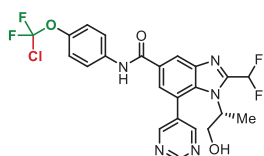


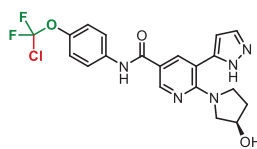
# Mixed Haloalkoxy Groups

## Introduction

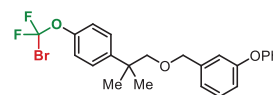
In 2021, the FDA approved asciminib (ABL001), an allosteric inhibitor of the Philadelphia tyrosine kinase, which plays a key role in leukemia development. The drug features a chlorodifluoromethoxy- ( $\text{ClF}_2\text{CO}-$ ) moiety, which embeds deeply within the myristate pocket. This group replaces the more commonly used  $\text{CF}_3\text{O}-$  moiety, doubling the binding affinity by forming a  $\text{Cl}\cdots\text{O}=\text{C}$  halogen bond with the backbone of Leu448.<sup>1</sup> Interestingly, the transition from  $\text{CF}_3\text{O}-$  to  $\text{ClF}_2\text{CO}-$  did not increase lipophilicity.<sup>2</sup> This example underscores the potential of mixed halogenated moieties for fine-tuning pocket interactions and optimizing drug pharmacology.<sup>3,4</sup>



**Embibatinib (TERN-701)**  
inhibitor of BCR-ABL1 tyrosine kinase  
Phase 1/2 trials for leukemia  
Terns/Merck

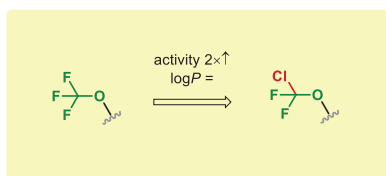


**Asciminib (ABL-001)**  
inhibitor of ABL/BCR-ABL1 tyrosine kinase  
FDA approved 2021 for leukemia  
Novartis

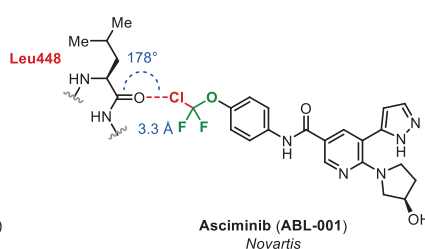


**Halfenprox (MTI-732)**  
sodium channel modulator  
insecticide and acaricide  
Mitsui Chemicals Agro

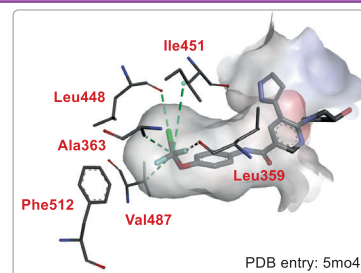
## Case study



inhibitor of tyrosine kinase BCR-ABL1 (Philadelphia chromosome)  
*Nature* **2017**, 543, 733; *J. Med. Chem.* **2018**, 61, 8120

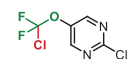


**Asciminib (ABL-001)**  
Novartis

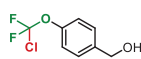


PDB entry: 5mo4

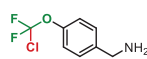
**We offer:** over 50 mixed haloalkoxy compounds from stock on 5-10 gram scale.



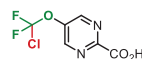
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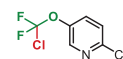
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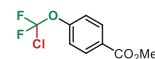
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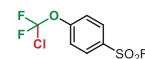
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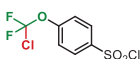
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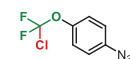
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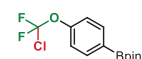
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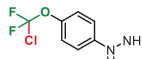
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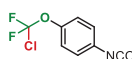
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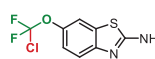
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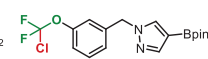
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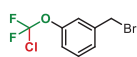
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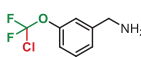
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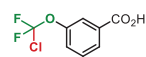
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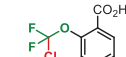
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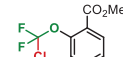
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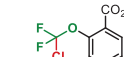
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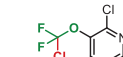
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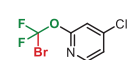
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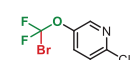
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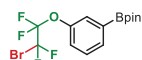
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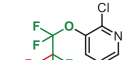
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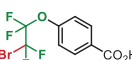
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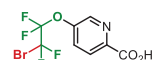
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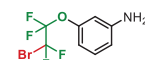
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EN300-22894591



EN300-39850960



EN300-37384691

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3. Y.-J. Wu et al. *J. Med. Chem.* **2026**, 69, 16143.
4. J. Sun et al. *Nat. Commun.* **2025**, 16, 4546.



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