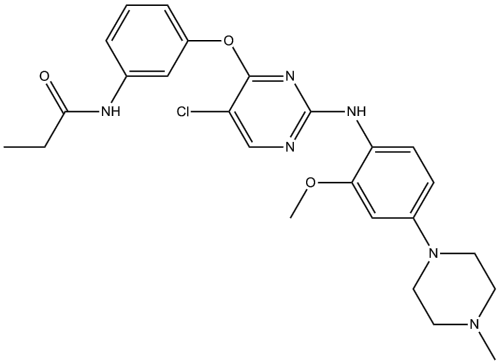
Product Data Sheet

Product Name: WZ4003
Cat. No.: GC16549

Chemical Properties

Cas. No.	1214265-58-3		
Chemical Name	N-[3-[5-chloro-2-[2-methoxy-4-(4-methylpiperazin-1-yl)anilino]pyrimidin-4-yl]oxyphenyl]propanamide		
SMILES	CCC(=O)NC1=CC(=CC=C1)OC2=NC(=NC=C2Cl)NC3=C(C=C(C=C3)N4CCN(CC4)C)OC		
Formula	$C_{25}H_{29}ClN_6O_3$	M.Wt	496.99
Solubility	≥ 7.85mg/mL in DMSO with gentle warming	Storage	Store at -20° C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure			

Protocol

Kinase experiment [1]:

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Kinase assays	In vitro activities of purified GST–NUAK1 were measured using Cerenkov counting of incorporation of radioactive 32P from [γ-32P]ATP into Sakamototide substrate peptide. Reactions were carried out in a 50 μl reaction volume for 30 min at 30°C and reactions were terminated by spotting 40 μl of the reaction mix on to P81 paper and immediately immersing in 50 mM orthophosphoric acid. Samples were washed three times in 50 mM orthophosphoric acid followed by a single acetone rinse and air drying. The kinase-mediated incorporation of [γ-32P]ATP into Sakamototide was quantified by Cerenkov counting.

Cell experiment [2]:

Cell lines	U2OS cell lines
Preparation method	The solubility of this compound in DMSO is >7.85mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37°C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Reacting condition	10 μM for 16h
Applications	WZ4003 impaired the invasive potential of U2OS cells in a 3D cell invasion assay to the same extent as NUAK1 knockdown, which indicates that WZ4003 will serve as useful chemical probes to delineate the biological roles of the NUAK kinases.

Caution: Product has not been fully validated for medical applications. For research use only.
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References:

[1] Banerjee S, Buhrlage SJ, Huang HT, et al. Characterization of WZ4003 and HTH-01-015 as selective inhibitors of the LKB1-tumour-suppressor-activated NUAK kinases. Biochem J, 2014, 457(1): 215-225.

Background

WZ4003 is a potent and selective inhibitor of NUAK1 and NUAK2 with IC50 values of 20 and 100 nM, respectively [1].

NUAK family SNF1-like kinase-1 (NUAK1) and the related NUAK2 belong to the AMP-activated protein kinase (AMPK) family and are activated by liver kinase B1 (LKB1) tumour suppressor protein kinase [1].

WZ4003 is a potent and selective NUAK1/2 inhibitor. In HEK-293 cells, WZ4003 inhibited the phosphorylation of myosin phosphate-targeting subunit 1 (MYPT1), which was phosphorylated by NUAK1 at Ser445. In HEK-293 cells overexpressing inhibitor-resistant NUAK1[A195T], WZ4003 didn't inhibit the phosphorylation of MYPT1 at Ser445. In mouse embryonic fibroblasts (MEFs), WZ4003 significantly inhibited migration in a wound-healing assay and inhibited MEFs proliferation. In a cell invasion assay, WZ4003 inhibited the invasive potential of U2OS cells [1]. In U2OS cells, WZ4003 (10 μM) inhibited phosphorylation of MYPT1 and reduced the cells in S-phase by 50%. Also, WZ4003 prevented cells from entering into mitosis [2].

References:
[1]. Banerjee S, Buhrlage SJ, Huang HT, et al. Characterization of WZ4003 and HTH-01-015 as selective inhibitors of the LKB1-tumour-suppressor-activated NUAK kinases. Biochem J, 2014, 457(1): 215-225.
[2]. Banerjee S, Zagórska A, Deak M, et al. Interplay between Polo kinase, LKB1-activated NUAK1 kinase, PP1βMYPT1 phosphatase complex and the SCFβTrCP E3 ubiquitin ligase. Biochem J, 2014, 461(2): 233-245.