Development of a Biocatalytic Cascade for the Manufacture of Islatravir

The chemistry community in general and the pharmaceutical industry in particular is focused on improving our environmental impact. To minimize the amount and toxicity of the waste we generate we have turned to a number of emerging technologies, with biocatalysis being one particularly effective approach. Initial applications featured simple functional group conversions where one stoichiometric reagent can be replaced with an enzyme catalyzed alternative. While these applications were effective for reducing waste, the early improvements were incremental. Leveraging biocatalysis to enable wholesale re-imagining of manufacturing processes has lead to far more dramatic improvements in overall efficiency. In the case of islatravir, a biocatalytic cascade process has been developed which allows simple building blocks to be converted to a high-value product in a single reaction stream. This presentation will cover the development efforts which have allowed for the reduction of a 16-step process with <1% over all yield to a 4 pot enzymatic cascade process proceeding in >50% overall yield.