

Antifungal library

Assessing the Landscape

Molecules in this set are based on the literature analysis of both targets and their respective ligands, specifically 4K known molecules with reported anti-bacterial and anti-fungal activities. In order to assemble the set, we used a) Kohonen self-organizing map, b) pharmacophore analysis, and c) bioisosteric replacement in order to select initial library of ca. 50,000 drug-like molecule. These were further prioritized based on relevance to the target/ligand of interest, IP potential, Lipinski-rule-of-five parameters and synthetic feasibility to yield final set of 6,000 molecules.

Antifungal library

Assessing the Landscape

Launched Drugs - Yes

Development Candidates - Yes

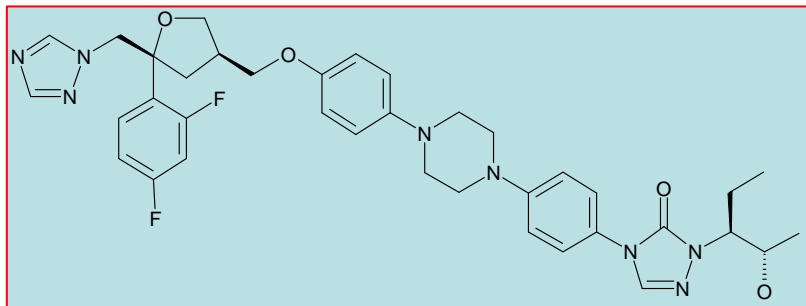
Compounds in Preclinical Development - Yes

In vivo model - No

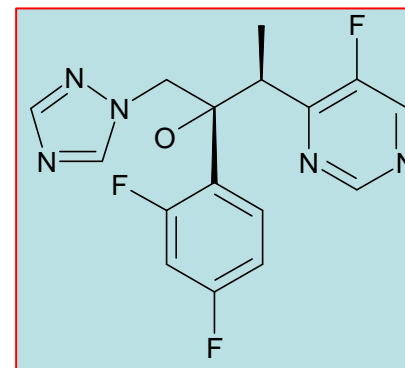
Lead Compounds - Yes

Antifungal library

Assessing the Landscape



**Posaconazole, Launched-2005,
Schering-Plough**



**Voriconazole, Launched-2002,
Pfizer**

Target:

Lanosterol 14 α -demethylase Inhibitors

**Therapeutic
Group:**

Antifungal Agents

Antifungal Agents

**Under Active
Development:**

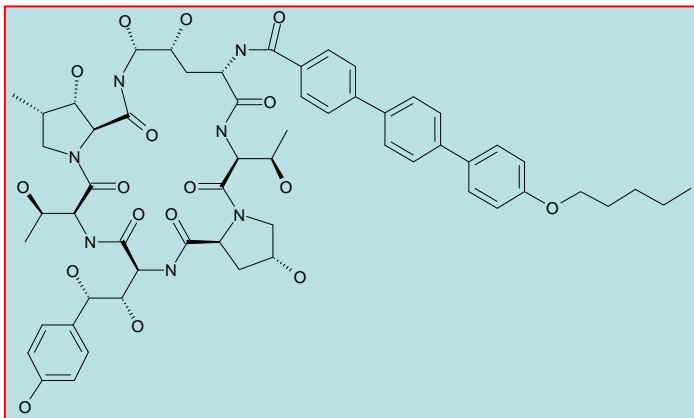
YES

YES

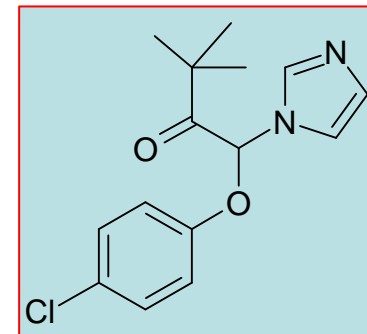
1. *Drug Data Rep.* 2005, 27(11): 1028
2. *Drug Data Rep.* 2002, 24(10): 918

