

Product Data Sheet

Product Name: SR-3029

Cat. No.: GC19336

Chemical Properties

Cas. No. 1454585-06-8

SMILES FC1=CC(N2C=NC3=C(NCC4=NC5=CC=C(F)C(F)=C5N4)N=C(N6CCOCC6)N=C23)=CC=C1

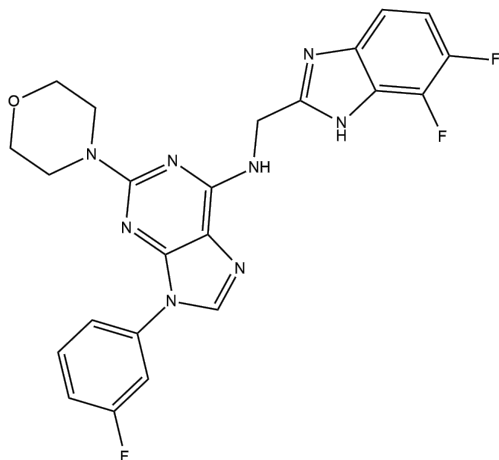
Formula $C_{23}H_{19}F_3N_8O$ M.Wt 480.45

Solubility DMSO : ≥ 30 mg/mL (62.44 mM); Water : < 0.1 mg/mL (insoluble) 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

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

**Kinase
experiment:**

Briefly, final assay concentrations for CK1 δ , Ulight peptide substrate (ULight-Topo-IIa(Thr1342) peptide) and ATP are 2 nM, 200 nM and 20 μ M respectively. The reaction is performed at room temperature in a 10 μ L final volume (384-well low volume plate) containing the following: 50 mM Hepes, pH 7.5, 5 mM MgCl₂, 0.1 mg/mL bovine serum albumin, 1 mM dl-dithiothreitol, 0.01% Triton X-100 and 1% DMSO. After 10 min, the reaction is terminated by addition of 10 μ L of 4 nM Eu-anti-p-Topo-IIa in Lance Detection Buffer. The fluorescent signal is detected using a plate reader. 10 point dose-response curves with 3-fold dilutions starting from 10 μ M for each compound (SR-3029) is generated in duplicate and data fit to a four parameter logistic[1].

Cell experiment:

Human A375 melanoma cells are cultured in Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10% fetal bovine serum, 1% penicillin/streptomycin and 1 $\times$ MEM Non-Essential Amino Acids at 37°C, 5% CO₂. To evaluate the anti-proliferative activity of newly synthesized CK1 δ/ϵ inhibitors, each compound (SR-3029) is subjected to MTT assays against A375 melanoma cells and their EC₅₀ values are determined. Briefly, A375 melanoma cells are plated into a 96-well plate and treated with a series of concentrations of each new inhibitor, vehicle (DMSO) or with SR-3029 or SR-1277 (positive controls). MTT assays are performed four days after treatment and data are analyzed using the GraphPad Prism5[1].

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Animal experiment: Stable pools of MDA-MB-231-Luc, MDA-MB-231, MDA-MB-468, SKBR3, or BT474 cells are established by injection of 2×10^6 cancer cells into the mammary fat pads of 6-week-old female athymic nude mice. Establishment of BCM-4013 patient-derived xenografts is performed. Briefly, fresh xenograft tumor fragments ($\sim 1 \text{ mm}^3$) are transplanted into the cleared mammary fat pad of recipient SCID/Bg mice. Mice are treated with SR-3029 or vehicle (10:10:80, DMSO:Tween-80:Water) at 20 mg/kg daily by i.p. injection. Tumor volumes are measured as the indicated intervals using calipers or by luminescence imaging with the IVIS 100 imager after subcutaneous injection of luciferin (15 mg/mL). Average radiance (p/s/cm²/sr) is determined from tumor region-of-interest (ROI) using Living-Image analysis software[2].

References:

- [1]. Bibian M, et al. Development of highly selective casein kinase 1 δ /1 ϵ (CK1 δ / ϵ) inhibitors with potent antiproliferative properties. Bioorg Med Chem Lett. 2013 Aug 1;23(15):4374-80.
[2]. Rosenberg LH, et al. Therapeutic targeting of casein kinase 1 δ in breast cancer. Sci Transl Med. 2015 Dec 16;7(318):318ra202.

Background

SR-3029 is a potent and ATP competitive CK1 δ and CK1 ϵ inhibitor, with IC₅₀s of 44 nM and 260 nM, respectively, and K_is of 97 nM for both kinases.

SR-3029 is a potent CK1 δ /CK1 ϵ inhibitor, with IC₅₀s of 44 nM and 260 nM, respectively. SR-3029 is ATP competitive, with K_is of 97 nM for CK1 δ /CK1 ϵ . SR-3029 also blocks CDK6/cyclin D3, CDK6/cyclin D1, CDK4/cyclin D3, CDK4/cyclin D1 and FLT3, with IC₅₀s of 427, 428, 368, 576, and 3000 nM, respectively. SR-3029 shows inhibitory effects on A375 cells, with an EC₅₀ of 86 nM[1]. CK1 δ is a necessary and sufficient driver of Wnt/ β -catenin signaling in human breast cancer. SR-3029 shows less potent activities against MCF7 and T47D breast cancer cells and the MCF10A cell line, which express low amounts of CK1 δ [2].

SR-3029 (20 mg/kg daily i.p.) exhibits anti-tumor effects in orthotopic MDA-MB-231, MDA-MB-468 (TNBC), SKBR3 and BT474 (HER2+) tumor xenografts with no overt toxicity in mice. SR-3029 (20

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

mg/kg daily i.p.) also effectively inhibits the growth of tumor in primary patient-derived xenograft (PDX) models. In addition, SR-3029 (20 mg/kg, i.p.) strongly reduces the expression of nuclear β -catenin in tumors of mice[2].

References:

- [1]. Bibian M, et al. Development of highly selective casein kinase 1 δ /1 ϵ (CK1 δ / ϵ) inhibitors with potent antiproliferative properties. *Bioorg Med Chem Lett*. 2013 Aug 1;23(15):4374-80.
- [2]. Rosenberg LH, et al. Therapeutic targeting of casein kinase 1 δ in breast cancer. *Sci Transl Med*. 2015 Dec 16;7(318):318ra202.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA