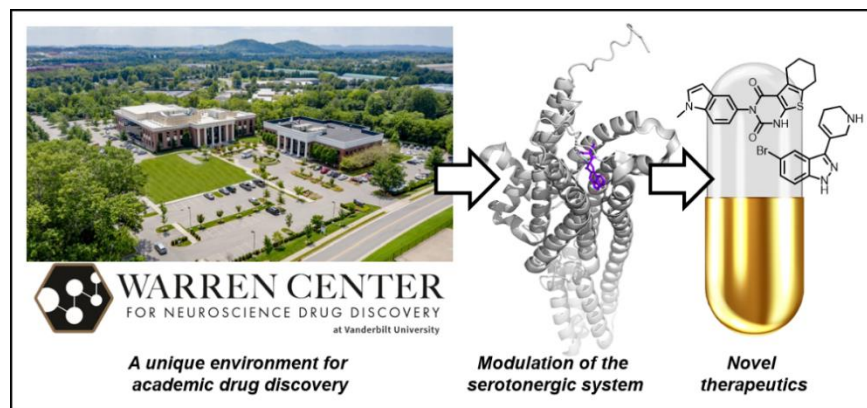


# CBAS Day Keynote Address

Tuesday, March 12<sup>th</sup>  
1:00-2:00 pm  
SCCM 105

Dr. Aaron Bender  
Assistant Director of Medicinal Chemistry  
Warner Center for Neuroscience Drug Discovery

## *New Opportunities for Serotonergic Drug Discovery*



### **Abstract:**

The Warren Center for Neuroscience Drug Discovery (WCNDD) is unique amongst academic drug discovery centers. By combining the infrastructure of the pharmaceutical industry with the resources of Vanderbilt University, the WCNDD has focused on novel therapeutic mechanisms for disorders of the central nervous system (CNS), a strategy that is traditionally viewed as “high risk” within the pharmaceutical industry. The WCNDD emphasizes allosteric target modulation, traditionally within the CNS realm, but is also actively engaged with targets related to cardiovascular and metabolic diseases. Recently, the WCNDD has added multiple projects targeting the serotonergic system to its pipeline portfolio.

Serotonin (5-hydroxytryptamine, 5-HT) is the endogenous ligand for the 14 known 5-HT receptors, where it acts as a neurotransmitter and growth factor through various signaling pathways. The 5-HT<sub>2</sub> family is further split into three distinct receptors (5-HT<sub>2A</sub>, 5-HT<sub>2B</sub> and 5-HT<sub>2C</sub>), and each subtype plays important roles in a variety of physiological processes. Ligands for the 5-HT<sub>2</sub> receptors have been developed for the modulation of diverse pathologies, including cognition, Alzheimer’s disease (AD), cluster headaches, substance abuse disorder, anxiety, pulmonary arterial hypertension (PAH), and valvular heart disease (VHD). While the 5-HT<sub>2</sub> receptors are well-established, highly druggable proteins, novel ligand chemotypes and/or modes of pharmacology may represent first-in-class approaches for many of these indications.

Toward this end, our laboratory is interested in developing compounds for 2 indications modulated by the 5-HT<sub>2</sub> receptor system: 1) the development of next-generation analogs of the classical psychedelic 5-HT<sub>2A</sub> agonists, specifically molecules which bind to unexplored, allosteric receptor sites, and 2) the development of novel 5-HT<sub>2B</sub> antagonists for the treatment of PAH and related cardiopathies, which have shown encouraging disease-modifying efficacy in rodent models. Although distinct with respect to indication and approach, each project highlights the immense utility of this receptor family in the treatment of unmet medical needs.

## Biography:



Dr. Bender earned his PhD in medicinal chemistry from the University of Michigan in 2016, where he worked on small molecules targeting the opioid system. He subsequently joined the Warren Center for Neuroscience Drug Discovery at Vanderbilt University as a postdoctoral scholar. Upon completion of his postdoctoral training, Aaron remained at Vanderbilt and is currently an Assistant Director of Medicinal Chemistry at the WCNDD. His research interests are in medicinal chemistry, particularly the development of therapeutics targeting G protein-coupled receptors, and organic methodology. Aaron is the primary author or co-author on over 30 publications, as well as several patents.