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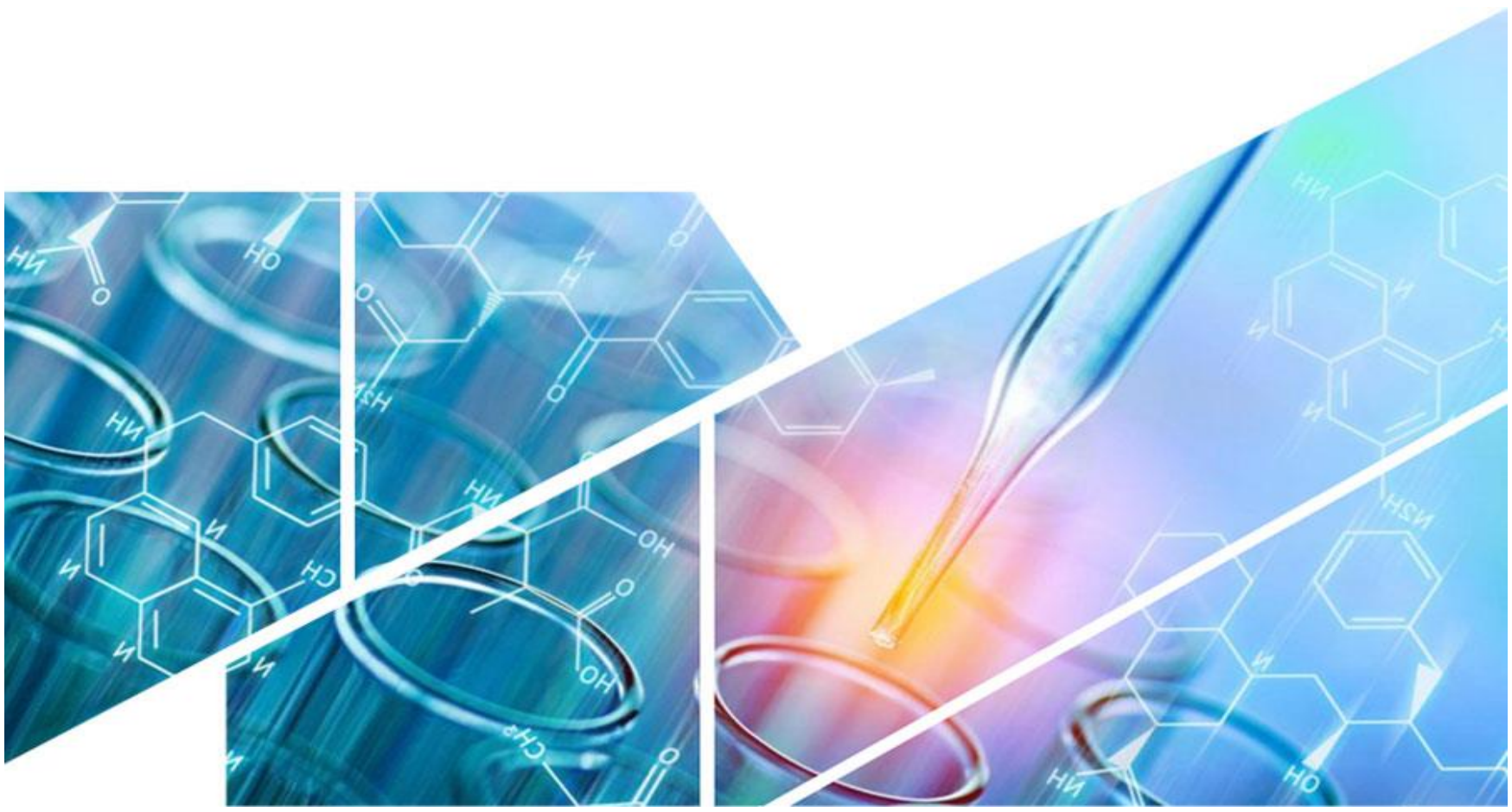
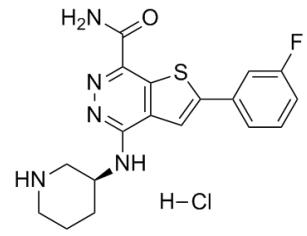
Chk (Checkpoint Kinase) Inhibitors

