

April 9, 2014

## Data Presented at AACR Support Potential of Peregrine's PS-Targeting Immunotherapy Bavituximab to Enhance Anti-Tumor and Immune-Stimulating Effects of Anti-CTLA-4 and Anti-PD-1 Treatments in Models of Melanoma and Colon Cancer

Combination Treatment With Upstream PS Checkpoint Inhibitor and Downstream CTLA-4 or PD-1 Inhibitors Provides Superior Protection Against Tumor Re-Challenge; Data Presented Show Significant Increases in Functional Tumor Specific T Cells and Increases in Inflammatory Cytokines Following PS and PD1 Inhibitor Combination Therapy

TUSTIN, CA -- (Marketwired) -- 04/09/14 -- Peregrine Pharmaceuticals, Inc. (NASDAQ: PPHM) (NASDAQ: PPHMP), today announced data from studies validating the immune-stimulatory mechanism of action of bavituximab and demonstrating that the combination of a preclinical phosphatidylserine (PS)-targeting antibody with the immune checkpoint inhibitors anti-CTLA-4 or anti-PD-1 antibodies yielded superior anti-tumor immune responses in animal models of melanoma and colon cancer compared to anti-CTLA-4 and PD-1 antibodies alone. These data were presented yesterday and today as a late-breaking poster

presentation and a poster presentation, respectively at the 105<sup>th</sup> Annual Meeting of the American Association for Cancer Research (AACR) being held in San Diego, California from April 5-9, 2014. Bavituximab is an investigational immunotherapy currently being evaluated in second-line, non-small cell lung cancer (NSCLC) as part of the SUNRISE pivotal Phase III clinical trial.

"Data from these combination studies are compelling as they provide further evidence that support the immune-stimulatory effects of bavituximab in reducing the prevalence of key immunosuppressive checkpoints in the tumor environment, reducing tumor-suppressive factors, reducing immune suppressor cells and providing increased tumor-specific immunity," said Jeff T. Hutchins, Ph.D., vice president of preclinical research at Peregrine. "These data also show that when combined with downstream immune checkpoint inhibitors such as anti-CTLA-4 and anti-PD-1, PS targeting mediates an improved protective tumor-specific immunity following tumor rechallenge. While these new downstream checkpoint inhibitors have been shown to strengthen the tumor-killing activity of T-cells and thus extend survival in some patients, there remains a need to increase the number of responders that mount anti-tumor T-cell responses in order to maximize the effects of these downstream checkpoint inhibitors. We believe a PS-targeting antibody, such as bavituximab, plays a key role in reducing tumor suppression and driving a more inclusive immune-mediated response. Insights from these data will influence our future clinical development plans including the soon to be opened investigator-sponsored trial assessing the potential of bavituximab and an anti-CTLA-4 antibody in patients with advanced melanoma."

In a poster titled: "Targeting of Phosphatidylserine by Monoclonal Antibodies Enhances Activity of Immune Checkpoint Inhibitors in Tumors," scientists from Peregrine Pharmaceuticals, led by Bruce Freimark, Ph.D., director of pre-clinical research oncology, reported that animals treated with the PS-targeting antibody ch1N11, the preclinical equivalent to bavituximab, in combination with anti-CTLA-4 or anti-PD-1 in melanoma and colon cancer tumor models demonstrated greater delayed tumor growth and suppression than anti-CTLA-4 or anti-PD-1 alone. Results also showed that the combination with anti-CTLA-4 reduced M2 macrophages in the melanoma tumor model, an important cell type responsible for facilitating tumor growth and proliferation. In addition, in the preclinical melanoma model, the combination of ch1N11 with anti-CTLA-4 or anti-PD-1 antibody developed protective tumor-specific immunity to tumor re-challenge than either the anti-CTLA-4 or anti-PD-1 antibody alone. Lastly, results showed that the combination treatment of ch1N11 and anti-PD-1 led to a proportional increase in tumor infiltrating cytotoxic T-cells, while decreasing PD-L1 expression on tumor derived CD45 cells such as tumor, endothelial and stromal cells as compared to anti-PD-1 alone.

"We now have compelling evidence from these preclinical studies in multiple tumor models that PS-targeting antibodies mediate a fundamental immune-stimulatory shift in the tumor environment, facilitating increased antigen presenting cells as well as tumor-specific cytotoxic T-cells," said Peregrine's Dr. Freimark. "With the use of immunohistochemical staining, we have seen that tumors from animals treated with ch1N11 in combination with anti-PD-1 antibody showed faster and more complete T-cell and macrophage tumor infiltration rates, which correlate with decreased tumor cells, than anti-PD-1 alone. We look forward to further exploring the potential of the bavituximab with other immune checkpoint inhibitors."

In a poster titled: "Phosphatidylserine-Targeting Antibody Synergizes with anti-PD-1 Antibody to Inhibit Tumor Growth in K1735 Mouse Melanoma Model," researchers from the University of Texas Southwestern Medical Center summarized their findings that PS-targeting antibodies block PS-mediated tumor immunosuppression while reactivating tumor immunity at multiple levels.

