

Paloma Pharmaceuticals presents at the 10th International Symposium on Anti-angiogenic Agents

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

Jamaica Plain, MA, Feb. 7, 2008 -- Paloma Pharmaceuticals, Inc. today presented its work on the Company's PI3K/Akt/mTOR inhibitor Palomid 529 (P529) at the 10th International Symposium on Anti-angiogenic Agents in La Jolla, California.

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.

"P529 is a potent anti-tumor agent acting through inhibition of the PI3K/Akt/mTOR pathway targeting both TORC1 and TORC2 complexes. TORC1 inhibitors have already shown activity in the clinic but their drawback is their lack of inhibition of signaling through TORC2. This inability appears to be problematic as cancer cells may use the TORC2 signalling to evade TORC1 antagonism resulting in tumor growth. P529 is unique and a first-in-class agent as it works by eliminating presence of both complexes resulting in a thorough inhibition of PI3K/Akt/mTOR signalling and interestingly enough does this without apparent systemic toxicity," 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 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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