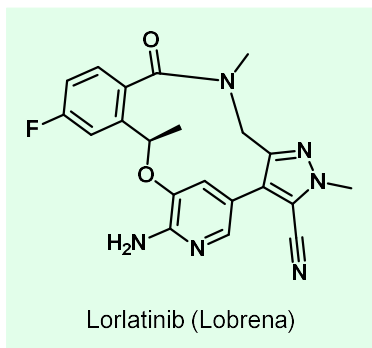
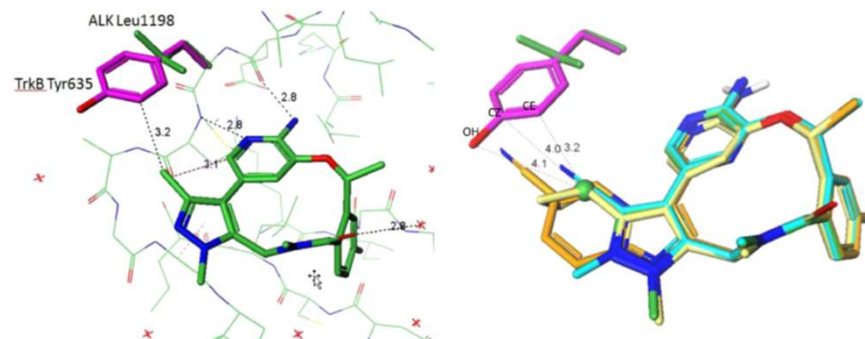


DOTW: Lorlatinib

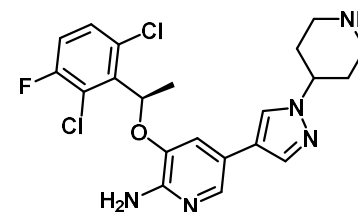
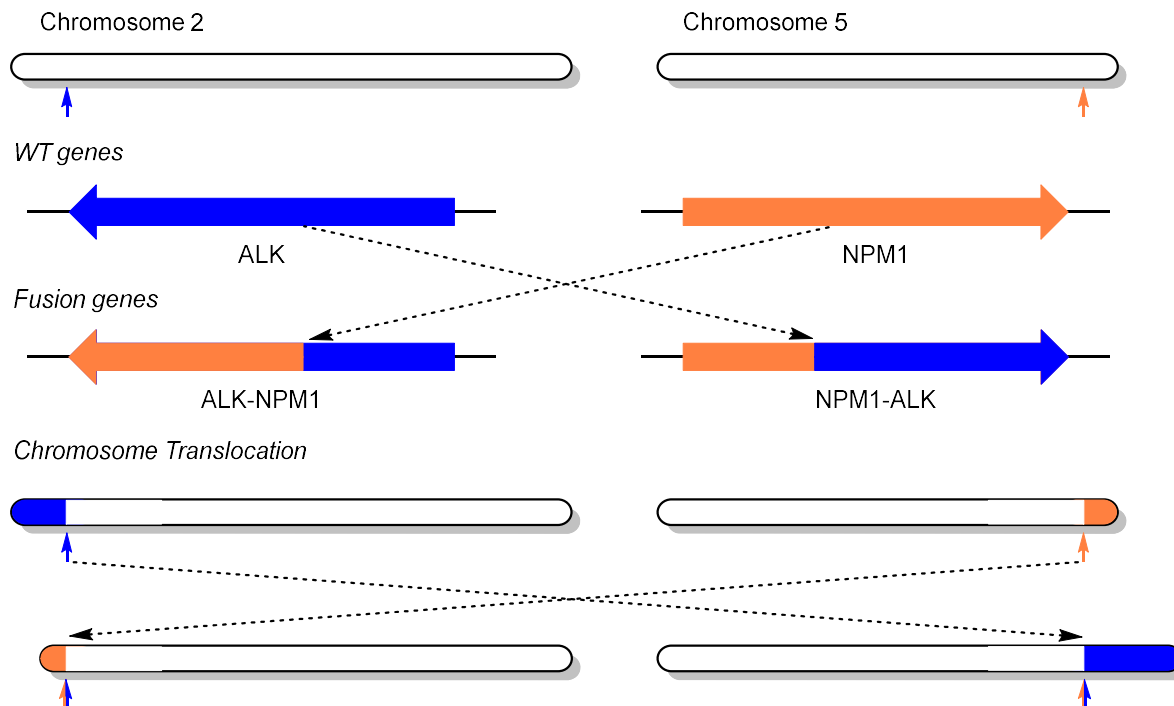


