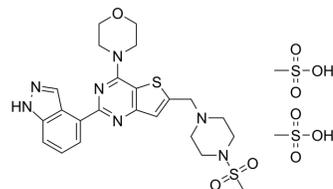


## Pictilisib dimethanesulfonate

<b>Cat. No.:</b>	HY-20180
<b>CAS No.:</b>	957054-33-0
<b>Molecular Formula:</b>	C <sub>25</sub> H <sub>35</sub> N <sub>7</sub> O <sub>9</sub> S <sub>4</sub>
<b>Molecular Weight:</b>	705.85
<b>Target:</b>	PI3K; Autophagy; Apoptosis
<b>Pathway:</b>	PI3K/Akt/mTOR; Autophagy; Apoptosis
<b>Storage:</b>	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



### SOLVENT & SOLUBILITY

#### In Vitro

H<sub>2</sub>O : 7.14 mg/mL (10.12 mM; ultrasonic and warming and heat to 60°C)  
DMSO : 7.14 mg/mL (10.12 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	1.4167 mL	7.0837 mL	14.1673 mL
	5 mM	0.2833 mL	1.4167 mL	2.8335 mL
	10 mM	0.1417 mL	0.7084 mL	1.4167 mL

Please refer to the solubility information to select the appropriate solvent.

### BIOLOGICAL ACTIVITY

#### Description

Pictilisib dimethanesulfonate (GDC-0941 dimethanesulfonate) is a potent inhibitor of PI3K $\alpha/\delta$  with IC<sub>50</sub> of 3 nM, with modest selectivity against p110 $\beta$  (11-fold) and p110 $\gamma$  (25-fold).

#### IC<sub>50</sub> & Target

p110 $\alpha$ 3 nM (IC <sub>50</sub> )	p110 $\alpha$ -H1047R 3 nM (IC <sub>50</sub> )	p110 $\alpha$ -E545K 3 nM (IC <sub>50</sub> )	p110 $\delta$ 3 nM (IC <sub>50</sub> )
p110 $\beta$ 33 nM (IC <sub>50</sub> )	p110 $\gamma$ 75 nM (IC <sub>50</sub> )	mTOR 0.58 $\mu$ M (Ki)	DNA-PK 1.23 $\mu$ M (IC <sub>50</sub> )
Autophagy			

#### In Vitro

Pictilisib (GDC-0941) and RP-56976 reduce tumor cell viability by 80% or greater in the breast cancer cell lines than single-agent treatment. GDC-0941 inhibits Akt phosphorylation and downstream targets of Akt signaling such as pPRAS40 and pS6 in Hs578T1.2 (PI3K $\alpha$  wild-type), MCF7-neo/HER2 (PI3K $\alpha$ -mutant), and MX-1 (PTEN-null) tumor models. Pictilisib (GDC-0941) decreases the time of RP-56976-induced mitotic arrest prior to apoptosis<sup>[1]</sup>. Pictilisib (GDC-0941) shows a high efficacy of antitumor activity in two ZD1839-resistant non-small cell lung cancer (NSCLC) cell lines, A549 and H460. Pictilisib (GDC-0941)

is highly efficacious in combination with U0126 in inducing cell growth inhibition, G0-G1 arrest and cell apoptosis. H460 cells with activating mutations of PIK3CA are relatively more sensitive to Pictilisib (GDC-0941) than A549 cells with wild-type PIK3CA<sup>[3]</sup>. Pictilisib (GDC-0941) reduces PI3K pathway activity in both cell lines, illustrated by decreased pAK. Pictilisib (GDC-0941) significantly reduces secreted VEGF detected in the medium after hypoxic/anoxic exposure in all cells<sup>[4]</sup>. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### In Vivo

Pictilisib (GDC-0941) (150 mg/kg, p.o.) leads to tumor stasis in MCF7-neo/HER2-bearing animals model. Pictilisib (GDC-0941) and RP-56976 result in tumor regressions during the treatment period leading to enhanced antitumor responses<sup>[1]</sup>. Tumours in the Pictilisib (GDC-0941)-treated mice show a marked non-linear shrinkage, and when the Pictilisib (GDC-0941) treatment ceased, the tumours in the test cohort mice grow again<sup>[2]</sup>. GDC-0941/Pictilisib (GDC-0941) (25 or 50 mg/kg) reduces tumor growth and PI3K and HIF-1 pathway activity in eGFP-FTC133 tumor-bearing mice<sup>[4]</sup>. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

