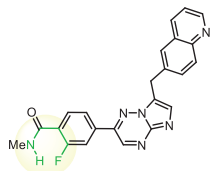


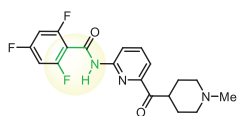
# ortho-Fluorine for Enhanced Permeability

## Introduction

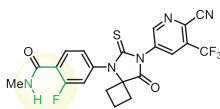
Aromatic amides represent a standard and robust molecular fragment in drugs. However, their high polarity often poses a problem, reducing bioavailability.<sup>1</sup> Incorporation of a fluorine atom in the vicinity of the amide enables temporary masking of the amide polarity through intramolecular hydrogen bonding, helping to improve pharmacokinetic features, especially permeability across membranes.<sup>2-4</sup> Discover Enamines's *ortho*-fluoro acids suitable for the synthesis of complex *ortho*-fluoroamides with improved permeability.



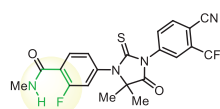
**Capmatinib**  
treatment of metastatic non-small cell lung cancer  
FDA approved 2020  
Novartis



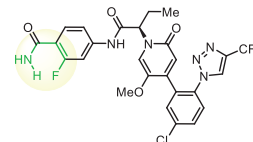
**Lasmiditan**  
treatment of migraine  
FDA approved 2019  
Eli Lilly



**Apalutamide**  
treatment of prostate cancer  
FDA approved 2018  
Janssen



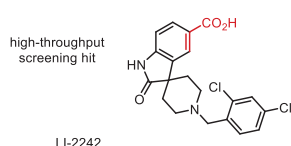
**Enzalutamide**  
treatment of prostate cancer  
FDA approved 2012  
Pfizer and Astellas



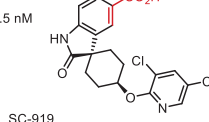
**Asundexian**  
preventing ischemic strokes  
Phase 3 trials  
Bayer

## Case study

inhibitor of inositol hexakisphosphate kinase

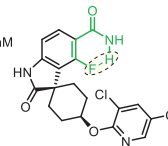


ACS Pharmacol. Transl. Sci. **2021**, 4, 780



IC<sub>50</sub> 2.5 nM  
*in vivo* mouse penetration  
[brain]/[plasma] 0.0075

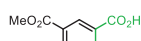
brain penetrant!



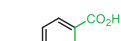
IC<sub>50</sub> 16 nM  
*in vivo* mouse penetration  
[brain]/[plasma] 1.3

J. Med. Chem. **2024**, 67, 13639

**We offer:** over 1,000 *ortho*-fluoro acids from stock on 5-10 gram scale.



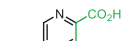
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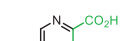
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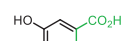
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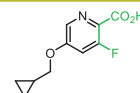
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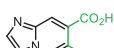
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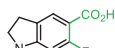
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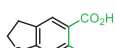
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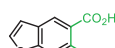
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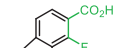
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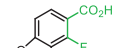
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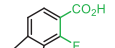
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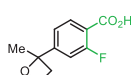
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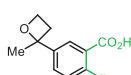
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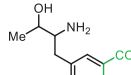
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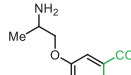
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EN300-7493826



EN300-7456654



EN300-3030728



EN300-3030724



EN300-3030729

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2. J. Scott et al. *J. Med. Chem.* **2023**, 66, 2918.

3. T. Heitmann et al. *J. Med. Chem.* **2024**, 67, 13639.
4. X.-Y. Zhao et al. *J. Med. Chem.* **2025**, 68, 11365.



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