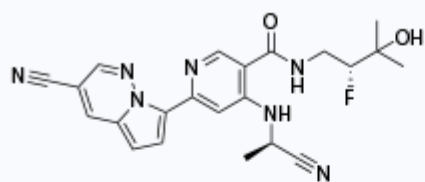


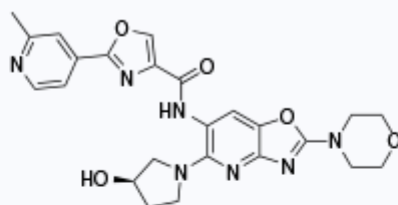
Building Blocks / Pharmaceutical Intermediates / Chemical Reagents

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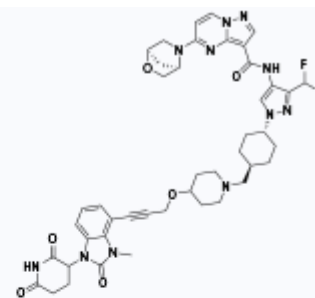
Interleukin-1 Receptor-Associated Kinase 4 (IRAK4) belongs to a family of four kinases (IRAK1, IRAK2, IRAK-M and IRAK4)<sup>[1]</sup>. IRAK4 is a serine/ threonine kinase which plays a crucial role in regulating Toll-Like receptors (TLR) and interleukin-1 receptors (IL-1R) signal. IRAK4 is recruited by the adaptor molecule Myeloid Differentiation primary response gene 88 (MyD88) after TLR activation, which results in activation of nuclear factor kappa B (NF-κB) and type I interferon (IFN) pathways. IRAK4 overactivation is linked with several autoimmune diseases, such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). In addition, IRAK4 has been shown to be associated with lymphocytic leukemia, lymphoma, and fibrotic disorders. Therefore, inhibitors of IRAK4 may be useful in the treatment of inflammatory disorders and cancers. To date, no IRAK4 inhibitors have been approved by FDA, but more than 14 promising IRAK4 inhibitors have entered into clinical trials<sup>[2-10]</sup>.



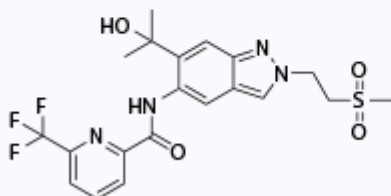
Edecisertib (Phase II)  
IRAK4 inhibitor



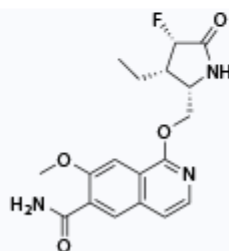
Emavusertib (Phase II)  
IRAK4 inhibitor



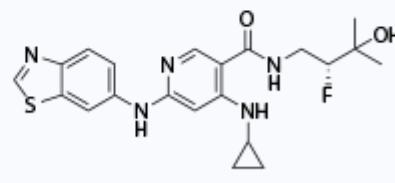
KT-474 (Phase II)  
IRAK4 degrader



Zabedoseritib (Phase II)  
IRAK4 inhibitor



Zimlovisertib (Phase II)  
IRAK4 inhibitor



BMS-978299 (Phase I)  
IRAK4 inhibitor

A series of building blocks will be used as molecular fragments  
in the design of IRAK4 inhibitors.

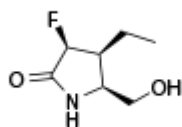
[1] Journal of Medicinal Chemistry (2019), 62, 13, 6223-6240.

[2] Journal of Medicinal Chemistry (2019), 62, 21, 9918-9930.

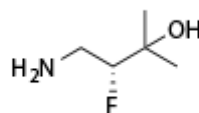
- [3] Journal of Medicinal Chemistry (2017), 60, 13, 5521-5542.  
 [4] European Journal of Medicinal Chemistry (2020), 190, 112092.  
 [5] European Journal of Medicinal Chemistry (2023), 258, 115616.  
 [6] European Journal of Medicinal Chemistry (2023), 256, 115453.  
 [7] ACS Medicinal Chemistry Letters (2022), 13, 4, 714-719.  
 [8] ACS Medicinal Chemistry Letters (2020), 11, 12, 2374-2381.  
 [9] Bioorganic & Medicinal Chemistry (2018), 26, 4, 913-924.  
 [10] Bioorganic & Medicinal Chemistry (2022), 63, 116729.



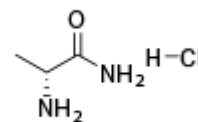
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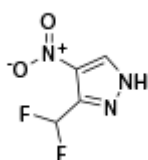
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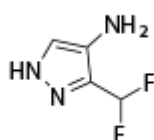
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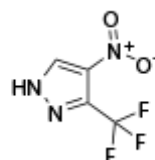
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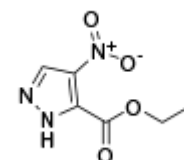
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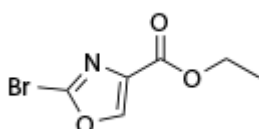
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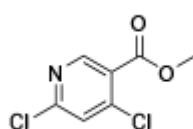
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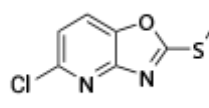
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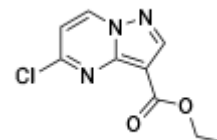
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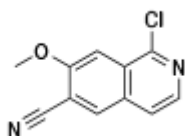
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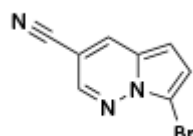
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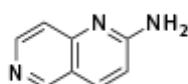
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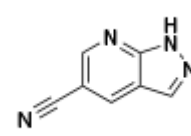
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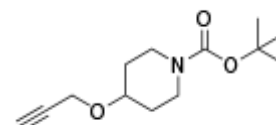
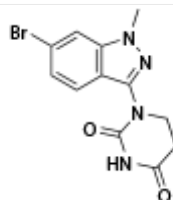
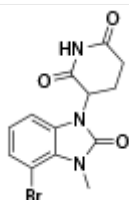
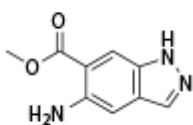
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