Lifirafenib (BGB-283)

Catalog No.C13058 Batch:C1305803

Product Datasheet

Technical Data

Formula	$C_{25}H_{17}F_3N_4O_3$					
Molecular Weight	478.42	**CAS No.**	1446090-79-4			
Solubility (25°C)*	In vitro	DMSO	95 mg/mL (198.57 mM)			
		Ethanol	95 mg/mL (198.57 mM)			
		Water	Insoluble			
	In vivo (Add solvents to the product individually and in order)	Oral Administration	Homogeneous suspension	CMC-NA	≥5mg/ml	Taking the 1 mL working solution as an example, add 5 mg of this product to 1 ml of CMC-Na solution, mix evenly to obtain a homogeneous suspension with a final concentration of 5 mg/ml.
		Injection	Clear solution	5%DMSO [1]→ 40%PEG300 [2]→ 5%Tween80 [3]→ 50%ddH2O Validated by Capsid Bio labs. Should you need adjustments to this formulation, contact our sales team for custom testing.	2.300mg/ml (4.81mM)	Taking the 1 mL working solution as an example, add 50 μL of 46 mg/ml clarified DMSO stock solution to 400 μL of PEG300, mix evenly to clarify it; add 50 μL of Tween80 to the above system, mix evenly to clarify; then continue to add 500 μL of ddH2O to adjust the volume to 1 mL. The mixed solution should be used immediately for optimal results.
			Clear solution	5% DMSO [1]→ 95% Corn oil Validated by Capsid Bio labs. Should you need adjustments to this formulation, contact our sales team for custom testing.	0.790mg/ml (1.65mM)	Taking the 1 mL working solution as an example, add 50 μL of 15.8 mg/ml clear DMSO stock solution to 950 μL of corn oil and mix evenly. The mixed solution should be used immediately for optimal results.

* <1 mg/ml means slightly soluble or insoluble.
* Please note that Capsid Bio tests the solubility of all compounds in-house, and the actual solubility may differ slightly from published values. This is normal and is due to slight batch-to-batch variations.
* Room temperature shipping (Stability testing shows this product can be shipped at 2-8°C for storage purposes.)

Preparing Stock Solutions

Concentration \ Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.0902 mL	10.4511 mL	20.9021 mL
5 mM	0.4180 mL	2.0902 mL	4.1804 mL
10 mM	0.2090 mL	1.0451 mL	2.0902 mL
50 mM	0.0418 mL	0.2090 mL	0.4180 mL

Biological Activity

Description	Lifirafenib (BGB-283, Beigene-283) potently inhibits RAF family kinases and EGFR activities in biochemical assays, with IC50 values of 23, 29 and 495 nM for the recombinant BRAFV600E kinase domain, EGFR and EGFR T790M/L858R mutant.
Targets	WT A-RAF [1] (Cell-free assay): 1 nM C-RAF (Y340/341D) [1] (Cell-free assay): 7 nM BRAF(V600E) [1] (Cell-free assay): 23 nM EGFR [1] (Cell-free assay): 29 nM BRAF WT [1] (Cell-free assay): 32 nM View More →
In vitro	Lifirafenib (BGB-283) potently inhibits BRAFV600E-activated ERK phosphorylation and cell proliferation in vitro. It demonstrates selective cytotoxicity and preferentially inhibits proliferation of cancer cells harboring BRAFV600E and EGFR mutation/amplification. In BRAFV600E colorectal cancer cell lines, this compound effectively inhibits the reactivation of EGFR and EGFR-mediated cell proliferation. It demonstrates selective cytotoxicity to cell lines harboring BRAFV600E or EGFR mutations. In A431 cells, it inhibits the EGF-induced EGFR autophosphorylation on Tyr1068 in a dose-dependent manner. In WiDr colorectal cancer cells, it is shown to be able to inhibit the feedback activation of EGFR signaling and achieves sustained inhibition of pERK[1].
In vivo	Lifirafenib (BGB-283) treatment leads to dose-dependent tumor growth inhibition accompanied by partial and complete tumor regressions in both cell line-derived and primary human colorectal tumor xenografts bearing BRAFV600E mutation. It is highly efficacious in BRAF(V600E) colorectal cancer xenograft models, including HT29, Colo205, and two primary tumor xenografts harboring BRAFV600E mutation. In addition, this compound shows compelling efficacy in a WiDr xenograft model where EGFR reactivation is shown to be induced upon BRAF inhibition. It induces tumor regression in HCC827 but not in A431 xenograft. BGB-283 inhibits phosphorylation of both ERK1/2 and EGFR and displays potent antitumor activity in WiDr tumor xenografts. It potently inhibits MEK and ERK phosphorylation and DUSP6 expression in vivo when dosed repeatedly. There is no detectable difference on AKT phosphorylation[1].

Protocol (from reference)

Cell Assay:[1]

- **Cell lines**
  A375 cells
- **Concentrations**
  0.03, 1, 10 μM
- **Incubation Time**
  3 days
- **Method**
  The number of cells seeded per well of a 96-well plate is optimized for each cell line to ensure logarithmic growth over the 3 days treatment period. Cells are left to attach for 16 hours and then treated with a 10-point dilution series of Lifirafenib (BGB-283) in duplicate. Following a 3-day exposure to the compound, a volume of CellTiter-Glo reagent equal to the volume of cell culture medium present in each well is added. Mixture is mixed on an orbital shaker for 2 minutes to allow cell lysing, followed by 10 minutes incubation at room temperature to allow development and stabilization of luminescent signal. Luminescent signal is measured

Animal Study:[1]

- **Animal Models**
  NOD/SCID and BALB/c nude mice
- **Dosages**
  2.5 to 30 mg/kg
- **Administration**
  p.o.

References

https://pubmed.ncbi.nlm.nih.gov/26208524/

RETURN POLICY

Capsid Bio's Unconditional Return Policy ensures a smooth online shopping experience for our customers. If you are in any way unsatisfied with your purchase, you may return any item(s) within 7 days of receiving it. In the event of product quality issues, either protocol related or product related problems, you may return any item(s) within 365 days from the original purchase date. Please follow the instructions below when returning products.

SHIPPING & STORAGE

Capsid Bio products are transported at room temperature. If you receive the product at room temperature, please rest assured, the Capsid Bio Quality Inspection Department has conducted experiments to verify that the normal temperature placement of one month will not affect the biological activity of powder products. After collecting, please store the product according to the requirements described in the datasheet. Most Capsid Bio products are stable under the recommended conditions.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

EU Headquarters
Gajeva ulica 28, HR-10000 Zagreb, Croatia

US Headquarters
12222 Merit Dr STE 130 Dallas, Texas, 75251

UK Headquarters
121 ABILITY HOUSE, BROOKER ROAD, EN9 1JH, ESSEX

Orders: Sales@capsidbio.com
Enquiries: info@capsidbio.com
www.capsidbio.com