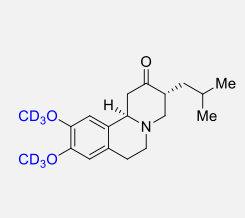
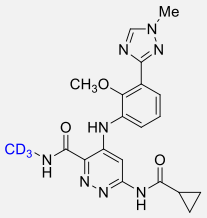
Deuterium-Containing Building Blocks for Drug Design

Introduction

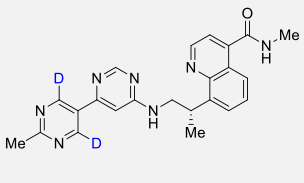
Selective incorporation of deuterium into organic molecules can profoundly alter their physical, chemical and biological properties. Compared to hydrogen, deuterium displays a smaller molar volume (by 0.140 cm^3/mol per atom), is less lipophilic (Δ logPoct = - 0.006) and might display a slightly different pKa. More importantly, C-D bonds are shorter (by 0.005 Å) and at times more stable to oxidative processes. This helps protect deuterated compounds from enzymatic degradation in the liver, increasing the compound's half-life.[1-4] In this context, Enamine offers a library of deuterium-containing building blocks for drug design.



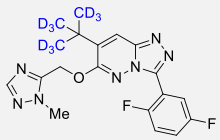
1st approved drug Deutetrabenazine
Treatment of choreas associated with Huntington's disease
Teva Pharmaceuticals



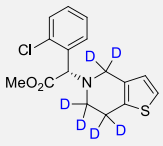
Deucravacitinib (BMS-986165)
Inhibitor of Tyk2 (Phase III)
Bristol Myers Squibb



VX-984
Selective DNA-PK inhibitor (Phase I)
Oncotarget **2018**, *9*, 25833.

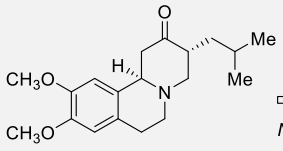


CTP-354
GABA-A modulator (Phase I)
Concert Pharmaceuticals



d_6-Clopidogrel
Inhibitory activity against ADP-induced platelet aggregation
ACS Med. Chem. Lett. **2013**, *4*, 349.

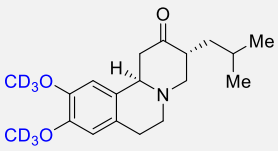
Design



drug Tetrabenazine

metabolic stability

Nat. Biotechnol. **2017**, *35*, 493.



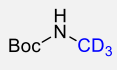
drug Deutetrabenazine
(Austedo)
Teva Pharmaceuticals

Advantages of D-compounds:

Novel chemical space

(patent-free)

We offer deuterium-containing building blocks from stock on a 5-10 g scale.



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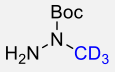

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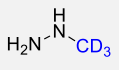

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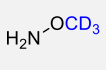

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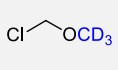

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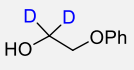

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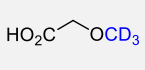

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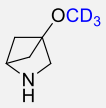

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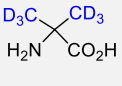

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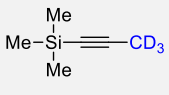

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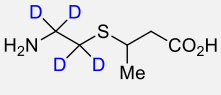

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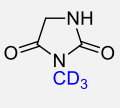

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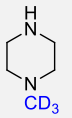

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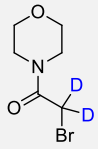

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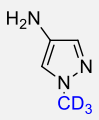

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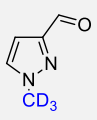

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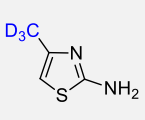

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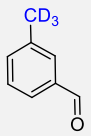

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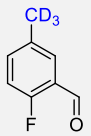

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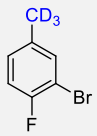

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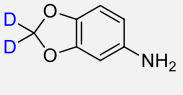

EN300-754577

References

1. T. Pirali et al. *J. Med. Chem.* **2019**, *62*, *11*, 5276.
2. R. Tung. *Innov. Pharm. Technol.* **2010**, *32*, 24.
3. C. Schmidt. *Nat. Biotechnol.* **2017**, *35*, 493.
4. S. Cargnin et al. *Future Med. Chem.* **2019**, *11*, 2039.