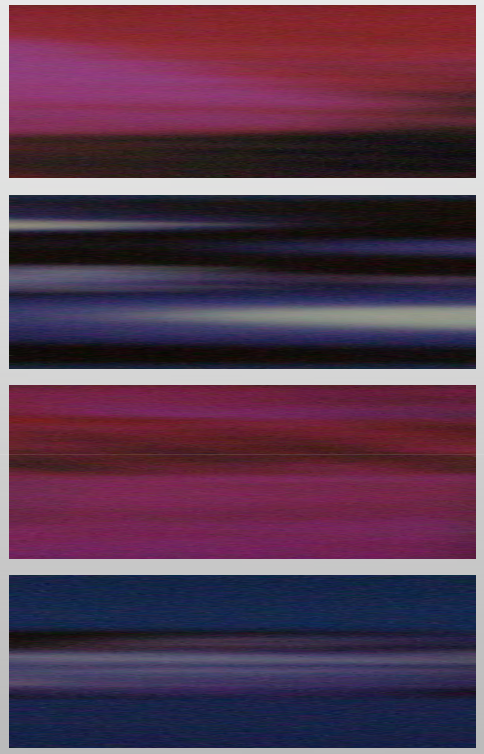
CHEM-X INFINITY



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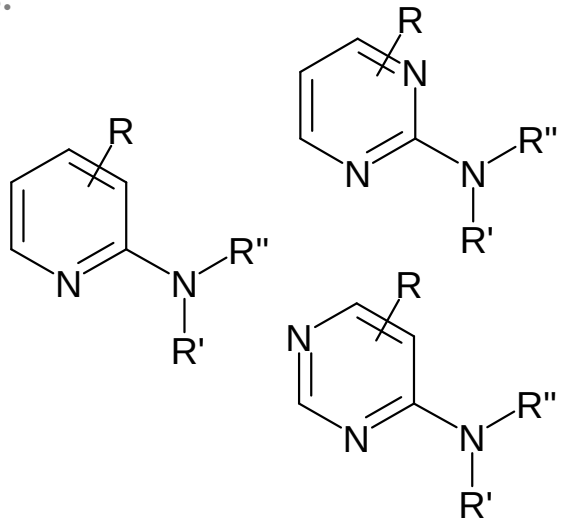
EXPLORA2

AMINOPYRIDINES & AMINOPYRIMIDINES

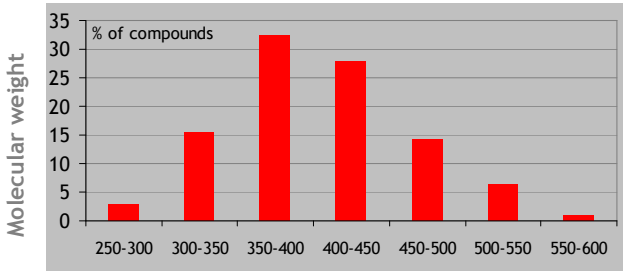
The scaffolds:

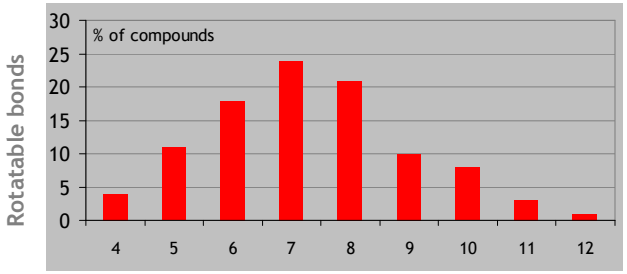


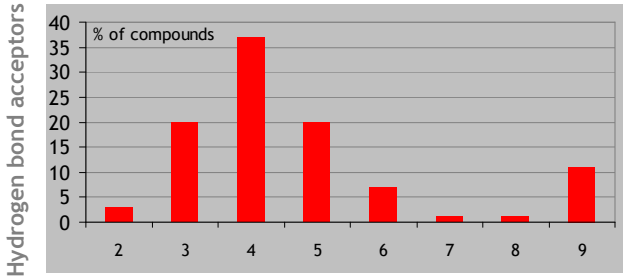
Bullet points:

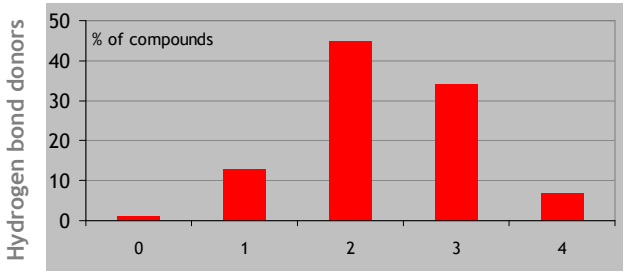
* highly diverse exploration of aminopyridines, aminopyrimidines and purine-like structures
* privileged structures for kinase and phosphodiesterase inhibitors, GPCR agonists and antagonists
* high diversity of potential targets
* scaffolds related to interesting leads for the exploration of the "kinome" and to natural derivatives with complex pharmacology
* sophisticated production process increasing diversity
* 700+ compounds based on 48 intermediates
* cherry-picking and custom format available

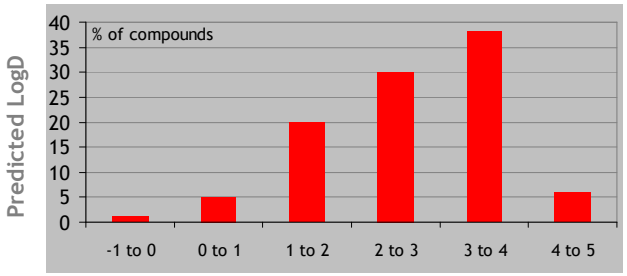
CHARACTERISTIC CHARTS

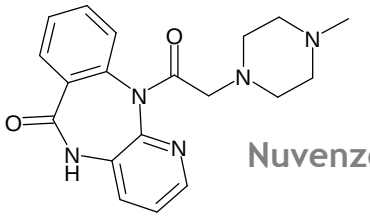




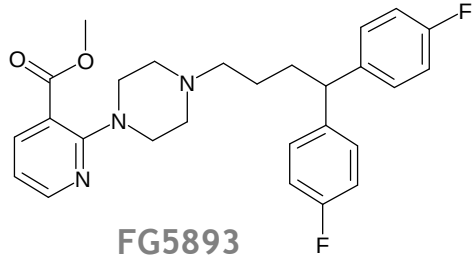




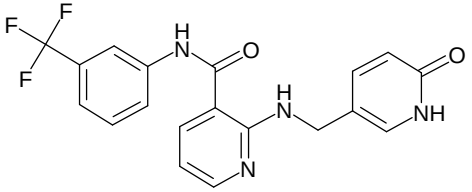




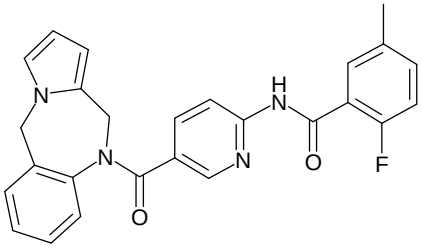
Nuvenzepine



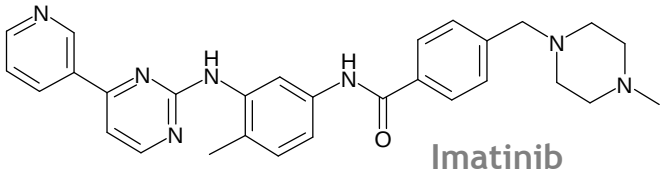
FG5893



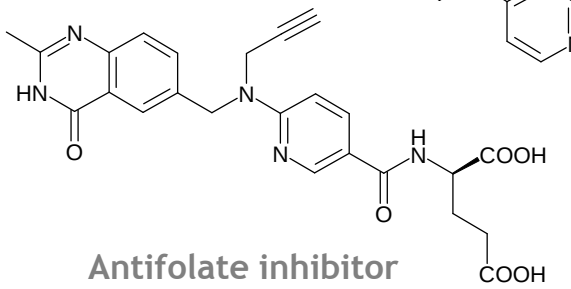
VEGFR kinase inhibitor



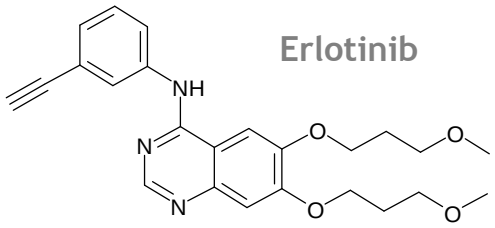
Vasopressin antagonist



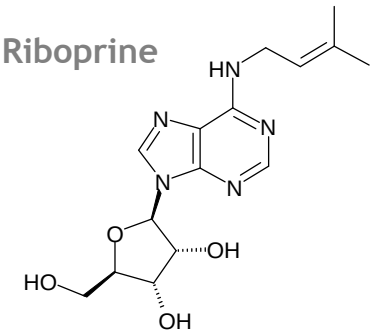
Imatinib



Antifolate inhibitor



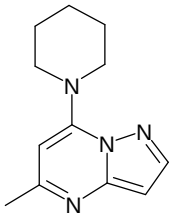
Erlotinib



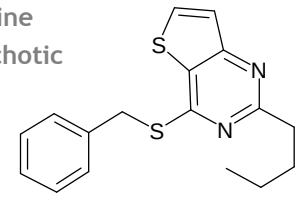
Riboprine

The aminopyridine fragment is present in several marketed and developed drugs. Cyclic series in pyridobenzodiazepinones produced M_1/M_3 antagonists[1] as nuvenzepine and rispenzepine or inhibitors of gastric secretion (pirenzepine)[2]. The fragment is also present in neviparine which is used for the treatment of HIV. FG5893 was studied for the treatment of alcoholic dependance[3]. More recently, 2-nicotinic benzamide was patented as potent and selective VEGFR kinase inhibitor[4]. The related 6-amino nicotinic amid is present as a linker to improve pharmacokinetic properties of a series of vasopressin antagonists[5] and in a series of antifolate inhibitors[6].

