产品名称：

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

产品别名：**Taselisib**

生物活性：

Description	Taselisib (GDC-0032) is a potent **PI3K** inhibitor targets PIK3CA mutations, with K_is of 0.12 nM, 0.29 nM, 0.97 nM, and 9.1 nM for PI3Kδ, PI3Kα, PI3Kγ and PI3Kβ, respectively.

IC_{50} & Target

PI3Kδ	PI3Kα	PI3Kγ	PI3Kβ
0.12 nM (Ki)	0.29 nM (Ki)	0.97 nM (Ki)	9.1 nM (Ki)

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 BRAFV600E/PTENNull 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].

Solvent&Solubility

In Vitro:

DMSO: 50 mg/mL (**108.57 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1714 mL	10.8571 mL	21.7141 mL
	5 mM	0.4343 mL	2.1714 mL	4.3428 mL
	10 mM	0.2171 mL	1.0857 mL	2.1714 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (5.43 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.43 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

	2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (5.43 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.43 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.43 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.43 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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]-1 H-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.

实验参考：

Cell Assay	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. [1]
Animal Administration	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. [1]
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.