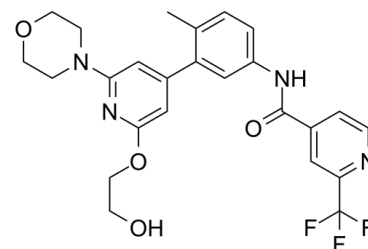


## Data Sheet

<b>Product Name:</b>	LXH254
<b>Cat. No.:</b>	CS-0043317
<b>CAS No.:</b>	1800398-38-2
<b>Molecular Formula:</b>	C <sub>25</sub> H <sub>25</sub> F <sub>3</sub> N <sub>4</sub> O <sub>4</sub>
<b>Molecular Weight:</b>	502.49
<b>Target:</b>	Raf
<b>Pathway:</b>	MAPK/ERK Pathway
<b>Solubility:</b>	DMSO : ≥ 83.3 mg/mL (165.77 mM)



### BIOLOGICAL ACTIVITY:

LXH254 is a potent **B/C RAF** inhibitor extracted from patent WO2018051306A1, Compound A. IC<sub>50</sub> & Target: CRAF, BRAF<sup>[1]</sup> **In Vitro:** LXH254 (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, LXH254 is also referred to as a c-RAF (or CRAF) inhibitor or a C-RAF/c-Raf kinase inhibitor. In cell-based assays, LXH254 has demonstrated anti-proliferative activity in cell lines that contain a variety of mutations that activate MAPK signaling. Moreover, LXH254 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<sup>[1]</sup>. **In Vivo:** Treatment with LXH254 (Compound A) generates tumor regression in several KRAS-mutant models including the NSCLC-derived Calu-6 (KRAS Q61K) and NCI-H358 (KRAS G12C). LXH254 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<sup>[1]</sup>.

### PROTOCOL (Extracted from published papers and Only for reference)

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

SCID beige female tumor-bearing NCI-H358 mice, n=8 per group, are randomized into 3 groups 14 days post tumor cell inoculation with an average tumor volume range of 259.44- 262.47mm<sup>3</sup>. Animals are administered an oral dose of either vehicle, LXH254 at 30mg/kg or 200mg/kg daily for 14 consecutive days at a dosing volume of 10 mL/kg of animal body weight during course of treatment. Tumor volumes are measured by digital caliper 3 times a week and body weights of all animals are recorded through the course of treatment.

Female nude tumor bearing Calu6 mice, n=6 per group are randomized into treatment groups on day 17 following tumor implantation, when the average tumor volume is 180 mm<sup>3</sup>. Treatments with LXH254 are initiated on Day 17 and continued for 16 days. Dosing volume is 10 mL/kg. Tumor volumes are collected at the time of randomization and twice weekly thereafter for the study duration.

Nude female mice tumor bearing NCI-H358, n=8 per group, are randomized into 2 groups with an average tumor volume range of 275.74 mm<sup>3</sup>. Animals are administered an oral dose of either vehicle or LXH254 at 100 mg/kg daily for 14 consecutive days at a dosing volume of 10 mL/kg of animal body weight during course of treatment. Tumor volumes are measured by digital caliper 3 times a week and body weights of all animals are recorded through the course of treatment<sup>[1]</sup>.

### References:

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

**CAIndexNames:**

4-Pyridinecarboxamide, N-[3-[2-(2-hydroxyethoxy)-6-(4-morpholinyl)-4-pyridinyl]-4-methylphenyl]-2-(trifluoromethyl)-

**SMILES:**

CC1=CC=C(NC(C2=CC(C(F)(F)F)=NC=C2)=O)C=C1C3=CC(N4CCOCC4)=NC(OCCO)=C3

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

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