- Potent inhibitor of the ALK-ROS1 fusion protein
- 2018 FDA approval for ALK+ non-small cell lung cancer (NSCLC)
- Given "breakthrough therapy designation" by the FDA



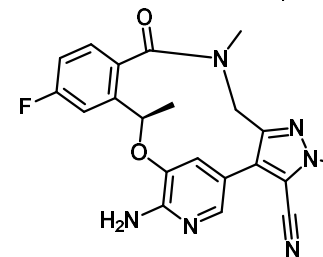
p(2;5)(p32;q35) ALK-NPM Translocation

As an example of translocation, here is the schematic for the ALK-NPM1 fusion kinase.



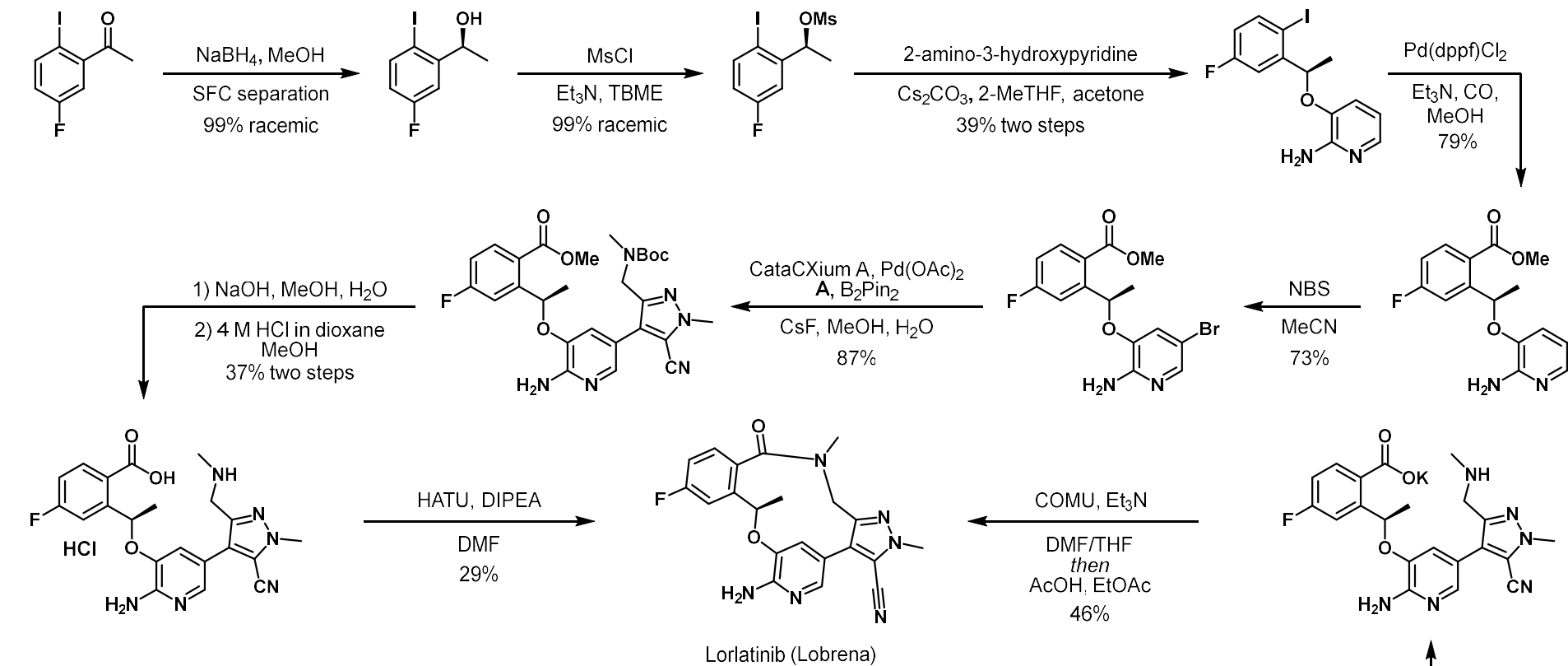
Optimization of lipophilic efficiency and molecular weight were targeted.

Macrocyclic structures found to fit the active site of the fusion protein to enforce binding conformation.



J. Med. Chem. **2014**, *57*, 4720.

Discovery Route



First Scale-Up Process Route

