

Product Data Sheet

Product Name: Domatinostat

Cat. No.: GC35893

Chemical Properties

Cas. No. 910462-43-0

SMILES O=C(NC1=CC=CC=C1N)/C=C/C2=CN(S(=O)(C3=CC=C(C4=CN(C)N=C4)C=C3)=O)C=C2

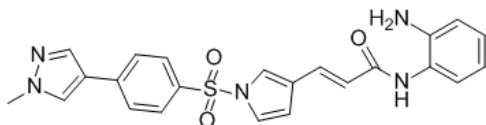
Formula $C_{23}H_{21}N_5O_3S$ M.Wt 447.51

Solubility DMSO: ≥ 58 mg/mL (129.61 mM) 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



Background

Domatinostat (4SC-202 free base) is a selective class I HDAC inhibitor with IC_{50} of 1.20 μM , 1.12 μM , and 0.57 μM for HDAC1, HDAC2, and HDAC3, respectively. It also displays inhibitory activity against Lysine specific demethylase 1 (LSD1). HDAC-3|0.57 μM (IC_{50})|HDAC-2|1.12 μM (IC_{50})|HDAC-1|1.2 μM (IC_{50})|HDAC-11|9.7 μM (IC_{50})|HDAC-5|11.3 μM (IC_{50})|HDAC-10|21 μM (IC_{50})|HDAC-9|50 μM (IC_{50})

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

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Domatinostat (4SC-202 free base) tosylate significantly reduces proliferation of all epithelial and mesenchymal UC cell lines (IC₅₀ 0.15-0.51 μ M), inhibits clonogenic growth and induces caspase activity[1]. Domatinostat (4SC-202 free base) tosylate provokes apoptosis activation in CRC cells, while caspase inhibitors (z-VAD-CHO and z-DVED-CHO) significantly alleviate Domatinostat (4SC-202 free base) tosylate-exerted cytotoxicity in CRC cells. Meanwhile, Domatinostat (4SC-202 free base) tosylate induces dramatic G2-M arrest in CRC cells. Further studies show that AKT activation might be an important resistance factor of Domatinostat tosylate. Domatinostat (4SC-202 free base) tosylate-induced cytotoxicity is dramatically potentiated with serum starvation, AKT inhibition (by perifosine or MK-2206), or AKT1-shRNA knockdown in CRC cells. On the other hand, exogenous expression of constitutively active AKT1 (CA-AKT1) decreases the sensitivity by Domatinostat tosylate in HT-29 cells. Notably, Domatinostat (4SC-202 free base) tosylate, at a low concentration, enhances oxaliplatin-induced in vitro anti-CRC activity[2]. Domatinostat (4SC-202 free base) tosylate treatment induces potent cytotoxic and proliferation-inhibitory activities against established HCC cell lines (HepG2, HepB3, SMMC-7721) and patient-derived primary HCC cells. Domatinostat (4SC-202 free base) tosylate induces apoptosis signal-regulating kinase 1 (ASK1) activation, causing it translocation to mitochondria and physical association with Cyp-D[3].

Oral gavage of Domatinostat (4SC-202 free base) inhibits HT-29 xenograft growth in nude mice, and when combined with oxaliplatin, its activity is further strengthened[2].

[1]. Pinkerneil M, et al. Evaluation of the Therapeutic Potential of the Novel Isotype Specific HDAC Inhibitor 4SC-202 in Urothelial Carcinoma Cell Lines. Target Oncol. 2016 Dec;11(6):783-798. [2]. Zhijun H, et al. Pre-clinical characterization of 4SC-202, a novel class I HDAC inhibitor, against colorectal cancer cells. Tumour Biol. 2016 Aug;37(8):10257-67. [3]. Fu M, et al. 4SC-202 activates ASK1-dependent mitochondrial apoptosis pathway to inhibit hepatocellular carcinoma cells. Biochem Biophys Res Commun. 2016 Mar 4;471(2):267-73 [4]. S.W.Henning, et al. Preclinical characterization of 4SC-202, a noval isotype specific HDAC inhibitor.

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