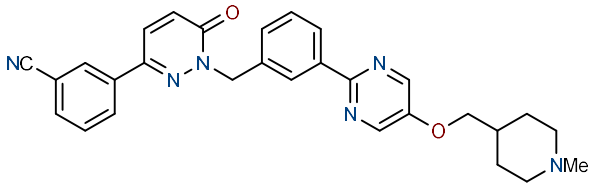
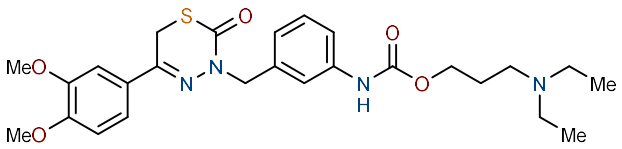
Tepotinib (Tepmetko)

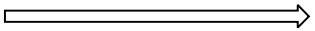
MERCK

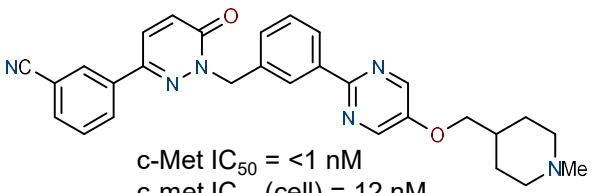


- Approved in February 2021 (granted breakthrough therapy in late 2019)
- First, once-daily oral MET inhibitor for patients with metastatic NSCLC with *Met*ex14 skipping
- MET (mesenchymal-epithelial transition factor) is a receptor tyrosine kinase
  - Activated by binding of hepatocyte growth factor (HGF)
  - Overexpressed or mutated in many tumor cells that has a role in tumor cell proliferation, survival, invasion, and mobilization
- Tepotinib is a tyrosine kinase inhibitor
  - Selectively binds to MET and disrupts onocogenic MET receptor signaling
  - Results in cell death in tumor cells overexpressing or expressing constitutively activated MET protein

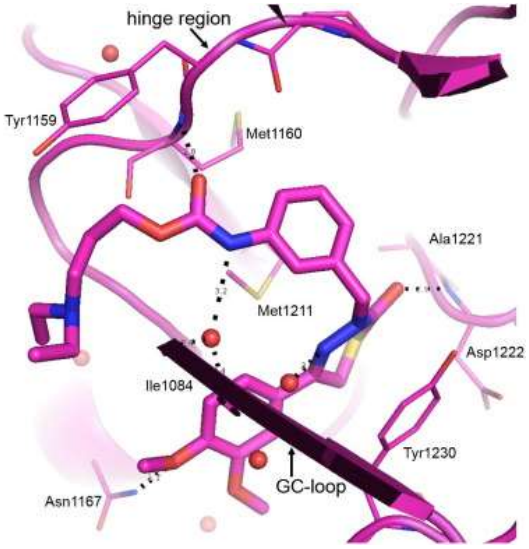


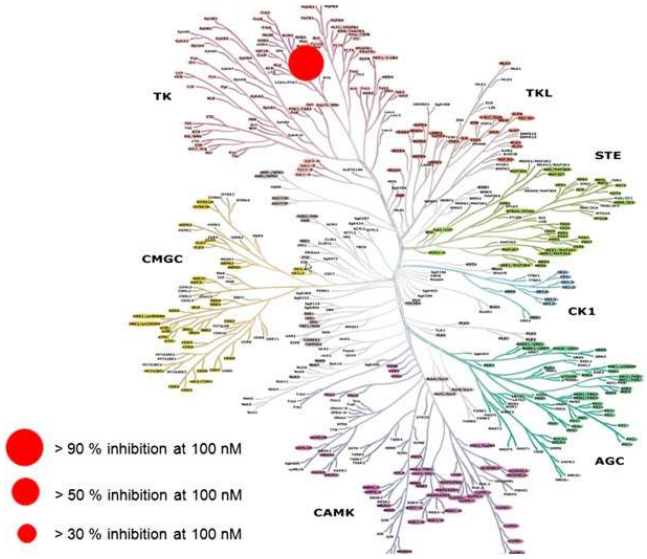
c-Met IC_{50} = 400 nM
c-met IC_{50} (cell) = 1100 nM

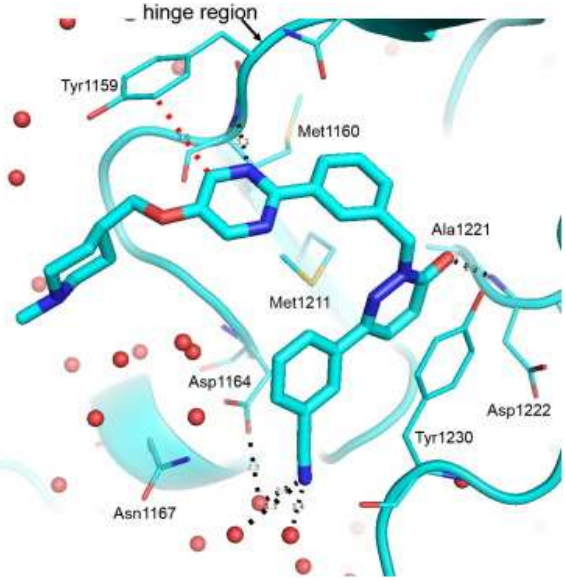




c-Met IC_{50} = <1 nM
c-met IC_{50} (cell) = 12 nM







Markham, A. *Drugs* **2020**, *80*, 829. https://doi.org/10.1007/s40265-020-01317-9. Dorsch, D. *Bioorg. Med. Chem. Lett.* **2015**, *7*, 1597. https://doi.org/10.1016/j.bmcl.2015.02.002

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Discovery Route: