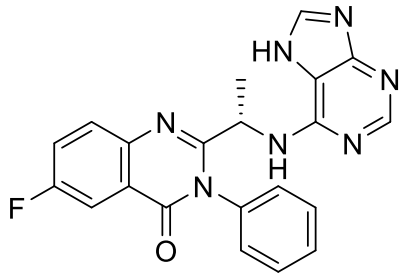
Product data sheet

MedKoo Cat#: 205966 Name: Acalisib CAS#: 870281-34-8 Chemical Formula: $C_{21}H_{16}FN_7O$ Exact Mass: 401.14004 Molecular Weight: 401.4	
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:

Acalisib, also known as GS-9820, is an inhibitor of the beta and delta isoforms of the 110 kDa catalytic subunit of class IA phosphoinositide-3 kinases (PI3K) with potential immunomodulating and antineoplastic activities. p110beta/delta PI3K inhibitor GS-9820 inhibits the activity of PI3K, thereby preventing the production of the second messenger phosphatidylinositol-3,4,5-trisphosphate (PIP3), which decreases tumor cell proliferation and induces cell death. PI3K-mediated signaling is often dysregulated in cancer cells; the targeted inhibition of PI3K is designed to preserve PI3K signaling in normal, non-neoplastic cells.

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	80	199.30

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.49 mL	12.46 mL	24.91 mL
5 mM	0.50 mL	2.49 mL	4.98 mL
10 mM	0.25 mL	1.25 mL	2.49 mL
50 mM	0.05 mL	0.25 mL	0.50 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. Shugg RP, Thomson A, Tanabe N, Kashishian A, Steiner BH, Puri KD, Pereverzev A, Lannutti BJ, Jirik FR, Dixon SJ, Sims SM. Effects of isoform-selective phosphatidylinositol 3-kinase inhibitors on osteoclasts: actions on cytoskeletal organization, survival, and resorption. J Biol Chem. 2013 Dec 6;288(49):35346-57. doi: 10.1074/jbc.M113.507525. Epub 2013 Oct 16. PMID: 24133210; PMCID: PMC3853283.

In vivo study

1. Lopez-Guadamillas E, Muñoz-Martin M, Martinez S, Pastor J, Fernandez-Marcos PJ, Serrano M. PI3Kα inhibition reduces obesity in mice. Aging (Albany NY). 2016 Nov 4;8(11):2747-2753. doi: 10.18632/aging.101075. PMID: 27816049; PMCID: PMC5191867.

7. Bioactivity

Biological target:

Acalisib (GS-9820, CAL-120) is a highly selective and potent p110δ inhibitor (IC50 = 14 nM) with 114- to 400-fold selectivity over the other class I PI3K enzymes and no activity against Class II and III PI3K family members or other PI3K-related proteins including mTOR and DNA-PK.

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In vitro activity

The novel PI3Kδ inhibitor GS-9820 (Acalisib) (Table 2A) was characterized using in vitro activity assays. It was found that GS-9820 was more selective for PI3Kδ relative to other PI3K class I enzymes (IC50: PI3Kα, 5,441 nm; PI3Kβ, 3,377 nm; PI3Kγ, 1,389 nm; and PI3Kδ, 12.7 nm) (Table 2B). GS-9820 was also 103-fold more selective against PI3Kδ than against related kinases, such as CIIβ, hVPS34, DNAPK, and mammalian target of rapamycin. EC50 values were characterized using in vitro cell-based assays. GS-9820 reduced PDGF-induced pAkt by only 50% at 11,585 nm, and LPA-induced pAkt by 50% at 2,069 nm (Table 2C). Expression of PI3Kγ and PI3Kδ is largely restricted to cells of hematopoietic origin, including basophils. GS-9820 suppressed FcεRI PI3Kδ-mediated CD63 expression with an EC50 of 14 nm, and fMLP PI3Kγ-mediated CD63 expression with an EC50 of 2,065 nm (supplemental Fig. S2). Thus, GS-9820 showed selectivity for PI3Kδ over the other class I PI3K isoforms and virtually no binding to a panel of other kinases.

Reference: J Biol Chem. 2013 Dec 6;288(49):35346-57. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/24133210/

In vivo activity

To dissect the relative contribution of PI3Kα inhibition in the reduction of obesity, obese hyperphagic ob/ob mice were treated with a selective PI3K δ inhibitor, GS-9820 (Acalisib). GS-9820 had no significant effect on body weight (Figure 1A and and 1B). It should be noted that 10 mg/kg of GS-9820 is sufficient to reduce the growth of multiple myeloma xenografts in mice. Obese ob/ob mice are insulin resistant and therefore their glycemic excursions were severe (up to 500 mg/dl) in the case of the two PI3Kα inhibitors, CNIO-PI3Ki and BYL-719, whereas GS-9820 had a comparatively minor effect (Figure 2A). GS-9820 had no detectable effect on serum lipids.

Refernece: Aging (Albany NY). 2016 Nov 4;8(11):2747-2753. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/27816049/