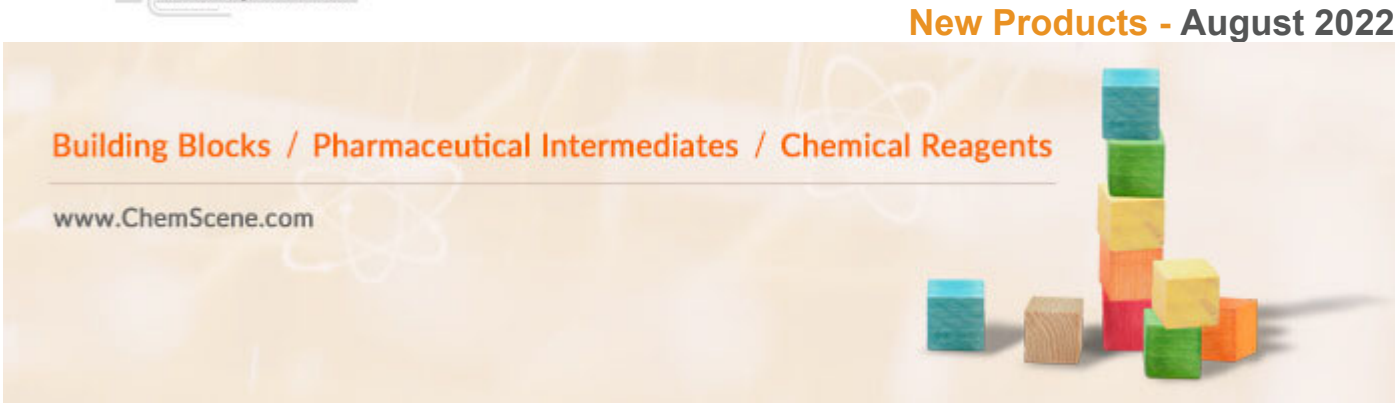
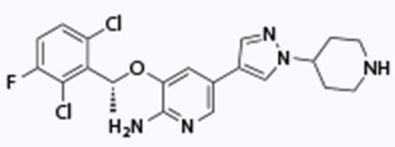
ChemScene
Chemical Reagents For Life Science

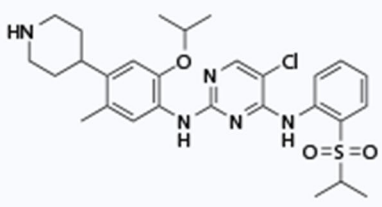
New Products - August 2022



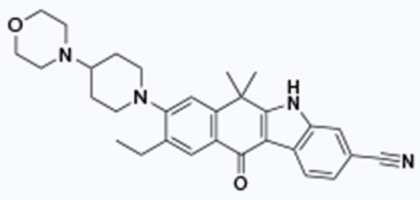
As a receptor tyrosine kinase of insulin receptor (IR) subfamily, anaplastic lymphoma kinase (ALK) has been validated to play important roles in various cancers, especially anaplastic large cell lymphoma (ALCL), non-small cell lung cancer (NSCLC), and neuroblastomas[1]. Currently, five small-molecule inhibitors of ALK, including Crizotinib, Ceritinib, Alectinib, Brigatinib and Lorlatinib, have been approved by the U.S. FDA against ALK-positive NSCLCs. To address the unmet need of the emergence of multiple combinations of acquired double ALK mutations, there are currently two 4G ALK TKIs (TPX-0131 and NVL-655) being developed. TPX-0131 has been designed with a novel compact macrocyclic structure and has shown preclinical potent inhibition of wildtype and numerous ALK mutations. NVL-655 is a novel brain-penetrant ALK-selective inhibitor created to overcome several limitations observed with currently available therapies and it started a phase 1/2 clinical trial on June 9, 2022[2-10].



