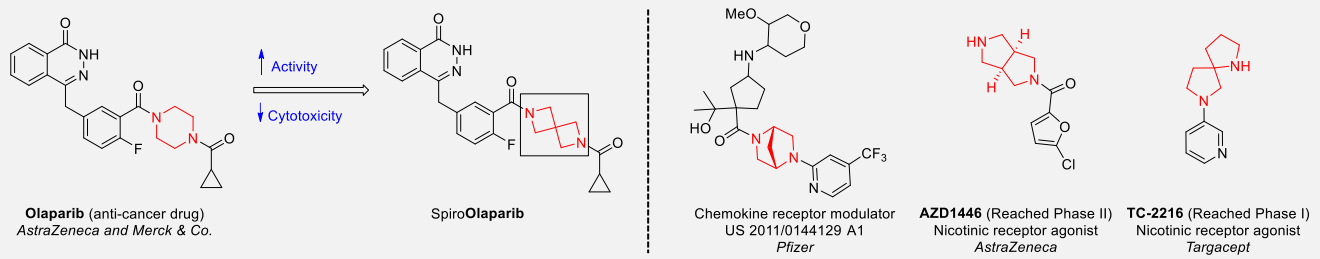
Piperazine Bioisosteres for Drug Design

Introduction

More than 100 FDA-approved drugs contain the piperazine moiety.[1] Piperazine-based analogues may advantageously alter important pharmacokinetic properties when grafted onto molecular scaffolds.[2-5] In 2018, chemists showed that replacing a piperazine ring in the drug Olaparib with the spirodiamine analogue beneficially affected activity and reduced cytotoxicity of the parent compound.[6] Herein we have designed and synthesized a library of piperazine analogues for drug design.



Olaparib (anti-cancer drug)
AstraZeneca and Merck & Co.

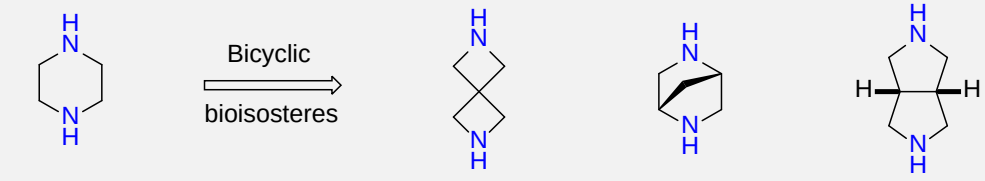
SpiroOlaparib

Chemokine receptor modulator
US 2011/0144129 A1
Pfizer

AZD1446 (Reached Phase II)
Nicotinic receptor agonist
AstraZeneca

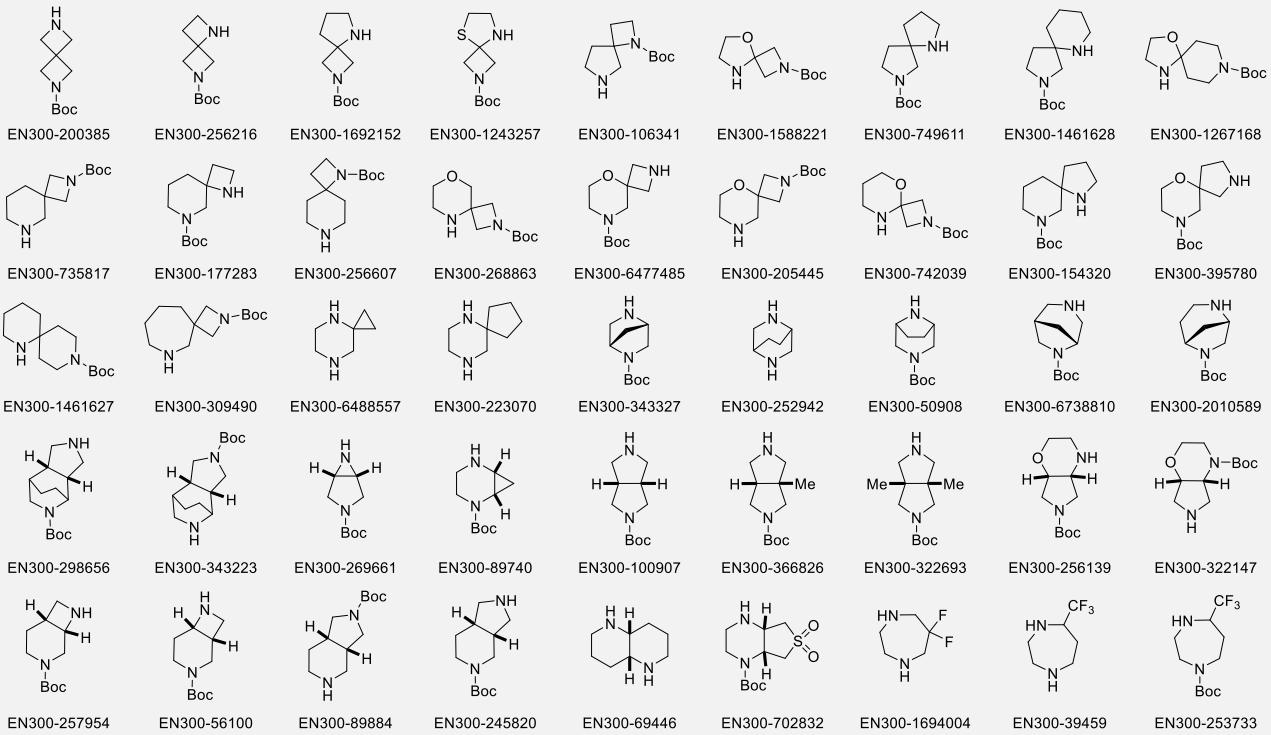
TC-2216 (Reached Phase I)
Nicotinic receptor agonist
Targacept

Design



Piperazine | Spiro | Bridged | Fused

We offer >100 unique piperazine analogues on a 5-50 g scale from stock.



EN300-200385 | EN300-256216 | EN300-1692152 | EN300-1243257 | EN300-106341 | EN300-1588221 | EN300-749611 | EN300-1461628 | EN300-1267168

EN300-735817 | EN300-177283 | EN300-256607 | EN300-268863 | EN300-6477485 | EN300-205445 | EN300-742039 | EN300-154320 | EN300-395780

EN300-1461627 | EN300-309490 | EN300-6488557 | EN300-223070 | EN300-343327 | EN300-252942 | EN300-50908 | EN300-6738810 | EN300-2010589

EN300-298656 | EN300-343223 | EN300-269661 | EN300-89740 | EN300-100907 | EN300-366826 | EN300-322693 | EN300-256139 | EN300-322147

EN300-257954 | EN300-56100 | EN300-89884 | EN300-245820 | EN300-69446 | EN300-702832 | EN300-1694004 | EN300-39459 | EN300-253733

References

1. www.drugbank.ca
2. J. A. Burkhard et al. *ANIE.* **2010**, *49*, 3524.
3. B. Chalyk et al. *Chem. Eur. J.* **2017**, *23*, 16782.
4. B. Chalyk et al. *Eur. J. Org. Chem.* **2017**, *31*, 4530.
5. A. Kirichok et al. *Chem. Eur. J.* **2018**, *24*, 5444.
6. S. W. Reilly et al. *J. Med. Chem.* **2018**, *61*, 5367.