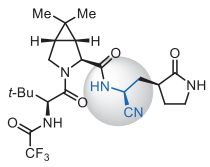
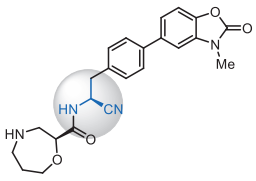
Aminonitrile Warheads for Cysteine Binding

Introduction

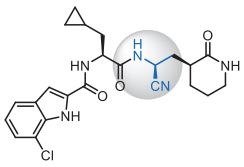
Warheads are reactive moieties that enable covalent binding to target enzymes. α-Aminonitriles are particularly effective for targeting cysteine residues, as they minimize off-target interactions with intracellular glutathione. Recently, aminonitrile-based inhibitors have been developed for dipeptidyl peptidase 1 (brensocatib)[1] and the SARS-CoV-2 main protease (nirmatrelvir, simnotrelvir, ibuzatrelvir).[2-4] Explore our aminonitriles for your cysteine-targeting applications!



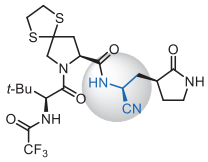
Nirmatrelvir (**PF-07321332**)
inhibitor of SARS-CoV2 main protease
FDA approved 2023
Prizer



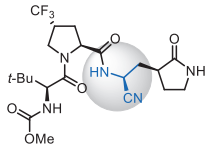
Brensocatib (**AZD7986**)
inhibitor of dipeptidyl peptidase 1
Phase 2 trials ongoing
AstraZeneca



Pomotrelvir (**PBI-0451**)
inhibitor of SARS-CoV2 main protease
Phase 2 trials 2023
Pardes Biosciences

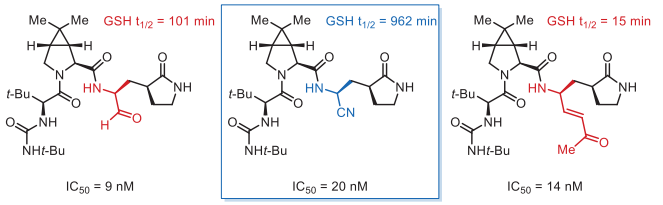


Simnotrelvir (SIM0417)
inhibitor of SARS-CoV2 main protease
approved in China in 2024
Simcere Pharmaceutical

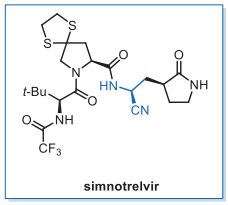


Ibuzatrelvir (**PF-07817883**)
inhibitor of SARS-CoV2 main protease
Phase 3 trials ongoing
Pfizer

Case study

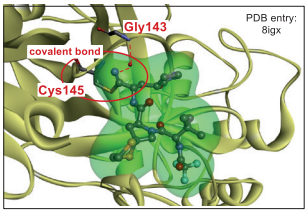


Nat. Commun. **2023**, *14*, 6463 GSH = glutathione

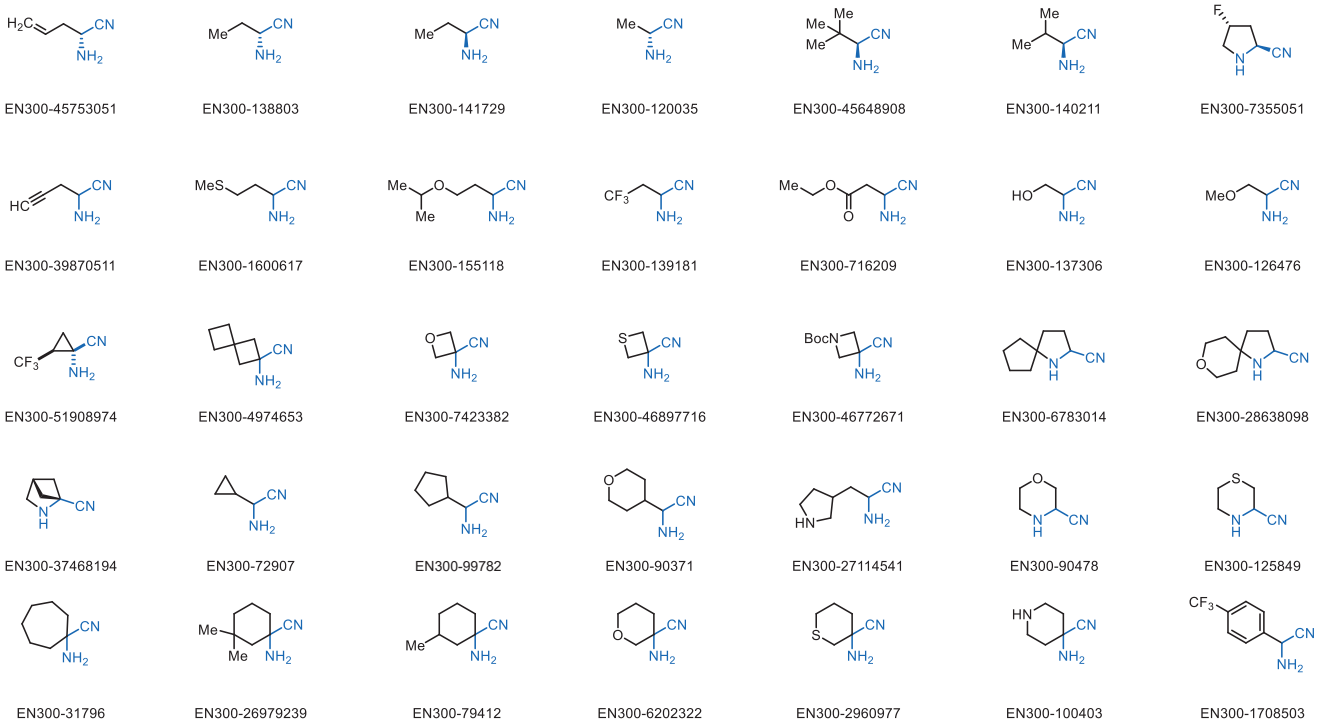


approved in 2023 against COVID-19 in China

SARS-CoV2 main protease with simnotrelvir



We offer: over 100 α-aminonitriles from stock on 5-10 gram scale.



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EN300-51908974 EN300-4974653 EN300-7423382 EN300-46897716 EN300-46772671 EN300-6783014 EN300-28638098

EN300-37468194 EN300-72907 EN300-99782 EN300-90371 EN300-27114541 EN300-90478 EN300-125849

EN300-31796 EN300-26979239 EN300-79412 EN300-6202322 EN300-2960977 EN300-100403 EN300-1708503

References

1. K. Doyle et al. *J. Med. Chem.* **2016**, *59*, 9457.
2. B. Cotrim et al. *Aust. J. Chem.* **2022**, *75*, 487.
3. X. Jiang et al. *Nat. Commun.* **2023**, *14*, 6463.
4. C. Allerton et al. *J. Med. Chem.* **2024**, *67*, 13550.

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