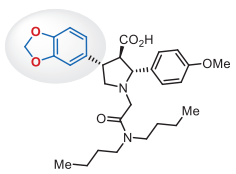
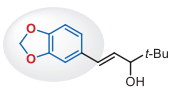
Aza Analogues of Benzodioxole

Introduction

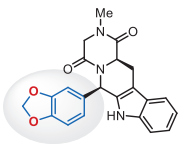
The benzodioxole and difluoro-benzodioxole motifs are important structural elements found in numerous recently developed drugs. Introducing heteroatoms into this scaffold increases polarity, which enhances solubility, reduces lipophilicity, and improves target binding by enabling interactions with polar protein side chains.[1] Notable applications of the aza-benzodioxole motif include AZD-0424, a tyrosine kinase inhibitor developed by *AstraZeneca* (Phase 1 trials),[2] and JNJ-67569762, a β-secretase inhibitor developed by *Janssen*.[3]



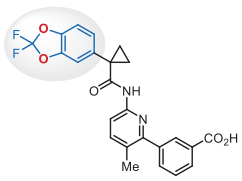
Atrasentan (**ABT-627**)
selective antagonist of endothelin A receptor
FDA approved 2025
Abbott/Novartis



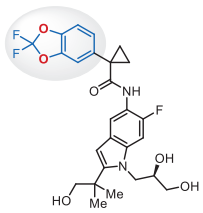
Stiripentol (**BCX-2600**)
allosteric modulator of GABA receptors
FDA approved 2018
Biocodex



Tadalafil (**IC-351**)
inhibitor of phosphodiesterase 5
FDA approved 2003
Glaxo//Eli Lilly

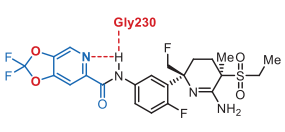


Lumacaftor (**VX-809**)
molecular chaperone for ΔPhe508 CFTR
FDA approved 2015
Vertex



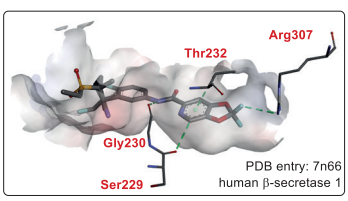
Tezacaftor (**VX-661**)
molecular chaperone for ΔPhe508 CFTR
FDA approved 2019
Vertex

Case studies

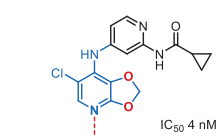


IC_{50} 2.7 nM

JNJ-67569762
β-secretase Inhibitor
Janssen



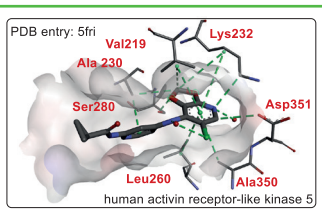
J. Med. Chem. **2021**, *64*, 14175



IC_{50} 4 nM

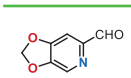
Asp351 ----- Lys232

inhibitor of activin receptor-like kinase 1
AstraZeneca



Med. Chem. Commun. **2016**, *7*, 1204

We offer: over 50 aza-benzodioxoles from stock on 5-10 gram scale.



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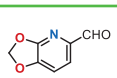

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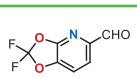

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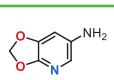

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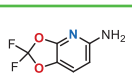

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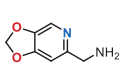

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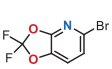

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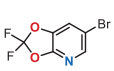

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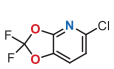

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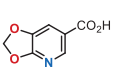

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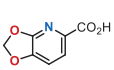

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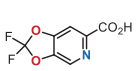

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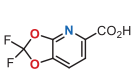

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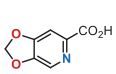

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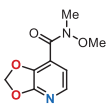

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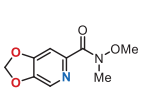

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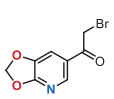

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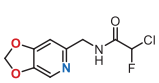

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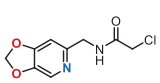

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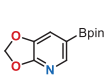

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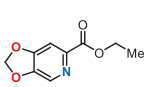

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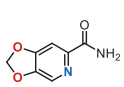

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References

1. F. Goldberg et al. *Med. Chem. Commun.* **2016**, *543*, 733.
2. L. Sun et al. *Eur. J. Med. Chem.* **2024**, *193*, 106678.
3. F. Rombouts et al. J. *Med. Chem.* **2021**, *64*, 14175.

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