



2023-2024 POCC Lecture Series

Sept 21, 2023, 7:30 PM

Dr. John Curto

Pfizer

Design and synthesis of small molecule GLP-I receptor agonists

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



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Abstract: The application of synthetic chemistry in medicinal chemistry has the power to access new chemical space, reduce cycle times in the “design, make, test” process and streamline mg to kg synthesis for testing in the clinic. Glucagon-like peptide-I (GLP-IR) receptor agonists comprise a growing class of agents that deliver unprecedented efficacy in diabetes and obesity. GLP-I is a 30 amino acid peptide hormone that activates the GLP-I receptor, a class B GPCR that is particularly challenging to stimulate with small molecules. Recently, Pfizer disclosed the structure of the orally bioavailable, small molecule, GLP-IR agonists PF-06882961 (danuglipron) and PF-07081532 (lotiglipron). This presentation will discuss the synthetic challenges for accessing PF-06882961 and PF-07081532. Large scale amenable routes to key fragments (amino-oxetane, 4-pyridyl-piperidine and benzimidazole) will be highlighted as well as the novel dioxolane functional group.

Bio: John started at Pfizer in Oct, 2014 in the Cardiovascular and Metabolism (CVMET) medicinal chemistry group. He joined the Inflammation and Immunology (I&I) medicinal chemistry group in Feb, 2017 and took on a lab head role in the recently formed Internal Medicine (IM) in Oct 2017. He supported the IM portfolio until Feb 2023 when he transitioned onto projects within Center for Therapeutic Innovation (CTI). His contributions have supported the advancement of three projects into human clinical trials including GLP-I agonists Danuglipron and Lotiglipron. He has managed the IM Library Optimization Center which drives internal parallel medicinal chemistry (PMC) efforts since 2018. He is active in recruiting, hiring and training as well as pursuing independent research. Since joining Pfizer he is a co-author on 6 manuscripts focusing on method development and medicinal chemistry as well an inventor on 7 patent applications. John received the WWRD team achievement award for the discovery of Danuglipron in 2019. He recently presented at the 2023 Fall ACS in celebration of receiving the Early Career Investigator award. John received his B.A. from the College of the Holy Cross and his PhD at University of Pennsylvania under the guidance of Marisa Kozlowski.