

Paloma Pharmaceuticals publishing seminal paper in Cancer Research and presentation at the AACR special conference in cancer research

-- Presentations highlight Palomid 529 as a first-in-class dual TORC1/TORC2 inhibitor--

Jamaica Plain, MA, Nov. 17, 2008 /PRNewswire/ -- Paloma Pharmaceuticals, Inc. today announced the publication of a first and seminal paper describing the Company's TOR complex inhibitor Palomid 529 (P529). The work was also presentation at the American Association of Cancer Research (AACR) special conference in cancer research, "Targeting the PI3-Kinase Pathway in Cancer".

P529 is a non-steroidal, synthetic, small molecule anti-tumor agent created through computational design, synthetic and medicinal chemistry, the result of three generations of Palomid design work. Palomid's broad activity as an anti-tumor agent is shown to reside in its ability to target and inhibit the Akt/mTOR signal transduction pathway through its dual TORC1/TORC2 inhibition.

Work constituting the Cancer Research paper, "Palomid 529, a Novel Small-Molecule Drug, Is a TORC1/TORC2 Inhibitor That Reduces Tumor Growth, Tumor Angiogenesis and Vascular Permeability", was conducted in the laboratory of Dr. Laura E. Benjamin of the Department of Pathology and Center for Vascular Biology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA. Dr. Benjamin expressed optimism for the "improvement that P529 represents over current TORC1 inhibitors with respect to the inhibition of Akt S473 signaling in tumor cells. I was also impressed that P529 was efficacious in animal models even when given orally".

"We were excited that Cancer Research chose our paper for their cover page of the November 15th issue of the journal honoring the work of Dr. Benjamin's laboratory and the importance of P529 in cancer research," said David Sherris, Ph.D., President and CEO of Paloma Pharmaceuticals.

"P529 is a potent anti-tumor agent acting through inhibition of the Akt/mTOR pathway targeting both TORC1 and TORC2 complexes. The dual nature of inhibition of TORC1/TORC2 complexes is notable and widely believed to be an improvement over existing TORC1 inhibitors by uniformly inhibiting signaling through the pathway and avoiding feedback loop activations. Work described in our Cancer Research paper and AACR presentation show the disappearance of both the TORC1 and TORC2 complexes within two hours of incubation of P529 with tumor cells. This inhibition results in significant tumor growth delay and inhibition of angiogenesis," said Dr. Sherris.

About the PI3K/Akt/mTOR Pathway

The PI3K/Akt/mTOR pathway has been implicated in a wide variety of biological responses and is considered a major therapeutic target in cancer. Activation of this signaling pathway,

via direct or indirect mutagenic events, is common in many types of human cancer resulting in deregulation of PI3K/Akt/mTOR pathway in cancer. Thus, agents capable of inhibiting the PI3K/Akt/mTOR pathway are attractive targets for therapeutic intervention in cancer. Central within the signalling pathway are two distinct protein complexes, one of which regulates growth through the signal transduction protein S6K, TORC1, and the other that regulates cell survival through Akt, TORC2. These complexes define both rapamycin-sensitive and insensitive branches of the PI3K/Akt/mTOR pathway. Inhibition of the TORC2 pathway suppresses the formation of tumors driven by the loss of the PTEN tumor suppressor, a gene which when lost contributes to carcinogenicity. Inhibitors of TORC2 may then have beneficial effects as anti-cancer agents without toxicity to normal tissues since loss of TORC2 through genetic alteration does not appear to affect normal tissue. TORC1 antagonists such as rapamycin and other rapalogs have shown activity in both animal models of cancer and in human clinical trials. As inhibition of both TORC1 and TORC2 should result in more complete inhibition of PI3K/Akt/mTOR signaling up-regulated in cancer, dual inhibitors are of active interest for pharmaceutical development.

About Paloma Pharmaceuticals

Paloma Pharmaceuticals, Inc. is an early stage drug development company focusing on cancer, ocular diseases (macular degeneration and diabetic retinopathy), arthritis, fibrotic diseases (pulmonary fibrosis) endometriosis, osteoporosis and skin diseases (psoriasis and atopic dermatitis). Paloma owns the intellectual property relating to a library of novel, proprietary, small molecule drugs created through an integrated design platform incorporating proprietary, customized and industry standard computational tools that has therapeutic potential for the treatment of the foregoing diseases.

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