# KRAS G12C inhibitor 57

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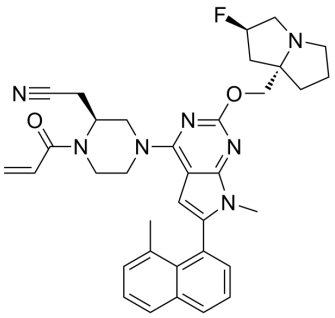
| **Cat. No.:** | HY-151968 |
| **CAS No.:** | 2821863-70-9 |
| **Molecular Formula:** | $C_{35}H_{38}FN_7O_2$ |
| **Molecular Weight:** | 607.72 |
| **Target:** | Ras |
| **Pathway:** | GPCR/G Protein |
| **Storage:** | Please store the product under the recommended conditions in the Certificate of Analysis. |



## BIOLOGICAL ACTIVITY

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| **Description** | KRAS G12C inhibitor 57 (Compound 50) is a potent, selective, covalent and orally active KRAS G12C inhibitor with an $IC_{50}$ of 0.21 μM in KRAS G12C/SOS1 binding assay. KRAS G12C inhibitor 57 induces cancer cell apoptosis[1]. |
| **$IC_{50}$ & Target** | KRAS(G12C)<br>0.21 μM ($IC_{50}$, KRAS G12C/SOS1 binding assay) |

**In Vitro**

KRAS G12C inhibitor 57 (Compound 50) (0-10 μM; 3 days) has selective inhibition on KRAS and KRAS-driven cell lines, together with strong inhibition on downstream signaling[1].
KRAS G12C inhibitor 57 (0.1-1 μM; 24 h) induces H358 cell apoptosis[1].
KRAS G12C inhibitor 57 (0.1-1 μM; 48 h) inhibits tumor metastasis in H358 cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

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| Cell Line: | H358 (KRAS p. G12C) cells |
| Concentration: | 0, 0.1, 0.3, 0.5, 1 and 5 μM |
| Incubation Time: | 4 and 24 h |
| Result: | Inhibited the active KRAS-GTP and the phosphorylation of ERK and AKT (MAPK and PI3K pathway) in the dose- and time-dependent manners, and strong inhibitory effects on the phosphorylation of ERK at the concentration of 0.1 μM. Increased the cleaved PARP and caspase-7 induction (24 h). |

Western Blot Analysis[1]

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| Cell Line: | H1975 cell line |
| Concentration: | 5, 10, and 20 μM |
| Incubation Time: | 4 h |
| Result: | Interrupted the phosphorylation of ERK. |

Cell Proliferation Assay[1]

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| Cell Line: | H358 cells harboring KRAS p.G12C, MIA Paca2 cells harboring KRAS p.G12C, H1975 cells harboring KRAS p.WT and A549 cells harboring KRAS p.G12S |
| Concentration: | 0-10 μM |
| Incubation Time: | 3 days |
| Result: | Displayed favourable inhibitory activities on H358 cells and MIA Paca2 cells with the $IC_{50}$ values of 0.16 μM and 0.87 μM, in sharp contrast with no obvious inhibition on cell proliferation on H1975 cells ($IC_{50}$ = 7.91 μM) and A549 cells ($IC_{50}$ = 29.9 μM). |

Apoptosis Analysis[1]

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| Cell Line: | H358 cell line |
| Concentration: | 0.1, 0.3, 0.5 and 1 μM |
| Incubation Time: | 24 h |
| Result: | Induced cellular apoptosis in dose-dependent manner. |

Cell Migration Assay [1]

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| Cell Line: | H358 cells |
| Concentration: | 0.1, 0.5 and 1 μM |
| Incubation Time: | 48 h |
| Result: | Significantly suppressed the migration. |

Cell Invasion Assay[1]

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|---|---|
| Cell Line: | H358 cells |
| Concentration: | 0.1, 0.5 and 1 μM |
| Incubation Time: | 48 h |
| Result: | Inhibited the cellular invasion and exhibited the dose-dependent inhibitory potency. |

**In Vivo**

KRAS G12C inhibitor 57 (Compound 50) (10 and 30 mg/kg; p.o.; daily for 20 days) shows anti-tumor efficacy in mice H358 xenograft model[1].

Pharmacokinetic data of KRAS G12C inhibitor 57 (Compound 50) in ICR mice. [1]

| Parameter | iv (3 mg/kg) | Parameter | po (30 mg/kg) |
|---|---|---|---|
| $AUC_{(0-t)}$ (h*ng/mL) | 801 | $AUC_{(0-t)}$ (h*ng/mL) | 600 |
| $AUC_{(0-\infty)}$ (h*ng/mL) | 804 | $AUC_{(0-\infty)}$ (h*ng/mL) | 835 |
| $C_0$ (ng/mL) | 1964 | $C_{max}$ (ng/mL) | 316 |
| $T_{1/2}$ (h) | 0.930 | $T_{1/2}$ (h) | 4.79 |

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|---|---|---|---|
| $V_{ss}$ (L/kg) | 4.98 | $T_{max}$ (h) | 0.083 |
| CL (mL/h/kg) | 3739 | F (%) | 10.4 |
| $AUC_{0-inf}$ (h*mg/mL) | 7060 ± 1020 (14.5%) | 21800 ± 2310 (10.6%) | 101000 ± 16700 (16.6%) |

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| Animal Model: | BALB/c-nu/nu mice, H358 xenograft model[1] |
| Dosage: | 10 mg/kg and 30 mg/kg |
| Administration: | Oral administration, daily for 20 days |
| Result: | Significantly inhibited the tumor growth in a dose-dependent manner with remarkable tumor regression at the dose of 30 mg/kg (tumor growth inhibition, TGI = 84.0%). All dosage groups were well-tolerated with no loss of body weight and no morphological damage to viscera including the heart, spleen, and kidney. Significantly suppressed the phosphorylation of ERK and AKT in tumors of nude mice when dosing orally at 10 mg/kg and 30 mg/kg. |

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|---|---|
| Animal Model: | ICR mice[1] |
| Dosage: | 3 mg/kg or 30 mg/kg |
| Administration: | IV or PO (Pharmacokinetic Analysis) |
| Result: | Displayed reasonable clearance and half-life by iv administration. Showed a moderate oral bioavailability (F) of 10.4%. |

## REFERENCES

[1]. Song Z, et al. Identification of novel Pyrrolo [2, 3-d] Pyrimidine-based KRAS G12C inhibitors with anticancer effects. European Journal of Medicinal Chemistry, 2022: 114907.

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

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