Product Data Sheet

Product Name: RAF265
Cat. No.: GC15818

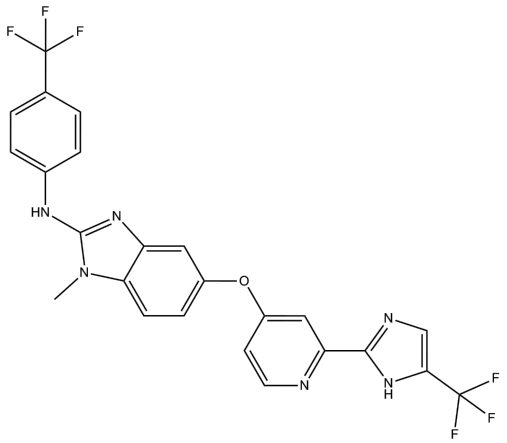
Chemical Properties

Cas. No.	927880-90-8		
Chemical Name	1-methyl-5-[2-[5-(trifluoromethyl)-1H-imidazol-2-yl]pyridin-4-yl]oxy-N-[4-(trifluoromethyl)phenyl]benzimidazol-2-amine		
SMILES	CN1C2=C(C=C(C=C2)OC3=CC(=NC=C3)C4=NC=C(N4)C(F)(F)F)N=C1NC5=CC=C(C=C5)C(F)(F)F		
Formula	$C_{24}H_{16}F_6N_6O$	M.Wt	518.43
Solubility	≥ 25.9mg/mL in DMSO, ≥ 7.97 mg/mL in EtOH with ultrasonic	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.		

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

Structure



Protocol

Cell experiment [1]:

Cell lines	A549, HCT116, HT29 and MDAMB231 cancer cell lines
Preparation method	The solubility of this compound in DMSO is >10 mM. 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.
Reaction Conditions	5 μM

Product Data Sheet

Applications	In all cell lines, RAF265 induced a decrease in clonogenic survival. In A549 cells, the combination of RAD001 and RAF265 enhanced the antiproliferative effect of RAF265.

Animal experiment [1]:

Animal models	Mice bearing H460 xenografts
Dosage form	12 mg/kg, p.o.; q.d.
Applications	In mice bearing H460 xenografts, RAD001 and RAF265 given alone showed limited effect on inhibition of tumor growth. When combined with RAD001, RAF265 significantly delayed tumor growth.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

[1]. Mordant P, Loriot Y, Leteur C, Calderaro J, Bourhis J, Wislez M, Soria JC, Deutsch E. Dependence on phosphoinositide 3-kinase and RAS-RAF pathways drive the activity of RAF265, a novel RAF/VEGFR2 inhibitor, and RAD001 (Everolimus) in combination. Mol Cancer Ther. 2010 Feb;9(2):358-68.

Background

RAF265, also known as CHIR-265, is a novel and orally available small molecule inhibitor of multiple intracellular kinases, including BRAFV600E, BRAF (wild-type), c-RAF, vascular endothelial growth factor receptor 2 (VEGFR2), platelet-derived growth factor receptor (PDGFR), colony-stimulating factor (CSF) 1R, RET, c-KIT, SRC and STE20, with half maximal inhibitory concentration IC50

Product Data Sheet

ranging from less than 20 nmo/L to more than 100 nmol/L, in which it exhibits the highest potency for BRAFV600E and VEGFR2 with half maximal effective concentration EC50 of 0.14 μM and 0.19 μM respectively. RAF265 has been found to inhibit proliferation of melanoma and colorectal cancer cell lines with active BRAF mutations and time- and dose-dependently suppress tumor regression in BRAFV600E melanoma and colorectal cancer xenograft models.

References:

[1]Huang T1, Karsy M, Zhuge J, Zhong M, Liu D. B-Raf and the inhibitors: from bench to bedside. J Hematol Oncol. 2013 Apr 25;6:30. doi: 10.1186/1756-8722-6-30.
[2]Garcia-Gomez A1, Ocio EM, Pandiella A, San Miguel JF, Garayoa M. RAF265, a dual BRAF and VEGFR2 inhibitor, prevents osteoclast formation and resorption. Therapeutic implications. Invest New Drugs. 2013 Feb;31(1):200-5. doi: 10.1007/s10637-012-9845-3. Epub 2012 Jul 7.
[3]Su Y1, Vilgelm AE, Kelley MC, Hawkins OE, Liu Y, Boyd KL, Kantrow S, Splittgerber RC, Short SP, Sobolik T, Zaja-Milatovic S, Dahlman KB, Amiri KI, Jiang A, Lu P, Shyr Y, Stuart DD, Levy S, Sosman JA, Richmond A. RAF265 inhibits the growth of advanced human melanoma tumors. Clin Cancer Res. 2012 Apr 15;18(8):2184-98. doi: 10.1158/1078-0432.CCR-11-1122. Epub 2012 Feb 20.