

MEETING DETAILS

Inositide Signaling in Pharmacology and Disease (X1)

Organizer(s): Marco Falasca, Nullin Divecha, John D. York and Pietro V. De Camilli
February 13 - 18, 2011

Keystone Resort · Keystone, Colorado

Abstract Deadline: October 14, 2010

Late Abstract Deadline: November 18, 2010

Scholarship Deadline: October 14, 2010

Early Registration Deadline: December 14, 2010

Sponsored by sanofi-aventis

Joint meeting: [PI 3-Kinase Signaling Pathways \(X2\)](#)

NOTE: Registration for meeting allows attendance at joint meeting (pending space availability).

AQX-1125, a Modulator of the SHIP1/PI3K Pathway, Suppresses Chemotaxis and Inflammation

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The phosphoinositide 3-kinase (PI3K)/Akt pathway is critical to immune cellular activation, proliferation, and survival. Pharmacological inhibition of the PI3K pathway as a means to control inflammatory disorders is a highly competitive area in the pharmaceutical industry. AQX-1125 is an orally administered small molecule with promising anti-inflammatory activities and a novel mechanism of action. AQX-1125 activates SH2-containing inositol-5'-phosphatase 1 (SHIP1), and exerts negative regulatory effects on the PI3K pathway.

AQX-1125 was evaluated for *in vitro* and *in vivo* anti-inflammatory activity. AQX-1125 was tested in *in vitro* leukocyte chemotaxis assays. The efficacy of AQX-1125 was also tested in a rat ovalbumin-mediated airway inflammation model, administered orally for 4 days at 0.1, 1 and 10 mg/kg before airway challenge. The degree of inhibition of leukocyte infiltration and mediator release in the bronchoalveolar lavage fluid (BALF) and lung tissue was measured.

AQX-1125 is a pan-selective inhibitor of *in vitro* leukocyte chemotaxis, with nM potency. *In vivo*, AQX-1125 at 1 and 10 mg/kg significantly reduced the total number of leukocytes recovered in the BALF of rats sensitized and challenged with ovalbumin. In the same model of allergic airway inflammation, AQX-1125 also inhibited inflammatory mediator content in the BALF and rat lung tissue. These data suggest that AQX-1125 has clinical potential for treatment of allergic and inflammatory diseases such as asthma and COPD.