Specifically, results showed that a PS-targeting antibody repolarized tumor-associated macrophages (TAM) from an M2 to a M1-phenotype, decreased the presence of myeloid-derived suppressor cells (MDSC), promoted dendritic cell maturation into cells having the phenotype of functional antigen presenting cells and elicited antitumor T cell immunity. In addition, statistically signifcant differences were seen in T-cell mediating markers IL-2 and gamma-interferon with the ch-1N11 and PD-1 combination. Researchers concluded that the combination of bavituximab with the anti-PD-1 checkpoint blockade should synergistically induce potent long-lasting antitumor immunity.

Abstract Details: Abstract Number 4978 Presentation Title: Targeting of phosphatidylserine by monoclonal antibodies enhances activity of immune checkpoint inhibitors in tumors Presentation Time: Wednesday, April 9, 2014, 8:00 AM -12:00 PM Author Block: Jian Gong, Van Nguyen, Shen Yin, Rich Archer, Jeff Hutchins, Bruce Freimark. Peregrine Pharmaceuticals, Inc., Tustin, California

Late-Breaking Abstract Number: LB-262

Presentation Title: Phosphatidylserine-targeting antibody synergizes with anti-PD-1 antibody to inhibit tumor growth in K1735 mouse melanoma model

Presentation Time: Tuesday, April 8, 2014, 1:00 PM - 5:00 PM

Author Block: Xianming Huang, Dan Ye, Rolf Brekken, Yi Yin. UT Southwestern Medical Center, Dallas, Texas

Copies of these posters are available on the front page of Peregrine's website.

## About Bavituximab: A Targeted Investigational Immunotherapy

Bavituximab is a first-in-class phosphatidylserine (PS)-targeting monoclonal antibody that represents a new approach to treating cancer. PS is a highly immunosuppressive molecule usually located inside the membrane of healthy cells, but "flips" and becomes exposed on the outside of cells that line tumor blood vessels, creating a specific target for anti-cancer treatments. PS-targeting antibodies target and bind to PS and block this immunosuppressive signal, thereby enabling the immune system to recognize and fight the tumor. These data detailing the immune-stimulatory mechanism of action of PS-targeting antibodies, such as the company's lead drug candidate bavituximab, are the subject of a manuscript published in the October 2013 issue of the American Association for Cancer Research (AACR) peer-reviewed journal, Cancer Immunology Research. Bavituximab is currently being evaluated in several solid tumor indications, including non-small cell lung cancer, breast cancer, liver cancer and rectal cancer with a trial in advanced melanoma anticipated to initiate in the near future.

## About SUNRISE Trial:

SUNRISE is a pivotal Phase III, randomized, placebo-controlled, double-blind, multinational clinical trial evaluating the efficacy and safety of bavituximab (bav i tux' i mab), a novel investigational immunotherapy, plus docetaxel versus placebo plus docetaxel as a second-line treatment for patients with Stage IIIb/IV non-squamous non-small cell lung cancer (NSCLC). For more information about the SUNRISE trial, please visit: <u>www.SunriseTrial.com</u>

## About Peregrine Pharmaceuticals, Inc.

Peregrine Pharmaceuticals, Inc. is a biopharmaceutical company with a pipeline of novel drug candidates in clinical trials for the treatment and diagnosis of cancer. The company is developing multiple clinical programs in cancer with its lead immunotherapy candidate bavituximab while seeking a partner to further advance its novel brain cancer agent Cotara®. Peregrine also has inhouse cGMP manufacturing capabilities through its wholly-owned subsidiary Avid Bioservices, Inc. (www.avidbio.com), which provides development and biomanufacturing services for both Peregrine and third-party customers. Additional information about Peregrine can be found at www.peregrineinc.com.

Safe Harbor Statement: Statements in this press release which are not purely historical, including statements regarding Peregrine Pharmaceuticals' intentions, hopes, beliefs, expectations, representations, projections, plans or predictions of the future are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. The forwardlooking statements involve risks and uncertainties including, but not limited to, the risk that results from human clinical studies involving combinations of bavituximab with approved or investigational immune checkpoint inhibitors may not correlate with the data from the preclinical studies. It is important to note that the Company's actual results could differ materially from those in any such forward-looking statements. Factors that could cause actual results to differ materially include, but are not limited to, uncertainties associated with completing preclinical and clinical trials for our technologies; the early stage of product development; the significant costs to develop our products as all of our products are currently in development, preclinical studies or clinical trials; obtaining additional financing to support our operations and the development of our products; obtaining regulatory approval for our technologies; anticipated timing of regulatory filings and the potential success in gaining regulatory approval and complying with governmental regulations applicable to our business. Our business could be affected by a number of other factors, including the risk factors listed from time to time in our reports filed with the SEC including, but not limited to, our annual report on Form 10-K for the fiscal year ended April 30, 2013 as well as any updates to these risk factors filed from time to time in the company's other filings with the Securities and Exchange Commission. The Company cautions investors not to place undue reliance on the forward-looking statements contained in this press release. Peregrine

Pharmaceuticals, Inc. disclaims any obligation, and does not undertake to update or revise any forward-looking statements in this press release.

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