

Striving for Zero Waste API Manufacture: A Fully Biocatalytic Synthesis of MK-8591

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With 37 million people around the world infected with HIV—and this number rising by almost 2 million a year—the search for newer, better medicines to treat this disease remains an important goal. MK-8591 is a nucleoside reverse transcriptase inhibitor currently undergoing clinical trials for the treatment of HIV.

In order to achieve a world-class manufacturing route to this target that is also green and sustainable, the process chemistry team has turned to biocatalysis. Specifically, the 4'-ethynyl-2'-deoxyribose sugar portion of the molecule is prepared via a highly efficient three-enzyme cascade sequence. Another multi-enzyme reaction system is then used to append the 2-fluoroadenine base, providing an unusual solution to a challenging glycosylation reaction.

This bold endeavor has posed numerous technical challenges in the optimization of complex multi-enzyme systems, the need for directed evolution of multiple enzymes, the detection and analysis of polar chromophore-free molecules and the isolation of unstable and highly water-soluble intermediates. An overview of the ongoing development and unique challenges—and opportunities—of this unprecedented fully-enzymatic manufacturing route will be presented.

Date: Wed, Sep. 25, 2019

Time: 4:30-5:30 pm

Location: 208 Clark Hall

Students, meet the speaker over coffee and cookies in the Bennett Conference room at 3:30 pm