



## 2023-2024 POCC Lecture Series

### The POCC Industrial Award Lecture:

Feb 15, 2024, 7:30 PM

**Dr. L.-C. Campeau**

Merck & Co.

*Changing the World One Reaction at A Time:  
Unique Challenges in the Development of a Robust  
and Sustainable Manufacturing Process to Belzutifan*

**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 Nobel Prize in Physiology or Medicine 2019 was awarded for the discovery of how cells sense and adapt to oxygen availability which uncovered a critical link with hypoxia-inducible factor  $2\alpha$  (HIF- $2\alpha$ ) and its potential role as a therapeutic target for Von Hippel-Lindau (VHL) disease and certain types of cancers. These insights eventually led to the discovery of belzutifan, a small molecule inhibitor of HIF- $2\alpha$  that achieved FDA breakthrough designation in 2020 and was approved in 2021 for VHL associated tumors and in 2023 for advanced renal cell carcinoma. Belzutifan has a unique stereochemical triad on the indanone ring featuring two secondary alkyl fluorides which posed significant challenges for its synthesis. We will present how the manufacturing process evolved from its initial scale-up route through to the final commercial manufacturing route, as well as highlight key innovations which enabled the manufacture and launch in 2021 of belzutifan including the development of a photo-flow bromination, direct enantioselective biocatalytic hydroxylation and a uniquely selective dehydrofluorination.

**Bio:** L.-C. Campeau obtained his Ph. D. degree in 2007 with the late Professor Keith Fagnou at the University of Ottawa in Canada as an NSERC Doctoral Fellow. He first joined Merck Research Laboratories at Merck-Frosst in Montreal in 2007 where he was recognized for key contributions to the discovery of Doravirine (MK-I439) a next generation non-nucleoside reverse transcriptase inhibitor for the treatment of HIV. In 2010, he moved from Quebec to New Jersey, where he has served in roles of increasing responsibility. He recently co-led the early development team for Merck's oral PCSK9 inhibitor MK-0616, ushering this first macrocyclic peptide in Merck's history into phase 3 clinical trials. L.-C. is currently Associate Vice President and the Head of Small Molecule Process Research and Development. Over his tenure at Merck, L.-C. and his team have made important contributions to >50 clinical candidates and 7 commercial products to date. Under his leadership, his organization was recognized with 4 EPA Green Chemistry Challenge Award and 2 Heroes of Chemistry Award. His passion for scientific excellence is exemplified by >85 publications and patents, several successful collaborations with key academics, and an extensive list of >95 invited lectures worldwide. L.-C. was elected Fellow of the Royal Society of Canada in 2022.

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