

Paloma Pharmaceuticals Presents at the AACR-NCI-EORTC International Conference Molecular Targets and Cancer Therapeutics

-- Presentation highlights Palomid 529 as a first-in-class dual TORC1/TORC2 inhibitor in Brain Cancer--

Jamaica Plain, MA, Nov. 16, 2009 /PRNewswire/ -- Paloma Pharmaceuticals, Inc. announced it will give a presentation today at the AACR-NCI-EORTC International Conference Molecular Targets and Cancer Therapeutics, "Palomid 529, a dual mTor1/2 inhibitor, efficiently penetrates the blood brain barrier and may be an attractive agent for treatment of glioblastoma" by Dr. Olaf van Tellingen, Ph.D. of The Netherlands Cancer Institute, Amsterdam, The Netherlands.

Palomid 529 (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 PI3K/Akt/mTOR signal transduction pathway as a dual TORC1/TORC2 inhibitor.

"Glioblastoma Multiforme is the most frequent primary brain tumor for which very few active drugs are available. The blood brain barrier is a major obstacle in the efficient delivery of drugs to the brain. In particular, the activities of ABC transporters such as P-glycoprotein and breast cancer-resistance protein (BCRP) are important. We were, therefore, pleased to see that Palomid 529 is only a very weak substrate of P-glycoprotein and BCRP and that high brain-to-plasma ratios were achieved following drug administration. This property makes Palomid 529 an attractive candidate for targeting this potentially important PI3K-Akt-mTOR signal transduction route in brain cancer" said Dr. Van Tellingen.

"Work from the laboratory of Dr. van Tellingen is significant in that it shows administration of P529 penetrates the brain-blood-barrier, enters the brain and is not affected by the ABC transporters a common problem in cancer therapy where cancer drugs are actively pumped out of cancer cells," said David Sherris, Ph.D., President and CEO of Paloma Pharmaceuticals. "This work adds to our mounting compendium of data showing P529 as a potent oral anti-tumor agent in variety of tumor animal models including breast, prostate and glioblastoma", 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 as rapamycin and other such 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 utilizing its PI3K/Akt/mTOR inhibitors focusing on cancer, ocular diseases (macular degeneration and diabetic retinopathy), CNS (epilepsy, Parkinson's disease, Alzheimer's disease), fibrotic diseases (pulmonary and renal fibrosis), antiviral (HIV, HCV) 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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