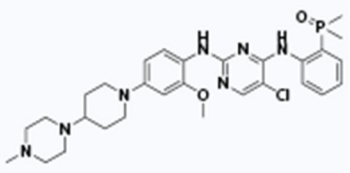
Crizotinib the first-generation ALK inhibitor



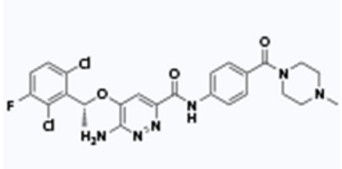
Ceritinib the second-generation ALK inhibitor



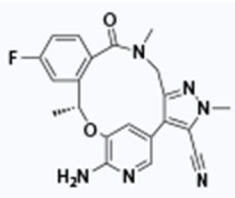
Alectinib the second-generation ALK inhibitor



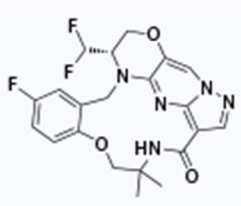
Brigatinib the second-generation ALK inhibitor



Ensartinib the second-generation ALK inhibitor



Lorlatinib the third-generation ALK inhibitor



TPX-0131 the fourth-generation ALK inhibitor

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

[1] Journal of Medicinal Chemistry (**2019**), 62, 24, 10927-10954.

[2] Journal of Medicinal Chemistry (**2019**), 62, 10, 4915-4935.

[3] Journal of Medicinal Chemistry (**2018**), 61, 9, 4249-4255.

[4] European Journal of Medicinal Chemistry (**2022**), 238, 114493.

[5] Bioorganic & Medicinal Chemistry (**2022**), 66, 116794.

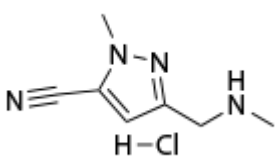
[6] Bioorganic & Medicinal Chemistry (**2020**), 28, 20, 115719.

[7] Bioorganic & Medicinal Chemistry (**2019**), 27, 20, 115051.

[8] Translational Oncology (**2021**), 14, 11, 101191.

[9] WO2021226208A2.

[10] WO2021226269A1.



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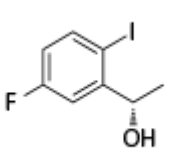

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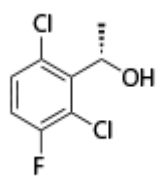

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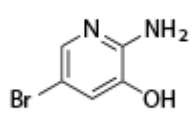

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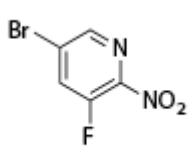

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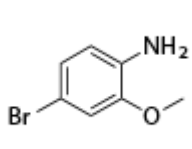

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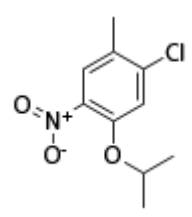

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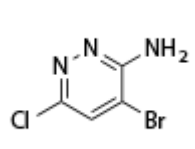

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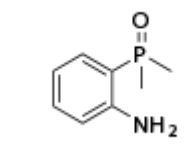

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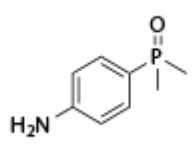

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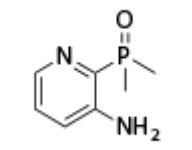

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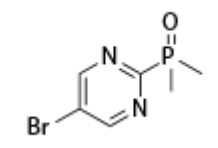

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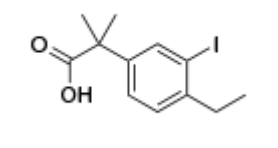

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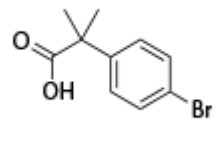

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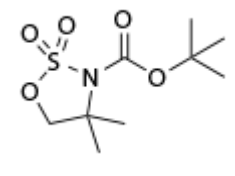

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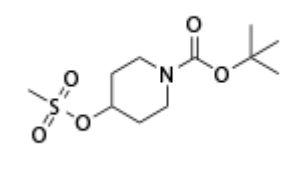

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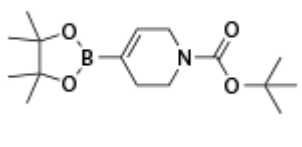

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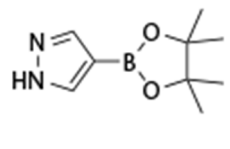

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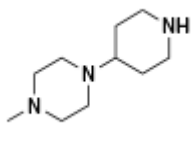

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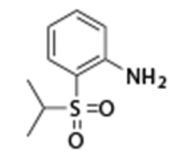

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