Product Datasheet

LXH254

Catalog No. **BP-02136** · CAS **1800398-38-2** · Form **free base** · Physical state **other** · Color **Off-white to light yellow** · Version **1.0** · Revision **2026-09-03**

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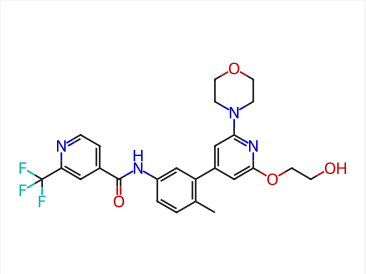
Target	Research area
Raf; p38 MAPK; Bcr-Abl	**Cancer**

Molecular formula	$C_{25}H_{25}F_3N_4O_4$
Molecular weight	**502.4856**

STRUCTURE



DESCRIPTION

LXH254 is a potent B/C RAF inhibitor extracted from patent WO2018051306A1, Compound A.

BIOLOGICAL ACTIVITY

In Vitro

Naporafenib (Compound A) is an adenosine triphosphate (ATP)-competitive inhibitor of BRAF (also referred to herein as b-RAF or b-Raf) and CRAF (also referred to herein as c-RAF or c- Raf) protein kinases. Throughout the present disclosure, Naporafenib is also referred to as a c-RAF (or CRAF) inhibitor or a C-RAF/c-Raf kinase inhibitor. In cell-based assays, Naporafenib has demonstrated anti-proliferative activity in cell lines that contain a variety of mutations that activate MAPK signaling. Moreover, Naporafenib is a Type 2 ATP -competitive inhibitor of both B-Raf and C-Raf that keeps the kinase pocket in an inactive conformation, thereby reducing the paradoxical activation seen with many B-Raf inhibitors, and blocking mutant RAS-driven signaling and cell proliferation.

Naporafenib (0-10 μM, 1 h) inhibits both monomeric and dimeric RAF and promotes RAF dimer formation[2].

Naporafenib has reduced ability to suppress MAPK signaling driven by ARAF and further that the contribution of ARAF to MAPK signaling increases in the absence of CRAF expression.

Naporafenib shows more sensitivity when cells lack ARAF.

In Vivo

Treatment with Naporafenib (Compound A) generates tumor regression in several KRAS-mutant models including the NSCLC-derived Calu-6 (KRAS Q61K) and NCI-H358 (KRAS G12C). Naporafenib exhibits efficacy in numerous MAPK-driven human cancer cell lines and in xenograft tumors representing model tumors harboring human lesions in KRAS, NRAS and BRAF oncogenes.

Naporafenib shows significant antitumor activity in models harboring BRAF mutations either alone or coincident with either activated NRAS or KRAS, and RAS mutants lacking ARAF are more sensitive to Naporafenib.

SOLUBILITY

Soluble in DMSO

REFERENCES

[1]. CAPONIGRO, Giordano, et al. THERAPEUTIC COMBINATIONS COMPRISING A RAF INHIBITOR AND A ERK INHIBITOR. WO 2018051306 A1 20180322

[2]. Kelli-Ann Monaco, et al. LXH254, a Potent and Selective ARAF-Sparing Inhibitor of BRAF and CRAF for the Treatment of MAPK-Driven Tumors. Clin Cancer Res. 2021 Apr 1;27(7):2061-2073.