SEMINAR
MEDICINAL CHEMISTRY

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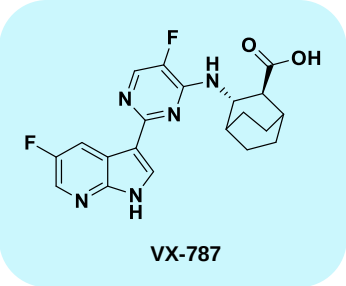
TUESDAY, September 19, 2017
12:00 NOON, CONFERENCE ROOM 323A

Discovery of a novel, first-in-class, orally bioavailable azaindole inhibitor (VX-787) of influenza PB2



VX-787

Influenza (Flu), a potentially deadly infectious disease, has imposed a substantial burden on human population in terms of morbidity and mortality. According to the Centers for Disease Control and Prevention (CDC), recent statistics suggest that, each year, 5% to 20% of the population in the United States are infected with influenza Virus during nonpandemic seasons. And there are estimated more than 200,000 hospitalizations on a yearly basis and an annual mortality rate ranging from 3,000 to 49,000 deaths. Occasionally, transmission of a new flu variant from other species to human can lead to an influenza pandemic, such as the 2009 H1N1 wine flu. In addition, the incidence of human infection by avian virus strains including the highly pathogenic H5N1 and H7N9 has potential global risk. The current standard of care (SOC) antivirals for influenza cases in the United States are the neuraminidase inhibitors oseltamivir and zanamivir. While these agents can be effective against a variety of influenza A and B, they have showed several limitations like the limited treatment window and the possibility of neuraminidase inhibitor resistance. It has been reported that oseltamivir-resistant H1N1 was prevalent during the 2008 to 2009 season and the H5N1 influenza virus has shown resistance to oseltamivir. This reinforces the critical need for new classes of antiviral agents with novel mechanisms of action. Recently, VX-787, a novel inhibitor of influenza virus replication, is reported as a promising antiviral agent for the treatment of influenza infection, as it has showed better research results, when compared with oseltamivir. This seminar will focus on how VX-787 has been successfully discovered and developed from phenotypic-assay-based screening.

Reference

Michael P. C.; Paul S. C. *et al.* Discovery of a novel, first-in-class, orally bioavailable azaindole inhibitor (VX-787) of influenza PB2. *J. Med. Chem.* **2014**, *57,* 6668-6678.

Randal A. B.; Paul S. C. *et al.* Preclinical activity of VX-787, a first-in-class, orally bioavailable inhibitor of the influenza virus polymerase PB2 subunit. *Antimicrob. Agents Chemother.* **2015**, *59,* 1569-1582.

Ervin F. The RNA polymerase of influenza A virus: mechanisms of viral transcription and replication. *Acta virologica.* **2013**, *57,* 113-122.

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