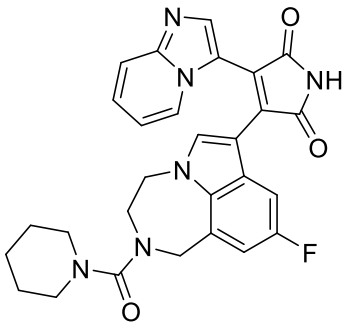
Product data sheet

MedKoo Cat#: 205518 Name: LY2090314 CAS#: 603288-22-8 Chemical Formula: $C_{28}H_{25}FN_6O_3$ Exact Mass: 512.19722 Molecular Weight: 512.53	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.



1. Product description:
LY2090314 is a potent inhibitor of glycogen synthase kinase-3 (GSK-3) which plays an important role in many pathways, including initiation of protein synthesis, cell proliferation, cell differentiation, and apoptosis. Pre-clinically LY2090314 i stabilizes β-catenin and enhances the efficacy of platinum based regimens.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	47.0	91.70
Ethanol	1.13	2.20

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.95 mL	9.76 mL	19.51 mL
5 mM	0.39 mL	1.95 mL	3.90 mL
10 mM	0.20 mL	0.98 mL	1.95 mL
50 mM	0.04 mL	0.20 mL	0.39 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Kunnimalaiyaan S, Schwartz VK, Jackson IA, Clark Gamblin T, Kunnimalaiyaan M. Antiproliferative and apoptotic effect of LY2090314, a GSK-3 inhibitor, in neuroblastoma in vitro. BMC Cancer. 2018 May 11;18(1):560. doi: 10.1186/s12885-018-4474-7. PMID: 29751783; PMCID: PMC5948712.
2. Atkinson JM, Rank KB, Zeng Y, Capen A, Yadav V, Manro JR, Engler TA, Chedid M. Activating the Wnt/β-Catenin Pathway for the Treatment of Melanoma--Application of LY2090314, a Novel Selective Inhibitor of Glycogen Synthase Kinase-3. PLoS One. 2015 Apr 27;10(4):e0125028. doi: 10.1371/journal.pone.0125028. PMID: 25915038; PMCID: PMC4411090.

In vivo study

1. Santoro R, Zanotto M, Simionato F, Zecchetto C, Merz V, Cavallini C, Piro G, Sabbadini F, Boschi F, Scarpa A, Melisi D. Modulating TAK1 Expression Inhibits YAP and TAZ Oncogenic Functions in Pancreatic Cancer. Mol Cancer Ther. 2020 Jan;19(1):247-257. doi: 10.1158/1535-7163.MCT-19-0270. Epub 2019 Sep 27. PMID: 31562256.
2. Atkinson JM, Rank KB, Zeng Y, Capen A, Yadav V, Manro JR, Engler TA, Chedid M. Activating the Wnt/β-Catenin Pathway for the Treatment of Melanoma--Application of LY2090314, a Novel Selective Inhibitor of Glycogen Synthase Kinase-3. PLoS One. 2015 Apr 27;10(4):e0125028. doi: 10.1371/journal.pone.0125028. PMID: 25915038; PMCID: PMC4411090.

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7. Bioactivity

Biological target:

LY2090314 is a potent inhibitor of glycogen synthase kinase-3 (GSK-3) with IC50 values of 1.5 nM and 0.9 nM for GSK-3α and GSK-3β, respectively.

In vitro activity

Several assays and imaging techniques were utilized to determine cellular growth patterns of 3 NB cell lines (NGP, SK-N-AS, and SH-SY-5Y) treated with LY2090314 or Tideglusib. Cells were plated and treated with LY2090314 in increasing nanomolar concentrations (20 nM, − 1000 nM), and proliferation was recorded using a colorimetric, MTT assay at 48 h, 72 h, and 96 h (Fig. 1). In Fig.1a, a steep reduction on average of 23% at 48 h, 42% at 72 h, and 61% at 96 h was noted in NGP cells treated with 20 nM of LY2090314. At higher concentrations of 25 nM – 1000 nM LY2090314 in the same cells, there was a more gradual reduction in cell growth, whereas, at 1000 nM a 37% reduction was seen at 48 h, 57% at 72 h, and 75% at 96 h. dditionally, a substantial decrease of 22 - 61% can be seen with the much lower concentrations of 20 nM of LY2090314 at 96 h in NGP, SK-N-AS, and SH-SY-5Y cells. SK-N-AS and SH-SY-5Y both showed similar decreases in growth, and like NGP, lower concentrations of LY2090314 in the nanomolar range more significantly inhibited growth compared to the micromolar range of Tideglusib. In summary, MTT assay data showed a significant decrease in cellular proliferation in all 3 cell lines treated with LY2090314 at concentrations of 20, 25, 50, 100, and 1000 nM during 48, 72, and 96 h. To confirm MTT results, CFU assays were performed in all cell lines with increasing concentrations of LY2090314 (10 nM – 50 nM) which showed a reduction in NB cells ability to form colonies (Fig. 2a). Lastly, to examine confluency of cells, Incucyte imaging data was collected every 3 h up to 4 days and graphed (Fig.2b). Decreasing confluency over time is noted in all cell lines treated with increasing concentrations of LY2090314. This is the first study in NB (neuroblastoma), and LY2090314 is a potential agent for the treatment of NB in future.

Reference: BMC Cancer. 2018; 18: 560. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5948712/

In vivo activity

It was sought to assess the ability of LY2090314 to activate the Wnt pathway in vivo and subsequently question if pathway elevation could lead to antitumor efficacy in melanoma. In mouse, LY2090314 is rapidly cleared and has a plasma half-life of 36 minutes (Fig 5A). In studies assessing the in vivo gene expression of Axin2, a Wnt responsive gene, a significant induction of Axin2 mRNA at 2 and 4 hours post dose of LY2090314 was observed in A375 xenograft tumor tissue (Fig 5B). This finding is in agreement with the in vitro experiments which also reveal Axin2 elevation 2–4 hours after initial drug exposure (Fig 1E). The rapid decline in Axin2 gene expression after 4 hours is consistent with the short half-life and pharmacokinetic properties of the compound in vivo (Fig 5A and 5B). Despite the transient elevation of the Wnt pathway with LY2090314 treatment, a single agent antitumor efficacy was able to be observed in subcutaneous A375 xenografts dosed every 3 days (Fig 5C, $p<0.003$). The in vitro and in vivo activity of LY2090314 in preclinical models suggests that the role of Wnt activators for the treatment of both BRAF and NRAS driven human melanoma should be further explored.

Reference: PLoS One. 2015; 10(4): e0125028. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4411090/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.