(inhibitors, agonists and modulators)



Checkpoint kinases are protein kinases that are involved in cell cycle control. Two checkpoint kinase subtypes have been identified, Chk1 and Chk2. Chk1 is a Serine/threonine-specific protein kinase that in humans, is encoded by the CHEK1 gene. Chk1 coordinates the DNA damage response (DDR) and cell cycle checkpoint response. Activation of Chk1 results in the initiation of cell cycle checkpoints, cell cycle arrest, DNA repair and cell death to prevent damaged cells from progressing through the cell cycle. CHEK2 is tumor suppressor gene that encodes the protein CHK2, a serine threonine kinase. Chk2 operates in an intricate network of proteins to elicit DNA repair, cell cycle arrest or apoptosis in response to DNA damage. Mutations to the CHEK2 gene have been linked to a wide range of cancers including breast cancer.

Thieno[2,3-d] pyridazine-7-carboxamide, 2-(3-fluorophenyl)-4-[(3S)-3-piperidinylamino]-, hydrochloride - CAS 1278405-51-8

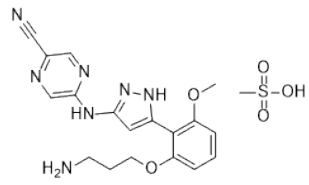


Catalog Number:

Molecular Weight:407.89 **Molecular Formula:** C18H19ClFN5OS

Description: An inhibitor of CHK1 and CHK2, with anti-proliferative activities.

Prexasertib mesylate - CAS 1234015-55-4

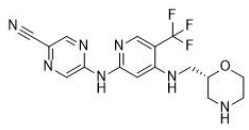


Catalog Number:

Molecular Weight: 461.49 **Molecular Formula:** C19H23N7O5S

Description: Prexasertib, also known as LY2606368, is an ATP-competitive CHK1 inhibitor (Ki= 0.9 nmol/L), with minor activity against CHK2 and RSK with IC50= 8 nM and 9 nM respectively in cell-free assay.

CCT245737 - CAS 1489389-18-5

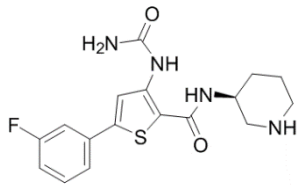


Catalog Number:

Molecular Weight: 379.347 **Molecular Formula:** C16H16F3N7O

Description: CCT245737 is an orally bioactive CHK1 inhibitor (IC50 of 1.4 nM), displaying >1,000-fold selectivity against CHK2 and CDK1. It potently inhibits cellular CHK1 activity (IC50 30-220nM) and enhances gemcitabine and SN38 cytotoxicity in multiple human tumor cell lines and human tumor xenograft models.

AZD-7762 - CAS 860352-01-8



Catalog Number: 860352-01-8

Molecular Weight: 362.42 **Molecular Formula:** C17H19FN4O2S

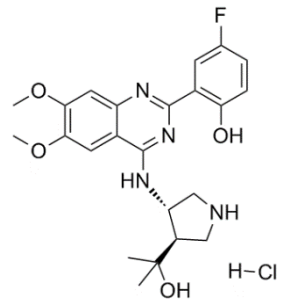
Description: AZD-7762 is a synthetic small molecule inhibitor of checkpoint kinases (Chks) with potential chemosensitizing activity. AZD7762 binds to and inhibits Chks, which may prevent cell cycle arrest and subsequent nucleotide excision repair in DNA-damaged tumor cells, resulting in tumor cell apoptosis.

CCT 241533 dihydrochloride - CAS 1431697-96-9

Catalog Number:

Molecular Weight: 515.41 **Molecular Formula:** C23H27FN4O4.2HCl

Description: CCT 241533 dihydrochloride is a potent Chk2 inhibitor (IC50 = 3 nM) displaying >63-fold selectivity for Chk1 over Chk2 and a panel of 84 other kinases. CCT 241533 inhibits Chk2 activation in response to etoposide-induced DNA damage in HT29 cells, and blocks ionizing radiation-induced apoptosis of mouse thymocytes.

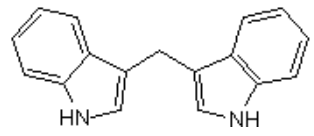


3,3'-Diindolylmethane - CAS 1968-05-4

Catalog Number:

Molecular Weight: 246.31 **Molecular Formula:** C17H14N2

Description: 3,3'-Diindolylmethane is an activator of checkpoint kinase 2 (Chk2) that induces G2/M cell cycle arrest in various cancer cell lines. It is used as an antineoplastic agent.

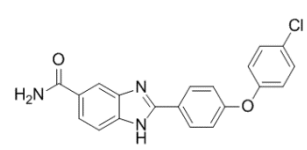


BML-277 - CAS 516480-79-8

Catalog Number: 516480-79-8

Molecular Weight: 363.80 **Molecular Formula:** C20H14ClN3O2

Description: BML-277 is a selective APT-competitive inhibitor of the DNA damage response signaling enzyme CHK2 (IC50 =15 nM).

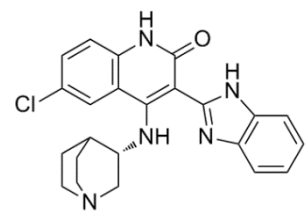


CHIR-124 - CAS 405168-58-3

Catalog Number: 405168-58-3

Molecular Weight: 419.91 **Molecular Formula:** C23H22ClN5O

Description: CHIR-124 is a quinolone-based small molecule Chk1 inhibitor, that is structurally unrelated to other known inhibitors of Chk1. It potently and selectively inhibits Chk1 in vitro (IC (50) = 0.0003 micromol/L).

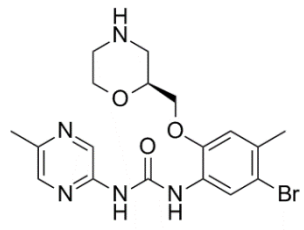


LY2603618 - CAS 911222-45-2

Catalog Number: 911222-45-2

Molecular Weight: 436.3 **Molecular Formula:** C18H22BrN5O3

Description: LY2603618 is a potent and selective small molecule inhibitor of Chk1 protein kinase activity in vitro (IC50=7 nM) and the first selective Chk1 inhibitor to enter clinical cancer trials.

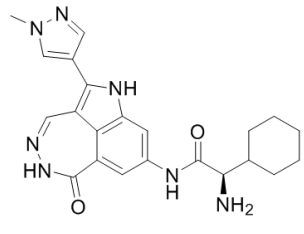


PF-477736 - CAS 952021-60-2

Catalog Number: 952021-60-2

Molecular Weight: 419.48 **Molecular Formula:** C22H25N7O2

Description: PF-477736 is a proprietary compound targeting cell cycle checkpoint kinase 1 (chk1) with potential chemopotentiation activity. Chk1 inhibitor PF-477736 inhibits chk1, an ATP-dependent serine-threonine kinase that is a key component in the DNA replication-monitoring S/G2 checkpoint system.

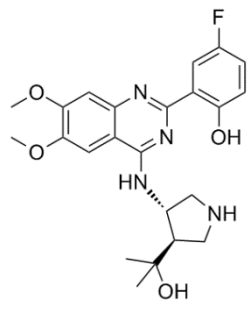


CCT241533 - CAS 1262849-73-9

Catalog Number: 1262849-73-9

Molecular Weight: 442.48 **Molecular Formula:** C23H27FN4O4

Description: CCT241533, a Chk2 inhibitor, has been found to improve the effect of genotoxic cancer therapies. IC50: 3 nM.

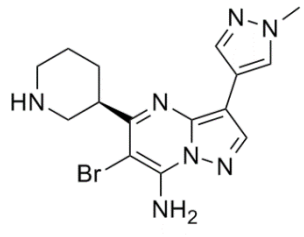


SCH900776 - CAS 891494-63-6

Catalog Number: 891494-63-6

Molecular Weight: 376.25 **Molecular Formula:** C15H18BrN7

Description: SCH900776, also known as MK-8776, is an agent targeting cell cycle checkpoint kinase 1 (Chk1) with potential radiosensitization and chemosensitization activities. Chk1 inhibitor SCH 900776 specifically binds to and inhibits Chk1, which may result in tumor cells bypassing Chk1-dependent cell cycle arrest in the S and G2/M phases to undergo DNA repair prior to entry into mitosis.

