEC7 and SIGLEC9 because they are expressed on a broad range of innate cells, and SIGLEC9 is also expressed on effector memory T cells.

According to BioCentury's BCIQ database, no other company has disclosed programs targeting either receptor, but several have products targeting CD33 (SIGLEC3). Pfizer Inc. markets Mylotarg gemtuzumab ozogamicin – a mAb against CD33 linked to the

calicheamicin cytotoxin – for acute myelogenous leukemia (AML). At least 10 other companies have products CD33-targeting products in preclinical to Phase II testing for cancer.

Broderick said differences in SIGLEC biology between humans and mice was an early barrier to glyco-immune checkpoint research, as humans have 10 of the receptors that mice don't have. Palleon has in-licensed a transgenic mouse model from The Rockefeller University and has since developed its own; each model expresses a different combination of human SIGLECs.

Palleon's third platform, Hydra, stratifies patients based on their individual glycan patterns to predict whether EAGLE or Convergence therapy will be more effective. Broderick said the former may be a better match for tumors with heterogeneous glycan patterns, while the latter may be more appropriate for homogeneous patterns. "We have not only a broad spectrum opportunity, in terms of hitting the innate and adaptive immune system, but a way to select patients that are most likely to respond."

The company launched in 2017 with a $47.6 million series A round led by SR One, the venture arm of GlaxoSmithKline plc.

Broderick said it's likely Palleon will conduct a financing of undisclosed type and size this year. The company hopes to submit INDs for a product each from the EAGLE and Convergence platforms in 2020.

COMPANIES AND INSTITUTIONS MENTIONED

American Association for Cancer Research (AACR), Philadelphia, Pa.
GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.
Palleon Pharmaceuticals Inc., Waltham, Mass.
Pfizer Inc. (NYSE:PFE), New York, N.Y.
The Rockefeller University, New York, N.Y.

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