SL-26. IRAK4 inhibitors

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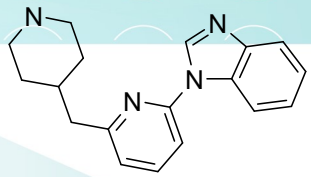
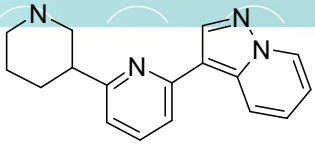
Ser/Thr kinase IRAK4 is a key factor in the transduction of signals from the interleukin receptor (IL-1) and toll-like receptors (TLRs) resulting in cytokine release and promotion of genes controlled by transcription factor NF-kB in response to infection [1]. IRAK4 deficiency leads to the blockade of the TLR4 receptor signaling pathway and consequent impairment of immune response to bacterial, fungal, parasitic, and viral infection. Recently several IRAK4 inhibitors have been studied against hematological tumors with oncogenic mutations of MyD88; for example, diffuse large cell lymphoma (ABC-DLBCL) and Waldenström's macroglobulinemia (WM) [2-4]. Thus small molecule IRAK4 inhibitors are an attractive therapeutic option for the treatment of inflammation and oncology-related disorders.

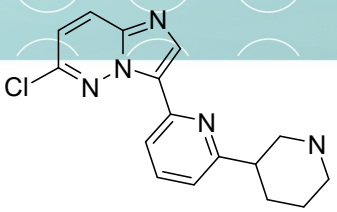
ASINEX has created a series of IRAK4-oriented compounds by combining the IRAK4 hinge binding motif with proprietary natural product-like fragments. Several compounds from this library were screened against IRAK4 kinase *in vitro* and showed sub-uM IC50. Sunitinib was also included in the library as a reference compound.



IC_{50} 0.7 µM



IC_{50} 0.4 µM



IC_{50} 0.9 µM

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Formats	Supplementary Information
80 compounds per plate 0.1 mg; 1 mg; 2 mg dry film/powder 0.1 µmol; 1 µmol DMSO solutions	SL#26_IRAK4 inhibitors_06-16.sdf

References:

1. *J Med Chem*. 2015, 58 (1):96-110. doi: 10.1021/jm5016044.
2. *Blood.* 2013, 122, 1222-123,. doi: 10.1182/blood-2012-12-475111
3. *Nature* 2011, 470, 115-119, doi: 10.1038/nature09671
4. *Cancer Res*. 2012, 72, 6209, doi: 10.1158/0008-5472.CAN-12-0337.

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