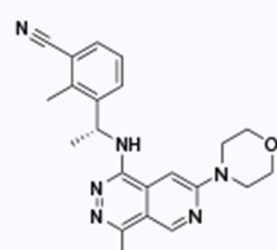


**Building Blocks / Pharmaceutical Intermediates / Catalysts & Ligands**

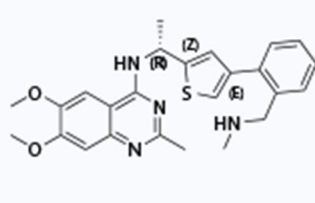
www.ChemScene.com



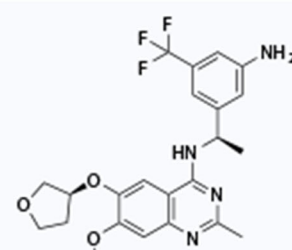
SOS1 (Son of sevenless homolog 1) is a guanine nucleotide exchange factor (GEF) that mediates the exchange of GDP for GTP, thereby activating RAS proteins<sup>[1]</sup>. SOS1 has two binding sites for RAS-family proteins; a catalytic site that binds GDP-bound RAS-family proteins to promote guanine nucleotide exchange and an allosteric site that binds GTP-bound RAS-family proteins which causes a further increase in the catalytic GEF function of SOS1. Stimulation of cells with growth factors leads to the association of SOS-Grb2 complexes with activated receptors and then to the stimulation of Ras through the juxtaposition of SOS and Ras at the membrane. A previous study showed that SOS1 promotes metastasis in ovarian cancer. It is established that SOS1 is important for the tumorigenesis and progress of tumors through the activation of Ras or Rac. Small molecule SOS1 inhibitors have been shown to be effective in downregulating active RAS in tumor cells with wild-type KRAS as well as tumor cells bearing a KRAS mutation. By preventing formation of the KRAS-SOS1 complex, the SOS1 inhibitors block reloading of KRAS with GTP, leading to antiproliferative activity<sup>[2-10]</sup>.



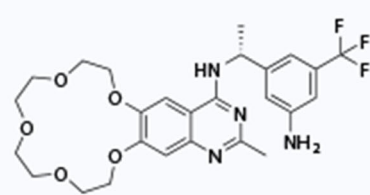
**MRTX0902**  
SOS1 inhibitor



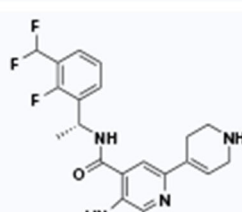
**BAY-293**  
SOS1 inhibitor



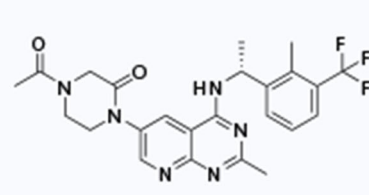
**BI-3406**  
SOS1 inhibitor



**Example 4 (WO2021203768)**  
SOS1 inhibitor



**Example 5 (WO2022146698A1)**  
SOS1 inhibitor



**Example 61 (WO2022058344A1)**  
SOS1 inhibitor

A series of building blocks will be used as molecular fragments in the design of SOS1 inhibitors.

[1] Journal of Medicinal Chemistry (2021), 64, 10, 6569-6580.

[2] Journal of Medicinal Chemistry (2022), 65, 14, 9678-9690.

[3] Journal of Medicinal Chemistry (2020), 63, 15, 8325-8337.

[4] Journal of Medicinal Chemistry (2022), 65, 5, 3923-3942.

[5] Journal of Medicinal Chemistry (2015), 58, 5, 2265-2274.

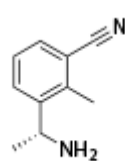
[6] European Journal of Medicinal Chemistry (2020), 185, 111844.

[7] ChemMedChem (2016), 11, 8, 814-821.

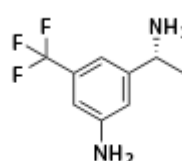
[8] WO2022146698A1.

[9] WO2022058344A1.

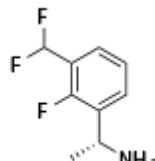
[10] WO2019122129A1.



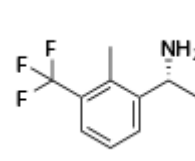
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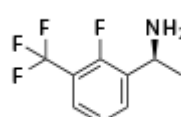
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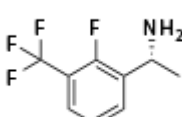
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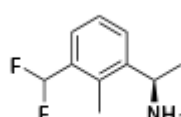
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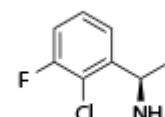
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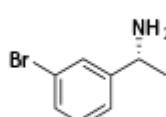
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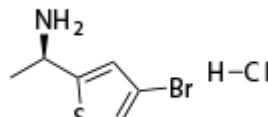
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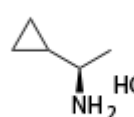
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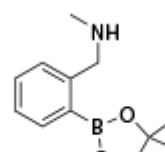
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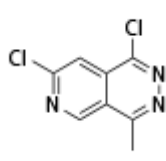
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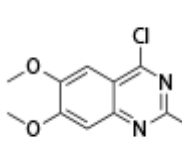
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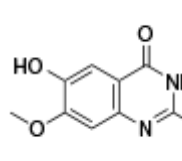
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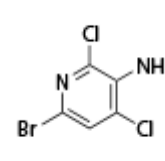
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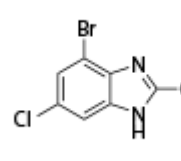
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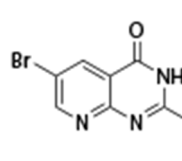
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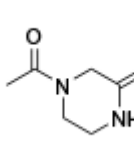
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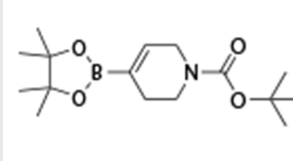
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