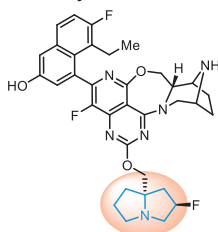


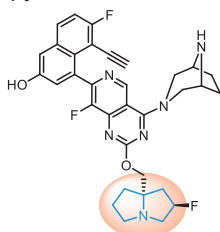
# Pyrrolizidines for Drug Design

## Introduction

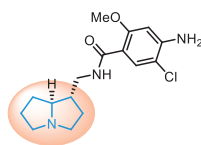
Pyrrolizidine is a tertiary amine found in the structures of natural alkaloids<sup>1</sup> and bioactive molecules.<sup>2-4</sup> Notably, it is present in various serotonin receptor agonists/antagonists<sup>2</sup> and KRAS mutant inhibitors undergoing clinical trials for anticancer therapy.<sup>3,4</sup> For example, in the structure of MRTX1133 (Phase 1 trials), the pyrrolizidine moiety forms a nonclassical hydrogen bond with Glu62 residue when binding to the cancerogenic KRAS protein, endowing the drug with better cellular potency and selectivity.<sup>3</sup> Discover our set of pyrrolizidine derivatives, homologues, and analogues!



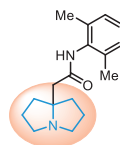
**HRS-4642**  
inhibitor of KRAS G12D  
Phase 2 trials  
Shanghai Zion Pharma



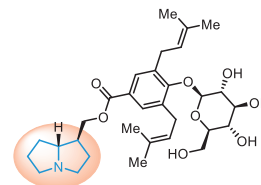
**MRTX1133**  
inhibitor of KRAS G12D  
Phase 1 trials  
Mirati Ther



**SC-53116**  
agonist of serotonin 5-HT<sub>4</sub> receptor  
Pfizer



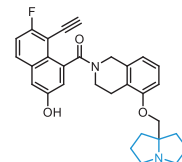
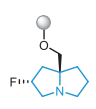
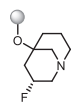
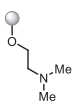
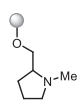
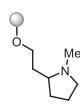
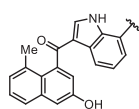
**Pilsicainide**  
antiarrhythmic agent  
approved in Japan  
Suntory



**Auriculine**  
liparic alkaloid  
Nagoya University

## Case study

### KRAS G12D inhibition



### pan-KRAS inhibitor

WT IC<sub>50</sub> 0.47  $\mu$ M  
G12V IC<sub>50</sub> 0.15  $\mu$ M  
G12D IC<sub>50</sub> 0.37  $\mu$ M  
G12C IC<sub>50</sub> 0.14  $\mu$ M  
G12R IC<sub>50</sub> 0.24  $\mu$ M  
G13D IC<sub>50</sub> 2.0  $\mu$ M

Insilico Medicine

ACS Med. Chem. Lett. 2025, 16, 1282

**We offer:** over 100 pyrrolizidine analogues from stock on gram scale.



EN300-190383



EN300-188244



EN300-7771057



EN300-26675672



EN300-112910



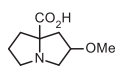
EN300-7384368



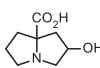
EN300-6489956



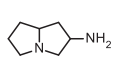
EN300-188008



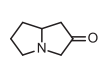
EN300-2394701



EN300-27755241



EN300-2492349



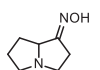
EN300-1177720



EN300-7727888



EN300-46764704



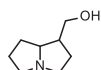
EN300-2496241



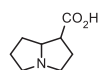
EN300-40523



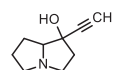
EN300-5092451



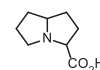
EN300-7698939



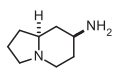
EN300-1693890



EN300-28253544



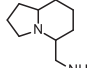
EN300-25388194



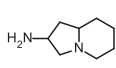
EN300-52652580



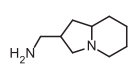
EN300-27719395



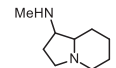
EN300-249927



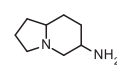
EN300-76687



EN300-80641



EN300-2993116



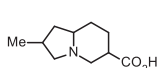
EN300-37391513



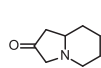
EN300-7112686



EN300-6480194



EN300-746578



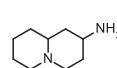
EN300-118485



EN300-6477816



EN300-7459441



EN300-343198

## References

1. J. Robertson & K. Stevens. *Nat. Prod. Rep.* **2014**, 31, 1721.
2. D. Becker et al. *J. Med. Chem.* **2006**, 49, 1125.

3. X. Wang et al. *J. Med. Chem.* **2022**, 65, 3123.
4. R. Kargbo. *ACS Med. Chem. Lett.* **2023**, 14, 1041.



Search & Buy on-line at **EnamineStore.com**  
Look for more at Chem-Space.com

BB@enamine.net, www.enamine.net