#### Cell Assay <sup>[1]</sup>

Cells are treated at EC<sub>50</sub> concentrations of Pictilisib (GDC-0941), RP-56976, or both for 4 or 24 hours and lysed in 1×Cell Extraction Buffer supplemented with protease inhibitors and Phosphatase Inhibitor Cocktails 1 and 2. Protein concentrations are determined using the Pierce BCA Protein Assay Kit. For immunoblots, equal amounts of protein are separated by electrophoresis through NuPAGE Bis-Tris 10% gradient gels, transferred onto polyvinylidene difluoride membranes using the Criterion system, and probed with monospecific primary antibodies. Specific antigen-antibody interactions are detected with IRDye 680 or IRDye 800 infrared secondary antibodies using a LI-COR imaging system<sup>[1]</sup>. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### Animal Administration <sup>[1]</sup>

Mice<sup>[1]</sup>  
Female nu/nu mice are inoculated subcutaneously with MCF7-neo/HER2 or MX-1 breast cancer cells. When tumors reach a mean volume of 200 to 250 mm<sup>3</sup>, animals are size-matched and distributed into groups consisting of 10 animals per group. RP-56976 formulated in 3% EtOH, 97% saline is administered intravenously once weekly. Pictilisib (GDC-0941), formulated in MCT (0.5% methylcellulose, 0.2% Tween-80) is dosed orally and daily. MAXF1162 is an HER2+/ER+/PR+ patient-derived breast cancer tumor xenograft model established by directly implanting tumors subcutaneously from patient to NMRI nu/nu mice. Tumor volume is calculated. Tumor sizes are recorded twice weekly over the course of a study. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## CUSTOMER VALIDATION

- Nature. 2018 Aug;560(7719):499-503.
- Cell. 2023 Jun 22;186(13):2929-2949.e20.
- Cell Metab. 2021 Nov 2;33(11):2247-2259.e6.
- Cell Metab. 2012 Mar 7;15(3):382-94.
- Cancer Discov. 2012 May;2(5):425-33.

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## REFERENCES

[1]. Wallin JJ, et al. GDC-0941, a novel class I selective PI3K inhibitor, enhances the efficacy of RP-56976 in human breast cancer models by increasing cell death in vitro and in vivo. Clin Cancer Res. 2012 Jul 15;18(14):3901-11. Epub 2012 May 14.

[2]. Wullschleger S, et al. Quantitative MRI establishes the efficacy of PI3K inhibitor (GDC-0941) multi-treatments in PTEN-deficient mice lymphoma. Anticancer Res. 2012

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Feb;32(2):415-20.

[3]. Zou ZQ, et al. The novel dual PI3K/mTOR inhibitor GDC-0941 synergizes with the MEK inhibitor U0126 in non-small cell lung cancer cells. Mol Med Report. 2012 Feb;5(2):503-8.

[4]. Burrows N, et al. GDC-0941 inhibits metastatic characteristics of thyroid carcinomas by targeting both the phosphoinositide-3 kinase (PI3K) and hypoxia-inducible factor-1 $\alpha$  (HIF-1 $\alpha$ ) pathways. J Clin Endocrinol Metab. 2011 Dec;96(12):E1934-43. Epub 2011 Oct

[5]. Folkes AJ, et al. The identification of 2-(1H-indazol-4-yl)-6-(4-methanesulfonyl-piperazin-1-ylmethyl)-4-morpholin-4-yl-thieno[3,2-d]pyrimidine (GDC-0941) as a potent, selective, orally bioavailable inhibitor of class I PI3 kinase for the treatment of can

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

Tel: 609-228-6898

Fax: 609-228-5909

E-mail: [tech@MedChemExpress.com](mailto:tech@MedChemExpress.com)

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA