New biologically active compounds based on pyrazolo[1,5-*a*]pyrimidine and its isosteres

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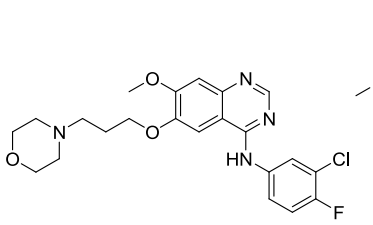
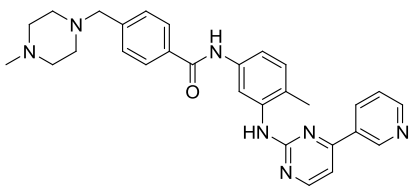
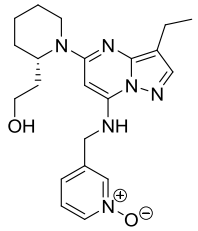
Since protein kinases play dominant roles in regulation of a wide range of cellular functions including initiation of cancer cells, tumor progression, and the development of metastatic diseases, many of them represent attractive targets for modern medicine. Some of these kinases have been targeted by modern oncology therapeutics (protein kinase inhibitors) for treatment of cancer (e.g. Gefitinib and Imatinib), and many other inhibitors are under clinical trials (e.g. Dinaciclib).[1]



Gefitinib (Iressa^{TM})



Imatinib (Gleevec^{TM})

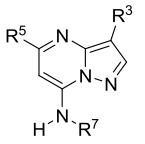


Dinaciclib (SCH 727965)

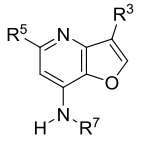
Because the majority of developed kinase inhibitors bind the kinase active site in the same manner as ATP, their scaffolds are often based on heterocycles (in many cases 5,6- and 6,6-condensed heterocycles) that imitate the adenine moiety and form highly analogous interactions with the kinase active site.[2]

Among a number of 5,6-condensed heterocyclic systems the pyrazolo[1,5-*a*]pyrimidine scaffold proved to be particularly suitable for development of protein kinase inhibitors. Numerous small organic molecules with pyrazolo[1,5-*a*]pyrimidine scaffold (depicted below) were designed and developed targeting different protein kinases.[3]

We have developed small libraries of kinase inhibitors with two different central pharmacophores: pyrazolo[1,5-*a*]pyrimidines and furo[3,2-*b*]pyridines.



pyrazolo[1,5-*a*]pyrimidine



furo[3,2-*b*]pyridine

[1] Thurston, D. E. *Chemistry and pharmacology of anticancer drugs*; CRC Press/Taylor & Francis: Boca Raton, 2007.

[2] (a) Roskoski, R. *Pharmacol. Res.* **2016**, *103*, 26. (b) Maddox, S. et al. *Future Med. Chem.* **2016**, *8* (3), 241.

[3] (a) Dwyer, M. P. et al. *Bioorg. Med. Chem. Lett.* **2011**, *21* (1), 467. (b) Le Roux, J. et al. *Bioorg. Med. Chem. Lett.* **2016**, *26* (2), 454.