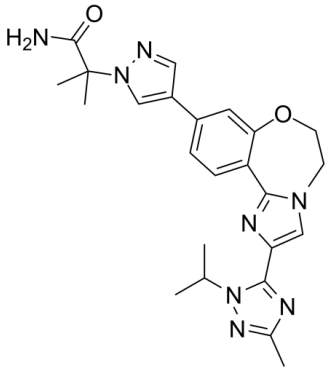
Data Sheet

Product Name:	Taselisib
Cat. No.:	CS-1817
CAS No.:	1282512-48-4
Molecular Formula:	C24H28N8O2
Molecular Weight:	460.53
Target:	PI3K
Pathway:	PI3K/Akt/mTOR
Solubility:	DMSO : 50 mg/mL (108.57 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

Taselisib (GDC-0032) is a potent **PI3K** inhibitor targets PIK3CA mutations, with **K_i**s of 0.12 nM, 0.29 nM, 0.97 nM, and 9.1 nM for PI3Kδ, PI3Kα, PI3Kγ and PI3Kβ, respectively. IC50 & Target: Ki: 0.29 nM (PI3Kα), 9.1 nM (PI3Kβ), 0.97 nM (PI3Kγ), 0.12 nM (PI3Kδ)[3] **In Vitro:** Taselisib (GDC-0032) (100 nM) inhibits AKT/mTOR signaling in PIK3CA mutant cell lines but not in cells with loss or mutation of PTEN; Taselisib (GDC-0032) enhances radiation-induced apoptosis and inhibits growth in head and neck cancer cell lines that are sensitive to its single-agent activiy[1]. Taselisib (GDC-0032) enhances the effects of MEK1/2 inhibition on both $BRAF^{V600E}$/$PTEN^{Null}$ human melanoma cells autochthonous mouse melanomas[2]. **In Vivo:** Taselisib (GDC-0032) (5 mg/kg, p.o.) potently impairs PI3K signaling and enhances the efficacy of fractionated radiotherapy; Taselisib (GDC-0032) and radiation is more effective than either treatment alone in nude mice implanted with subcutaneous Cal-33 xenografts[1]. The vehicle-treated BRAFV600E/PTENNull melanoma-bearing mice experiencs initial tumor regression after treatment with Taselisib (GDC-0032) (22.5 mg/kg, p.o.)[2].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: Taselisib (GDC-0032) is dissolved in DMSO.[1]Cells are seeded in replicates of 6 in 96-well plates with 500 to 5,000 cells/well overnight and then treated with Taselisib (GDC-0032). After 4 days, the media are removed and the cells are fixed with 4% glutaraldehyde for 30 minutes. Fixed cells are stained with 0.1% crystal violet for 2 minutes, then washed, and dissolved in 10% acetic acid. **Animal Administration:** Taselisib (GDC-0032) is dissolved in sterile water, 0.5% methyl-cellulose, and 0.2% Tween-80.[1]Six-week-old Nu/Nu mice are injected bilaterally with 5×10^5 cells resuspended in 200 µL of culture media and Matrigel mixed in a 1:1 ratio. After tumors reache approximately 100 to 200 cm^3, mice are randomized into treatment arms with 8 to 10 tumors per group. Taselisib (GDC-0032) (5 mg/kg) is dissolved in a vehicle containing 0.5% methylcellulose with 0.2% TWEEN-80 and is administered via daily oral gavage.

References:

[1]. Zachary S. Zumsteg, et al. Taselisib (GDC-0032), a Potent β-Sparing Small Molecule Inhibitor of PI3K, Radiosensitizes Head and Neck Squamous Carcinomas Containing Activating PIK3CA Alterations. Clin Cancer Res. 2016 Apr 15; 22(8): 2009–2019.

[2]. Marian M. Deuker, et al. PI3′-Kinase Inhibition Forestalls the Onset of MEK1/2 Inhibitor Resistance in BRAF-Mutated Melanoma. Cancer Discov. 2015 Feb; 5(2): 143–153.

[3]. Ndubaku CO, et al. Discovery of 2-<3-[2-(1-isopropyl-3-methyl-1H-1,2-4-triazol-5-yl)-5,6-dihydrobenzo[f]imidazo[1,2-d][1,4]oxazepin-9-yl]-1H-pyrazol-1-yl>-2-methylpropanamide (GDC-0032): a β-sparing phosphoinositide 3-kinase inhibitor with high unbound exposure and robust in vivo antitumor activity. J Med Chem. 2013 Jun 13;56(11):4597-610.

CAIndexNames:

1H-Pyrazole-1-acetamide, 4-[5,6-dihydro-2-[3-methyl-1-(1-methylethyl)-1H-1,2,4-triazol-5-yl]imidazo[1,2-d][1,4]benzoxazepin-9-yl]-α,α-dimethyl-

SMILES:

CC(C)N1C(C2=CN3C(C(C(OCC3)=C4)=CC=C4C5=CN(C(C)(C(N)=O)C)N=C5)=N2)=NC(C)=N1

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