2008-2009 POCC Lecture Series

May 14, 2009, 8:00 PM

Dr. Christopher Dinsmore

Merck Research Laboratories

"Discovery of a Unique c-Met Inhibitor for the Treatment of Cancer"

Carolyn Hoff Lynch Lecture Hall
Chemistry Building, University of Pennsylvania

The Philadelphia Organic Chemist's Club

POCClub.org

Dr. Christopher Dinsmore completed his undergraduate studies at Bowdoin College in chemistry, and then earned his Ph.D. degree in synthetic organic chemistry under the direction of Professor Thomas Hoye at the University of Minnesota, Minneapolis. In 1991 he moved to Harvard University, where he carried out postdoctoral research in the laboratory of Professor David Evans, and in 1994, he joined Merck Research Laboratories in West Point, PA as a Senior Research Chemist. He has been a member of drug discovery project teams in areas of oncology, cardiovascular disease and neuroscience, and has been closely associated with several drug candidates that have undergone clinical studies. Dr. Dinsmore is currently a Director of Medicinal Chemistry at the Merck Boston research site. He has co-authored over 45 publications in chemistry and drug discovery, is a co-inventor on 27 patents and 26 patent applications, and is a proud past officer of the POCC.

Abstract: Organic chemistry is a crucial driver in the discovery of small molecule therapeutics when practiced in close collaboration with other life sciences. An example in cancer research will be described. Aberrant c-Met activity has been implicated in the pathogenesis of a variety of human tumors and is therefore an attractive target for therapeutic intervention. Building from a novel structure scaffold, we have identified a potent and selective ATP-competitive c-Met kinase inhibitor that is equally potent against wild type enzyme and naturally occurring oncogenic mutants, including activation loop mutants. The compound inhibits in vitro c-Met-driven phosphorylation events and phenotypic changes in cells. In a cancer xenograft model driven by MET gene amplification, well tolerated oral doses of the compound inhibited kinase autophosphorylation, downstream signal transduction and tumor growth. These preclinical data provided support for clinical evaluation as a potential targeted therapy for patients with c-Met driven tumors.