NEWS RELEASE

Omeros Discovers New Cancer-Immunity Pathways Controlled by GPR174

2019-09-10

-- The Company's GPR174 Inhibitors Enhance Anti-Tumor Activities of Adenosine Pathway Inhibitors by up to 25-Fold --

SEATTLE--(BUSINESS WIRE)--Sep. 10, 2019-- Omeros Corporation (Nasdaq: OMER) today announced a new approach to cancer immunotherapy that targets inhibition of GPR174, a member of the family of G protein-coupled receptors (GPCRs), which can be combined with and significantly improve the tumor-killing effects of adenosine pathway inhibitors. GPR174-targeting immunotherapy is expected to be applicable to all solid tumors (e.g., breast, lung, pancreas, colon, brain, etc.).

The new cancer-immunotherapy approach is based on a series of discoveries by Omeros related to GPR174, which include:

- The identification of cancer-immunity pathways controlled by GPR174
- The identification of phosphatidylserine (PS) as a potent natural ligand for GPR174
- A collection of novel small-molecule inhibitors of GPR174
- A dramatic and synergistic enhancement of "tumor-fighting" cytokine production by T cells following the combined inhibition of both GPR174 and the adenosine pathway (e.g., A2A and/or A2B), another key metabolic pathway that regulates tumor immunity

GPR174 and A2A/A2B Adenosine Receptors

Like GPR174, A2A/A2B adenosine receptors are GPCRs. Central components of the adenosine pathway, A2A/A2B receptors are being targeted for cancer immunotherapy by several companies. GPR174 and A2A/A2B receptors share certain features. First, each of them increases intracellular cyclic adenosine monophosphate (cAMP), which is well known for suppressing the type of immune response necessary for killing tumor cells. Second, these receptors are activated by molecules (i.e., PS and adenosine, respectively) that are highly enriched in the tumor microenvironment. Strikingly, in experiments with total human peripheral blood mononuclear cells (PBMCs) where PS and adenosine are naturally abundant, GPR174 inhibitors synergized with A2A/A2B inhibitors to increase T-cell responses dramatically. Findings include the following:

- A2A/A2B inhibition alone yielded, on average, 2-fold increases in both interferon-gamma (IFN-γ) and tumor necrosis factor (TNF) and smaller increases in granulocyte-macrophage colony stimulating factor (GM-CSF) and interleukin-2 (IL-2)
- GPR174 inhibition alone averaged increases of 2.8-fold for IFN-γ, 2.7-fold for TNF, 1.7-fold for IL-2, and 1.4-fold for GM-CSF
- Combining a GPR174 inhibitor with A2A and/or A2B inhibition increased the average IFN-γ and TNF levels 8- to 9-fold and the average IL-2 and GM-CSF levels nearly 3-fold, with maximum increases reaching 25-fold for IFN-γ and TNF and over 4-fold for IL-2 and GM-CSF

“Our GPR174-related discoveries open a wholly new approach to targeting the tumor microenvironment for cancer immunotherapy,” said Marc Gavin, Ph.D., Omeros’ director of immunology who previously pioneered research on cAMP signaling in regulatory T cells and initiated and led Amgen’s groundbreaking IL-2 mutein program. “The adenosine pathway has been a focus of immunotherapy drug development efforts across the pharmaceutical industry. We have now shown that a relatively modest boost in cytokine production by T cells observed with inhibition of the A2A or A2B receptors, singly or together, is synergistically augmented when combined with GPR174 inhibitors. Furthermore, the discovery that PS itself stimulates an immunosuppressive GPCR – namely GPR174 – on all lymphocytes represents a significant advancement in our understanding of how PS regulates tumor immunity. New animal data from our group support these collective findings, and I look forward to clinical studies with GPR174 inhibitors, which could potentially become a treatment for most or all solid malignancies.”