Aminopyrimidine and purine building blocks are also highly represented in natural products and in synthetic drugs. One of the most recent and exciting field for the development of their analogues is kinase inhibition. The first three kinase inhibitors to reach the market are N-aryl pyrimidines or quinazolines: imatinib in 2001, gefitinib in 2003 and erlotinib in 2004. N-aryl purines, as purvanalol A[7], and simple 2,4 and 4,6 diarylpyrimidines[8] are specific inhibitors of CDKs. Adenosine derivatives are still a very active field of research. For example riboprine has been developed as an anti-neoplastic agent.This family has also applications as phosphodiesterase inhibitors like pyrazolo[1,5-a]pyrimidine and thieno[3,2-d]pyrimidine[9,10].Finally, the pyrimidine-2-piperazine scaffold has been used in many GPCR and CNS acting drugs, as the anxiolytic buspirone or atypical antipsychotic agents with strong sigma interactions[11].



PDE inhibitors



The Explora 2 library has thus applications in many medicinal chemistry fields and is a valuable tool for the exploration of the promiscuous scaffolds aminopiridine and aminopyrimidine.

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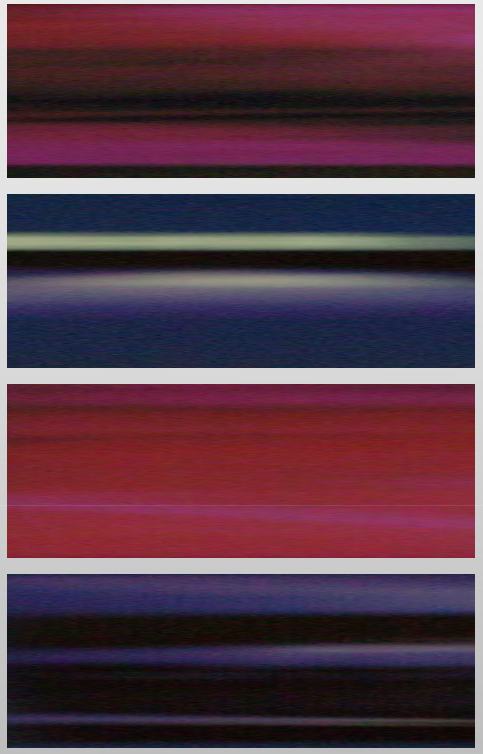

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[2] *Ophtalmic Physiol. Opt.*, **1995,** *15,* 351
[3] *Pharmacol. Bioc. Behav.*, **1996,** *53,* 33
[4] *Eur. J. Cancer,* **2004,** *2,* 172
[5] *Bioorg. Med. Chem. Lett.*, **1999,** *9,* 737
[6] *J. Med. Chem.*, **1996,** *39,* 695
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[9] *J. Med. Chem.*, **1998,** *8,* 4021
[10] *J. Med. Chem.*, **1982,** *25,* 235
[11] *J. Med. Chem.*, **1988,** *31,* 618