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Design, synthesis and biological evaluation of 7*H*-pyrrolo[2,3-*d*]pyrimidin-4-amine derivatives as selective Btk inhibitors with improved pharmacokinetic properties for the treatment of rheumatoid arthritis

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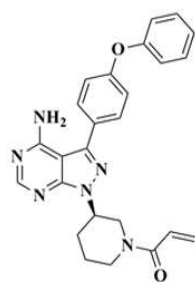
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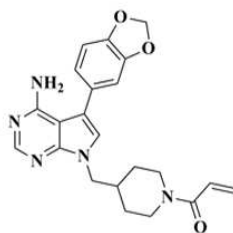
**Ibrutinib**Btk IC_{50} = 0.81 nMhERG IC_{50} = 0.97 μ M

ClogP = 4.07

aqueous solubility < 0.01 mg/ml

F % in rats: 18-23%

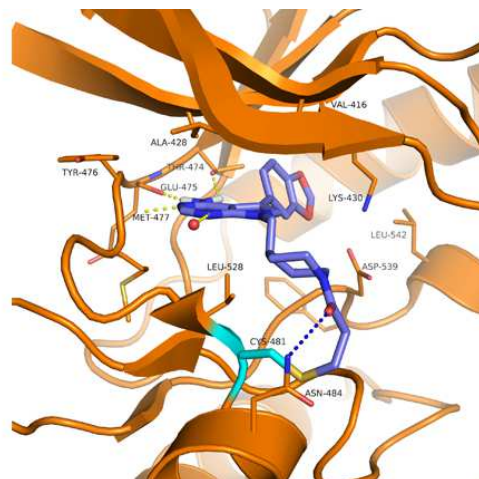
structure-based design
PK studies and preliminary
druglikeness evaluation

**B16**Btk IC_{50} = 21.70 nMhERG IC_{50} = 11.10 μ M

ClogP = 2.53

aqueous solubility \approx 0.1 mg/ml

F% in SD rat: 49.15%



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