2022-2023 POCC Lecture Series

March 23, 2023, 7:30 PM

Dr. Kristi Leonard

Janssen R & D

Discovery of a Gut-Restricted JAK Inhibitor for the Treatment of Inflammatory Bowel Disease & Identification of Quinazoline-based Covalent Inhibitors of KRAS^{G12C} for the Treatment of Solid Tumors

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

POCClub.org

with support from ADSE

@POCC_Chem

@adse_penn

Sponsored by:

ADESIS
A Universal Display Company

Abstract: To identify Janus kinase (JAK) inhibitors that selectively target gastrointestinal tissues with limited systemic exposures, a class of imidazopyrrolopyridines with a range of physical properties was prepared and evaluated. We demonstrate the utility of JAK inhibitors with low intrinsic permeability as a feasible approach to develop gut-restricted, pharmacologically active molecules with a potential advantage over systemically available compounds that are limited by systemic on-target adverse events.

A novel series of mutant-selective KRAS^{G12C} quinazoline-based covalent inhibitors demonstrating high potency in a biochemical target engagement assay were optimized. SAR, parallel optimization of both potency and physicochemical properties, as well as in vivo efficacy and pharmacokinetic/pharmacodynamic markers assessment in tumor xenograft models will be discussed.

Bio: Kristi Leonard is currently a Scientific Director in Global Discovery Chemistry at Janssen and has over 20 years of experience in Medicinal Chemistry working in several therapeutic areas including Immunology and Oncology. She has been a project leader for multiple projects including RORγt, Gut-restricted JAK, and KRAS and has contributed to the advancement of several compounds to clinical development. She has authored 30 scientific publications and been a co-inventor on over 40 patents. Kristi obtained her Ph.D. in Medicinal Chemistry at the University at Buffalo in New York and was a post-doctoral fellow in Chemistry at Yale University..