



2023-2024 POCC Lecture Series

Oct 19, 2023, 7:30 PM

Dr. Daniel Paone

GSK

Discovery of an MRGPRX2 Antagonist Clinical Candidate for the Treatment of Mast Cell Diseases

IN PERSON @:

Carolyn Hoff Lynch Lecture Hall Chemistry Building,

University of Pennsylvania

6:30 Reception in the Nobel Hall

Food and drinks to be provided!

The Philadelphia Organic Chemist's Club



POCCclub.org

with support from ADSE



@POCC_Chem

@adse_penn

Sponsored by:



FOX CHASE THERAPEUTICS DISCOVERY, INC.

Abstract: MRGPRX2 is a GPCR that has been implicated in a number of mast cell pathologies, including various skin disorders. As part of a Discovery Partnerships with Academia (DPAc) collaboration, we began working with Professor Xinzhong Dong at Johns Hopkins University to explore the possibility of developing small molecule, orally dosed MRGPRX2 antagonists. This presentation will highlight the progression of an initial HTS hit to clinical candidate selection, overcoming challenges related to mitochondrial dysfunction.

Bio: Dan received his B.S. in Chemistry at the University of Delaware where he performed undergraduate research for Professor Cynthia McClure. He then attended the University of Pennsylvania to pursue graduate studies while working in the laboratories of Professor Amos B. Smith, III towards the total synthesis of (-)-cylindrocyclophane A. After receiving his Ph.D., Dan accepted a post-doctoral position with Professor Larry Overman at the University of California, Irvine where he completed total syntheses of polypyrroloindoline alkaloids including (-)-chimonanthine and ditryptophenaline. He began his medicinal chemistry career at Merck (West Point) in 2001 where he contributed significantly to the design of multiple preclinical candidates, including telcagepant, a CGRP receptor antagonist for acute migraine which advanced through Phase III clinical trials. In 2014, Dan joined GlaxoSmithKline as a member of the Discovery Partnerships with Academia team. In that role, he coordinated the medicinal chemistry efforts of multiple small molecule drug discovery programs, leading large chemistry matrix teams and serving on project joint steering committees while working collaboratively with scientists at academic institutions. Additionally, he was responsible for guiding the externalization of chemistry, DMPK, and biology operations for the broader DPAc group with the accompanying logistics/operations and financial responsibilities, and was highly involved in identifying and evaluating potential projects at research institutions. In 2019, Dan joined the newly created Medicinal Chemistry department, where he continued to direct the chemistry efforts on the MRGPRX2 program through to candidate selection, and currently occupies both medicinal chemistry leadership and people management roles.