Antifungal library

Assessing the Landscape



Ecalta, Launched-2006, Pfizer



Climbazole, Launched, Bayer

Target: 1,3-beta-Glucan Synthase Inhibitors

Enzyme Inducers

Therapeutic Group: Antifungal Agents

Antifungal Agents
Dermatologic Drugs

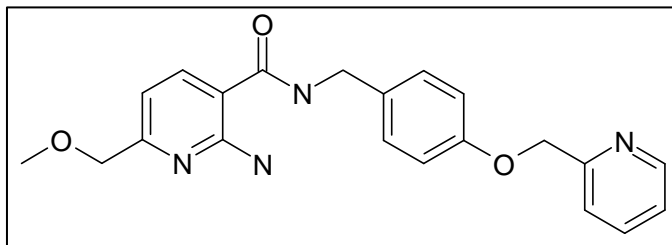
Under Active Development: YES

NO

1. *Drug Data Rep.* 2006, 28(6): 543
2. *Kobayashi, Y.; et al. Biol. Pharm. Bull.* 2002, 25(1): 53

New available libraries of analogues

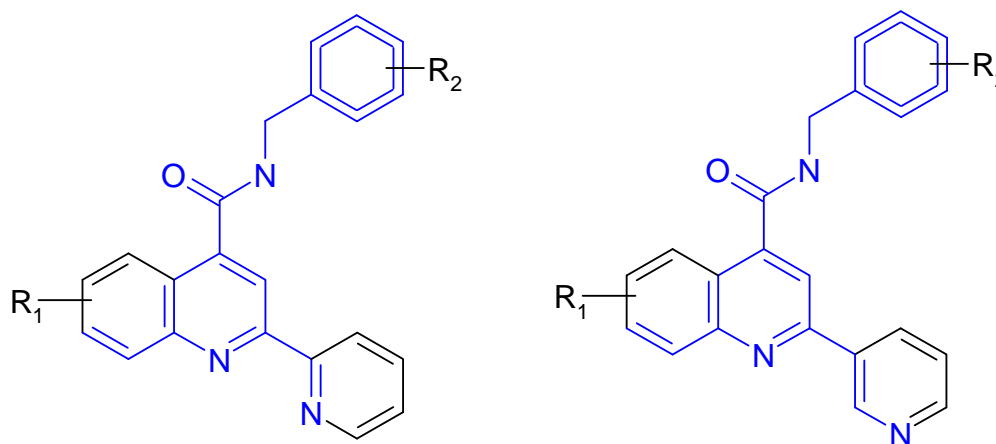
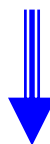
Bioisosteric core replacement
More flexibility
More diversity
More interesting heterocyclic system



Diverse substituents looking at donating/withdrawing properties, H-bond acceptor/donors as well lipophylicity and solubility

Antifungal Agents, Eisai

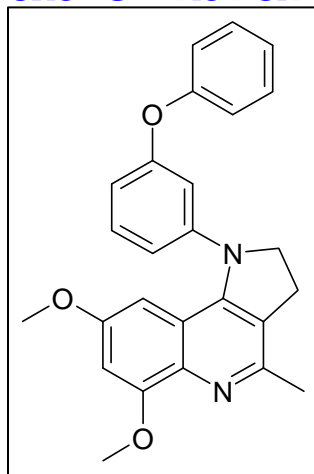
1. *Drug Data Rep.* 2005, 27(7): 651
2. Nakamoto, K.; et al. *WO 2005033079* Apr 14, 2005



~ 400 compounds

New available libraries of analogues

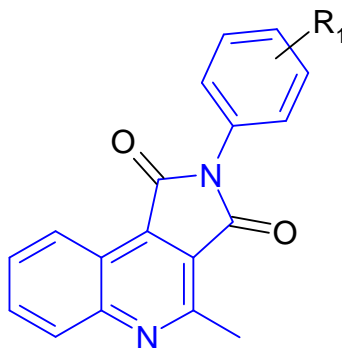
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Diverse substituents looking at donating/withdrawing properties, H-bond acceptor/donors as well lipophylicity and solubility

