2017-2018 POCC Lecture Series

January 25, 2018, 7:30 PM

The Women in Chemistry Lecture at POCC

Dr. Ruth R Wexler

Bristol-Myers Squibb

Adventures in the Discovery of Novel Oral Anticoagulants: New Frontiers and Lessons Learned

Carolyn Hoff Lynch Lecture Hall
Chemistry Building, University of Pennsylvania

The Philadelphia Organic Chemist's Club

POCClub.org

Dr. Ruth Wexler received a B.A. in Chemistry with a minor in biology from Boston University in 1977, and a Ph.D. in Organic Chemistry from the University of Pennsylvania in 1982. She joined DuPont as a Research Chemist in the Medicinal Chemistry Section of the Biomedical Products Division and was promoted to positions of increasing leadership responsibility becoming an Executive Director in 1998. In 2001, she moved to Bristol-Myers Squibb (post-acquisition of DuPont Pharmaceuticals Company) where she currently heads the medicinal chemistry efforts in Cardiovascular Diseases and the Chemotype Discovery and Optimization group. During her career, Dr. Wexler has led research groups focused on the design and synthesis of drug candidates directed at Cardiovascular/Metabolic Diseases (hypertension, atherosclerosis, thrombosis, heart failure and obesity), Inflammatory Diseases, and Alzheimer's Disease. Her group has been involved in many innovative advances most notably in the Cardiovascular area, where their research efforts have resulted in two marketed Cardiovascular drugs: Cozaar®, an angiotensin II receptor antagonist; and Eliquis®, a factor Xa inhibitor, as well as the discovery of 24 additional compounds which were selected for clinical evaluation across a wide range of mechanisms of action.

Dr. Wexler has been active in the American Chemical Society where she served the Medicinal Chemistry Division on the Long Range Planning Committee (1996-1999), Pre-doctoral Fellowship program Committee (1998-2001), and as Industrial Councilor (2003-2005), and the Organic Division as a member of the Executive Committee (1997-2000). She also served as a member of the NIH Medicinal Chemistry A Study Section (1999-2003). She was honored in 2004 as one of twelve Outstanding New Jersey Women in Research by the New Jersey Association for Biomedical Research. In 2011, she was a recipient of the Bristol-Myers Squibb Ondetti and Cushman Award for her leadership role in the discovery of Eliquis®. Ruth was elected to the ACS Medicinal Chemistry Division Hall of Fame in 2014, and more recently she was awarded the 2015 American Chemical Society E.B. Hershberg Award for Important Discoveries in Medicinally Active Substances. Ruth has co-authored over 215 peer-reviewed scientific publications and patents, and has contributed several review articles and book chapters largely in the area of cardiovascular research.

Abstract: Cardiovascular disease is the leading cause of death and disability worldwide. A common component of the end stage of these diseases is thromboembolic disorders which account for over 50% of cardiovascular related deaths. This large unmet medical need resulted in intense activity to discover and develop novel antithrombotic agents. Over the past few decades, drug discovery directed at the treatment and prevention of thromboembolic diseases has been challenged by the need to balance robust efficacy with exquisite safety. Perhaps the most impactful advance to date in the area of oral anticoagulants, has been the recent introduction into clinical practice of the new class of orally bioavailable small molecule factor Xa (FXa) inhibitors. At Bristol-Myers Squibb our efforts culminated in the discovery of Eliquis® (apixaban), a novel oral FXa inhibitor. This presentation will highlight the key learnings from the discovery efforts which led to Eliquis, and applications of these learnings to structure-based drug design of small molecule macrocyclic Factor XIa inhibitors which have the potential to provide the next generation of antithrombotic drugs..