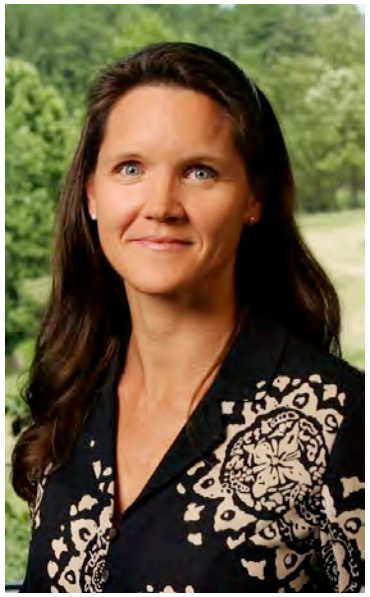

2009-2010 POCC Lecture Series

December 3, 2009, 8:00 PM

Dr. Karen Lackey

GlaxoSmithKline Pharmaceuticals

" Tykerb® and Kinome Drug Discovery "

Carolyn Hoff Lynch Lecture Hall
Chemistry Building, University of Pennsylvania

The Philadelphia Organic Chemist's Club

POCClub.org

Karen Lackey is currently a Vice President of Molecular Discovery Research Chemistry, GlaxoSmithKline, with accountability for exploratory chemistry, compound collection enhancement and new technology with research groups on five sites in the UK and US. In her previous role as International Medicinal Chemistry Director her team advanced more than 55 early stage programs in multiple therapeutic areas, including cardiovascular, oncology, inflammation, psychiatry, neurology, respiratory, gastrointestinal diseases, metabolic diseases, infectious diseases, and virology. Karen has over 75 published articles, patents and book chapters covering various aspects of drug discovery with an emphasis in oncology, infectious diseases, and cell signaling research. She has been involved in drug discovery for over 20 years, and of her accomplishments, she is most proud of the Discovery of Tykerb®, a Dual ErbB1/2 Tyrosine Kinase Inhibitor, approved in March of 2007 in the treatment of advanced breast cancer.

Abstract: Protein Kinases offer opportunities for drug intervention since phosphorylation is considered one of the most common post-translational modifications. Fortunately, protein kinases are among the most successfully pursued drug targets in industry and academia for oncology.[1] The focus of this presentation will be on the highlights of a drug discovery effort and the lessons learned from using a tool compound in the generation of a highly effective signalling inhibitor, Tykerb®, a dual inhibitor of EGFR and ErbB-2, also known as transmembrane Type 1 receptor tyrosine kinases of the HER family of receptors. Type 1 receptors are over-expressed in a variety of cancers and generally correlate with poor prognosis. Many other tractable kinases are being pursued where the small molecules' design also aims to bind in the ATP binding site of the intracellular portion of kinase proteins to block the aberrant signalling events that lead to disease. Well characterized tool compounds provide a means to better associate kinase activity with disease, thus ensuring the right combination or selectivity profile was achieved for emerging oncology drugs.

1. I. Walker and H. Newell, Nature Reviews: Drug Discovery. Do Molecularly targeted agents in oncology have reduced attrition rates? 2009, 8, 15 - 16.