Antifungal Agents, Antibacterial Drugs,
Helperby Therapeutics

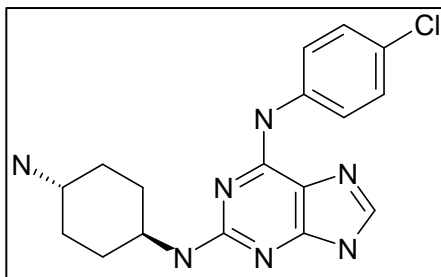
1. Beck, P.H.; et al. WO 2007054693 May 18, 2007



~ 60 compounds

New available libraries of analogues

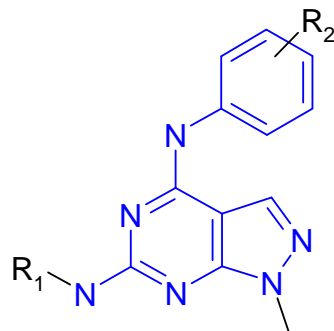
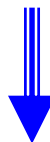
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Diverse substituents looking at donating/withdrawing properties, H-bond acceptor/donors as well lipophylicity and solubility

Antifungal Agents, sanofi-aventis

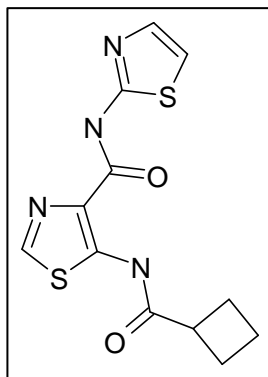
1. *Drug Data Rep.* 2002, 24(9): 820
2. Haesslein, J.-L., Bordon-Pallier, F. WO 2002051843 Jul 4, 2002



~ 300 compounds

New available libraries of analogues

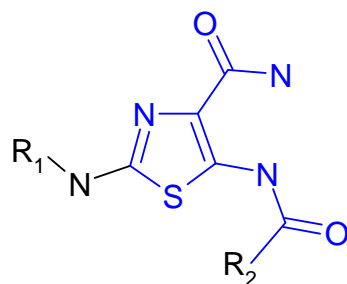
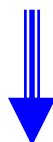
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Diverse substituents looking at donating/withdrawing properties, H-bond acceptor/donors as well lipophylicity and solubility

Antifungal Agents, Antibacterial Drugs,
University of Kansas

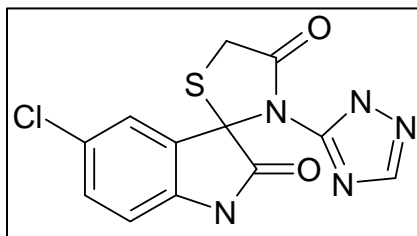
1. Cui, Y.-M.; et al. *Bioorg. Med. Chem. Lett.*
2005, 15(16): 3732



~ 20 compounds

New available libraries of analogues

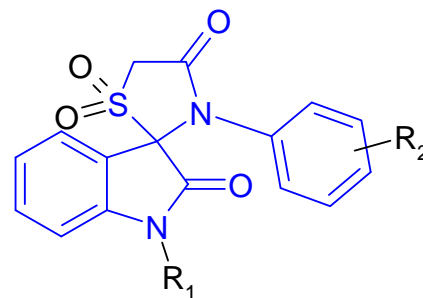
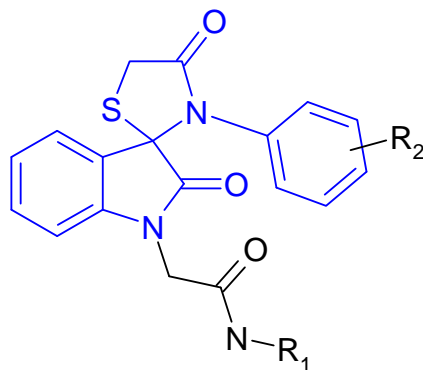
Bioisosteric core replacement
More flexibility
More diversity
More interesting heterocyclic system



Diverse substituents looking at donating/withdrawing properties, H-bond acceptor/donors as well lipophylicity and solubility

Antifungal Agents, Universite Paris-Sud

1. Dandia, A.; et al. *Bioorg. Med. Chem.* 2006, 14(7): 2409



~ 400 compounds

Summary

Antifungal library

ChemDiv prepares most diverse set of over 6000 compounds based on active prototypes and their bioisosterically replaced cores.

The database is represented by 115 templates