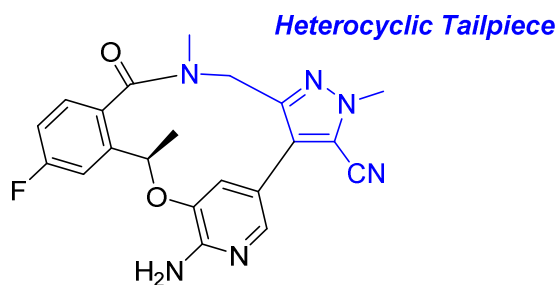


Synthesis and Conformational Studies of Small Molecule Macrocyclic Inhibitors of ALK/ROS1 – Discovery of PF-06463922

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This talk will focus on the synthesis of the chemical properties of the macrocyclic inhibitors developed for the EML4 ALK program for the treatment of NSCLC leading to the discovery of the clinical candidate PF-06463922. The work disclosed will feature (i) variations of the heterocyclic tailpiece of the molecule, and the synthetic chemistry to incorporate these into the macrocyclic ring through either macrolactamization or direct arylation, (ii) conformational studies and atropisomerism of specific macrocyclic ring systems, and (iii) optimization and scale-up of the clinical candidate including the evolution of the synthesis of the pyrazole tailpiece.



PF-06463922