# Brigimadlin

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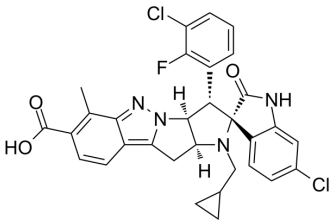
| **Cat. No.:** | HY-152859 |
| **CAS No.:** | 2095116-40-6 |
| **Molecular Formula:** | $C_{31}H_{25}Cl_2FN_4O_3$ |
| **Molecular Weight:** | 591 |
| **Target:** | E1/E2/E3 Enzyme; MDM-2/p53 |
| **Pathway:** | Metabolic Enzyme/Protease; Apoptosis |
| **Storage:** | Powder -20°C 3 years<br>4°C 2 years<br>In solvent -80°C 6 months<br>-20°C 1 month |



## BIOLOGICAL ACTIVITY

**Description**

Brigimadlin (BI 907828) is an orally active E3 ubiquitin-protein ligase MDM-2 inhibitor, preventing MDM-2 from negatively regulating the tumor suppressor p53. Brigimadlin can be used for antineoplastic research[1][2][3][4].

**In Vitro**

Brigimadlin (0-10 nM, 48 h) inhibits viability and induces cell death in brain tumor stem cells (BTSCs)[3].
Brigimadlin (1-50 nM, 48 h) induces apoptosis and increases p53 transcriptional targets (p21 and PUMA) in BT48, BT67, BT73 cells[3].
Brigimadlin (1 nM, 48 h) disrupts the interaction between MDM2 and wild-type p53 in brain tumor stem cells (BTSCs)[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[3]

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| Cell Line: | BT48, BT50, BT67, BT69, BT89, BT94 |
| Concentration: | 0-10 nM |
| Incubation Time: | 48 h |
| Result: | $IC_{50}$: 58.5, 21.1, 37.9, 89.8, 16.7, 46.8 pM. |

Western Blot Analysis[3]

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|---|---|
| Cell Line: | BT48, BT67, BT73 cells |
| Concentration: | 0-50 nM |
| Incubation Time: | 48 h |
| Result: | Upregulated p21 and PUMA, and increased cleaved PARP level. |

**In Vivo**

Brigimadlin (15 and 50 mg/kg, p.o., once a week) inhibits tumor growth and increases median survival in orthotopic xenografts of both a MDM2 amplified (BT48) and a normal CN (BT67), TP53 wild-type BTSC model[3].
Brigimadlin (50 mg/kg, p.o., a single dose) increasees PD biomarkers (CDKN1a and GDF15) in the brain in orthotopic GBM patient-derived BTSC models (BT48 and BT67) in SCID mice, and has low systemic clearance[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## REFERENCES

[1]. Gollner Andreas, et al. Preparation of spiroindolepyrrolidinone derivatives for use as MDM2-p53 inhibitors: World Intellectual Property Organization, WO2017060431. 2017-04-13.

[2]. WHO Drug Information-World Health Organization (WHO).

[3]. Hao X, et al. BI-907828, a novel potent MDM2 inhibitor, inhibits glioblastoma brain tumor stem cells in vitro and prolongs survival in orthotopic xenograft mouse models. Neuro Oncol. 2023 May 4;25(5):913-926.

[4]. Yoo C, et al. Brightline-2: a phase IIa/IIb trial of brigimadlin (BI 907828) in advanced biliary tract cancer, pancreatic ductal adenocarcinoma or other solid tumors. Future Oncol. 2024 Jan 12.



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