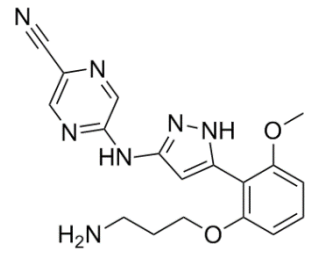


LY2606368 - CAS 1234015-52-1

Catalog Number: B0084-462722 **Price:** $198/10 mg

Molecular Weight: 365.39 **Molecular Formula:** C18H19N7O2

Description: LY2606368 is a potent and selective ATP competitive inhibitor (IC50=1.5 nM in SW1990 cell) of the Chk1 protein kinase.

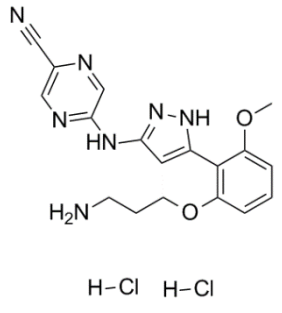


LY2606368 dihydrochloride - CAS 1234015-54-3

Catalog Number: 1234015-54-3

Molecular Weight: 438.31 **Molecular Formula:** C18H21Cl2N7O2

Description: The dihydrochloride salt form of LY2606368 which also known as prexasertib, is an inhibitor of checkpoint kinase 1 and has potential effect in antineoplastic. It is still under Phase II clinical trial against breast cancer and some other sorts of cancers.

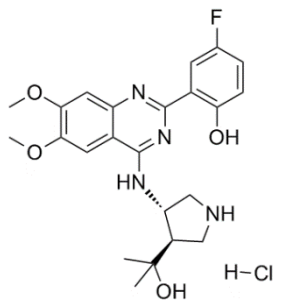


CCT241533 (hydrochloride) - CAS 1431697-96-9

Catalog Number: 1431697-96-9

Molecular Weight: 478.94 **Molecular Formula:** C23H28ClFN4O4

Description: CCT241533 (hydrochloride) is the hydrochloride salt form of CCT241533. As a potent Chk2 inhibitor, CCT241533 blocked CHK2 activity in human tumor cell lines in answer to DNA damage and potentiate PARP inhibitor cell killing. Chk2: IC50=3nM.

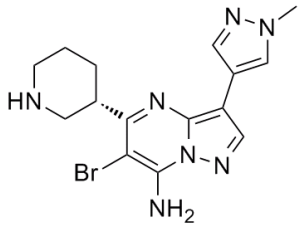


SCH900776 S-isomer - CAS 891494-64-7

Catalog Number: 891494-64-7

Molecular Weight: 376.25 **Molecular Formula:** C15H18BrN7

Description: SCH900776 S-isomer is the S-isomer form of SCH900776, which is a potent, selective and orally bioavailable inhibitor of checkpoint kinase Chk1. It can be used as a protein kinase inhibitor useful in the treatment of protein kinase-mediated diseases.

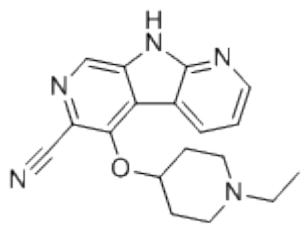


GDC-0425 - CAS 1200129-48-1

Catalog Number: 1200129-48-1

Molecular Weight: 321.38 **Molecular Formula:** C18H19N5O

Description: This active molecular is a selective Checkpoint kinase 1 (Chk1) inhibitors and it enhances gemcitabine efficacy in tumor xenograft models. GDC-0425 was safe and yielded responses in patients with a variety of cancers.



CCT245737 - CAS 1489389-23-2

Catalog Number: 1489389-23-2

Molecular Weight: 379.14 **Molecular Formula:** C16H16F3N7O

Description: CCT245737, a nitrogen heterocycle compound, has been found to be a CHK1 inhibitor that could probable be effective in antineoplastic studies. It is still under Phase I trial for Solid tumours. IC50: 30-220 nM.