Relevance of Findings

Omeros’ findings are also particularly relevant for patients resistant to checkpoint inhibitors, such as anti-PD-1 (e.g., Keytruda® and Opdivo®) and anti-CTLA-4 (Yervoy®), and to emerging cellular therapies such as CAR-T cells and adoptive T-cell therapy. Checkpoint inhibitors are only effective in a minority of patients, and high levels of adenosine-generating molecules have been observed in non-responding patients. Furthermore, overcoming natural

immunosuppression in solid tumors represents a major hurdle for cellular therapies. Because PS and adenosine are both products of cell stress and death in solid tumors, it is expected that patients resistant to checkpoint inhibitors or cellular therapies would benefit greatly from the combined inhibition of the GPR174 and adenosine pathways.

“Our team’s discovery of the GPR174-controlled cancer-immunity pathways and their interrelationships with the adenosine pathway have been methodically elucidated and defined,” said Gregory A. Demopulos, M.D., Omeros’ chairman and chief executive officer. “Simply put, Omeros has discovered that there are two feet on the cAMP brake pedal restraining immunity against the tumor and, to enable effective tumor-killing activity, both GPR174 and the adenosine pathway must be inhibited. We are optimizing our small-molecule GPR174 inhibitors with the objective of moving orally available therapeutics into the clinic as rapidly as possible. We look forward to providing physicians and patients with a new and broadly applicable option in cancer immunotherapy.”

Omeros is preparing a manuscript for publication detailing its GPR174-related discoveries and data and plans to present these same discoveries and data beginning this year at upcoming oncology international congresses.

Omeros is establishing an expansive and exclusive intellectual property position directed to GPR174 inhibitors as well as to inhibition of the GPR174 receptor, both alone and in combination with other cancer therapies, for the treatment of any tumor or malignancy.

About Omeros Corporation

Omeros is a commercial-stage biopharmaceutical company committed to discovering, developing and commercializing small-molecule and protein therapeutics for large-market as well as orphan indications targeting inflammation, complement-mediated diseases, disorders of the central nervous system and immune-related diseases, including cancers. The company’s drug product OMIDRIA (phenylephrine and ketorolac intraocular solution) 1% / 0.3% is marketed in the U.S. for use during cataract surgery or intraocular lens (IOL) replacement to maintain pupil size by preventing intraoperative miosis (pupil constriction) and to reduce postoperative ocular pain. In the European Union, the European Commission has approved OMIDRIA for use in cataract surgery and other IOL replacement procedures to maintain mydriasis (pupil dilation), prevent miosis (pupil constriction), and to reduce postoperative eye pain. Omeros has multiple Phase 3 and Phase 2 clinical-stage development programs focused on: complement-associated thrombotic microangiopathies; complement-mediated glomerulonephropathies; cognitive impairment; and addictive and compulsive disorders. In addition, Omeros has a diverse group of preclinical programs and a proprietary G protein-coupled receptor (GPCR) platform through which it controls 54 new GPCR drug targets and corresponding compounds, a number of which are in preclinical development. The company also exclusively possesses a novel antibody-generating platform.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, which are subject to the “safe harbor” created by those sections for such statements. All statements other than statements of historical fact are forward-looking statements, which are often indicated by terms such as “anticipate,” “believe,” “could,” “estimate,” “expect,” “goal,” “intend,” “likely”, “look forward to,” “may,” “plan,” “potential,” “predict,” “project,” “prospects,” “should,” “slated,” “targeting,” “will,” “would” and similar expressions and variations thereof. Forward-looking statements, including statements regarding Omeros’ research and development programs and the therapeutic application of Omeros’ research findings, are based on management’s beliefs and assumptions and on information available to management only as of the date of this press release. Omeros’ actual results could differ materially from those anticipated in these forward-looking statements for many reasons, including, without limitation, availability and timing of data from ongoing clinical trials and the results of such trials, unproven preclinical and clinical development activities, regulatory oversight, intellectual property claims, competitive developments, litigation, and the risks, uncertainties and other factors described under the heading “Risk Factors” in the company’s Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 1, 2019. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements, and the company assumes no obligation to update these forward-looking statements, even if new information becomes available in the future.

View source version on businesswire.com: **https://www.businesswire.com/news/home/20190910005467/en/**

Source: Omeros Corporation

Jennifer Cook Williams
Cook Williams Communications, Inc.
Investor and Media Relations
360.668.3701
jennifer@cwcomm.org