Paloma Pharmaceuticals presents at the Association for Research in Vision and Ophthalmology 2009 Meeting

-- Presentation describes Palomid 529 as a first-in-class Dual TORC1/TORC2 complex inhibitor of the PI3K/Akt/mTOR pathway showing efficacy in retinal scarring caused by retinal detachment –

Jamaica Plain, MA, May. 6, 2009 -- Paloma Pharmaceuticals, Inc. presented “Palomid 529, An Inhibitor of the Akt/mTOR Pathway Reduces Photoreceptor Cell Death Following Experimental Retinal Detachment”, today at the annual meeting of the Association for Research in Vision and Ophthalmology 2009 (ARVO 2009), This study, presented by Geoffrey P. Lewis, Ph.D. (along with G. Luna, J. Byun, E.A. Chapin and S.K. Fisher*)* of the Neuroscience Research Institute and Molecular Cell & Developmental Biology Department of the University of California, Santa Barbara, CA. has been accepted for publication in the journal Investigative Ophthalmology and Visual Science.

Work from this study indicates that intravitreally administered Palomid 529 slows photoreceptor cell death following retinal detachment in a seven day rabbit study without obvious side effects to the retina. This suggests that inhibiting the PI3K/Akt/mTor signal transduction pathway by Palomid 529 may be neuroprotective to photoreceptors and perhaps represents a novel therapy for other retinal diseases such as proliferative vitreoretinopathy, macular degeneration and diabetic retinopathy. “We are excited over the results of this study in that it further adds to our data showing the versatility of Palomid 529 for diseases of retinal and subretinal origin. Furthermore, results from a separate six month intravitreal ocular biodistribution study, shows the presence of Palomid 529 in the eye for at least six months. This observation coupled with efficacy data described here and in earlier studies indicates that Palomid 529 may be administered infrequently, possibly as little as once a year”, says David Sherris, Ph.D., President and CEO of Paloma Pharmaceuticals.

“Retinal detachment can occur following trauma or as part of certain diseases of the eye resulting in blindness in the affected area. In some cases, blindness or other visual deficits may be permanent, and related to the death of photoreceptor cells, the cells responsible for capturing light in the retina. We have presented data at ARVO demonstrating that a single intraocular injection of Palomid 529, a drug originally designed as an anti-angiogenic agent,

can significantly reduce this death in an animal model of retinal detachment. In addition, we show that Palomid 529 also reduces the activation of glial cells and subsequently slows the formation of subretinal scar tissue, a condition that can prevent the regeneration of photoreceptors following successful retinal reattachment surgery. Taken together these data suggest that Palomid 529 may be neuroprotective to photoreceptors and reduce the incidence of subretinal fibrosis without obvious side effects to the retina", says Dr. Lewis, study investigator.

About Retinal Detachment

Retinal detachments can occur for a variety of reasons and, in general, can be repaired by retinal surgeons. Two potentially devastating complications of retinal detachment, however, are proliferative vitreoretinopathy (PVR) and subretinal fibrosis (scarring). When the retina becomes separated from the retinal pigment epithelium (RPE) because a tear or hole occurs in the retina, many cell types undergo proliferation and consequently have the potential to form retinal scars. When such cell types are present in the space between the retina and the RPE, subretinal fibrosis is the result and can prevent the recovery of photoreceptor cells even though the retina is reattached. When such cells grow on the vitreal surface of the retina, they can form contractile scar tissue leading to re-detachment of the retina. Together, these conditions are termed proliferative vitreoretinopathy (PVR). PVR remains the most common cause of retinal reattachment surgery failure still occurring in about 5-12% of cases. Although advances in the surgical management of PVR have improved the ability of surgeons to ultimately reattach the retina, the visual prognosis remains poor, with only 11-25% of patients achieving a visual acuity of 20/100. Presumably this permanent decrease in visual acuity is due, in part, to the loss of photoreceptors since apoptosis is a clear consequence of detachment and can continue at low levels even after the retina is reattached. While there have been numerous attempts to reduce the incidence of PVR, to date no effective pharmacological treatment has been found.

About the PI3K/Akt/mTOR Pathway and Palomid 529

The PI3K/Akt/mTOR pathway has been implicated in a wide variety of biological responses and is considered a major therapeutic target in several different diseases. Activation and

subsequent deregulation of this signaling pathway, via direct or indirect mutagenic events, is common in many types of human diseases. Thus, agents capable of inhibiting the pathway are attractive targets for therapeutic intervention. Central to the signalling pathway are two distinct protein complexes, one of which, TORC1, regulates cell growth by acting on the signal transduction protein S6K, while the other, TORC2, regulates cell survival through Akt. These complexes define the rapamycin-sensitive and insensitive branches of the PI3K/Akt/mTOR pathway. Inhibitors of TORC2 may have beneficial effects without toxicity to normal tissues since loss of TORC2 in genetically altered mice does not appear to affect normal tissue. TORC1 antagonists such as rapamycin (Sirolimus) have shown activity in both animal models of ocular disease and in human clinical trials. The inhibition of both TORC1 and TORC2 should result in more complete inhibition of aberrant PI3K/Akt/mTOR signaling and are therefore of active interest for pharmaceutical development. Palomid 529 is a first-in-class dual TORC1/TORC2 inhibitor.

About Paloma Pharmaceuticals

Paloma Pharmaceuticals, Inc. is an early stage drug development company focusing on cancer, ocular diseases (macular degeneration, diabetic retinopathy and proliferative vitreoretinopathy), arthritis, fibrotic diseases (pulmonary fibrosis), viral (HIV) 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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