# LLK203

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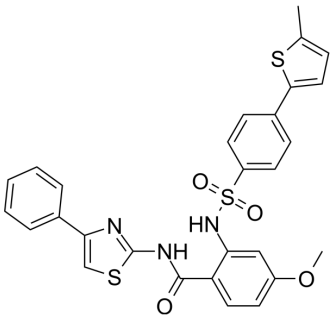
| **Cat. No.:** | HY-162312 |
| **CAS No.:** | 2758090-62-7 |
| **Molecular Formula:** | $C_{28}H_{23}N_3O_4S_3$ |
| **Molecular Weight:** | 561.69 |
| **Target:** | Deubiquitinase; Apoptosis |
| **Pathway:** | Cell Cycle/DNA Damage; Apoptosis |
| **Storage:** | Please store the product under the recommended conditions in the Certificate of Analysis. |



## BIOLOGICAL ACTIVITY

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| **Description** | LLK203 is a potent USP2/USP8 dual-target inhibitor with $IC_{50}$s of 0.89 μM and 0.52 μM, respectively. LLK203 leads a degradation of ERα and induces apoptosis of breast cancer MCF-7 cells. LLK203 demonstrates antitumor activities against the 4T1 tumor mice model[1]. |

| **$IC_{50}$ & Target** | USP2 | USP8 |
|---|---|---|
| | 0.89 μM ($IC_{50}$) | 0.52 μM ($IC_{50}$) |

**In Vitro**

LLK203 (0-100 μM; 36 h) demonstrates high inhibitory activity on MCF-7 cells ($IC_{50}$=3.4 μM) compared with ML364 ($IC_{50}$=9.3 μM). LLK203 demonstrates a 4-fold increase in USP2 activity and a 9-fold increase in USP8 activity compared to ML364 (HY-100900)[1].

LLK203 (10-50 μM; 24 h) increases the ratio of apoptotic cells and remaines largely in G1 phas on MCF-7 cells[1].

LLK203 (2-50 μM; 24 h) can degrade various proteins (MDM2, Cyclin D1, Her2, ERα) in a dosedependent manner[1].

LLK203 (2-50 μM; for 7 days) shows a robust ability of inhibiting clone formation at the concentration of 10 μM[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Cytotoxicity Assay[1]

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| Cell Line: | MCF-7 and MCF10A cells |
| Concentration: | 0-100 μM |
| Incubation Time: | 36 h |
| Result: | Exhibited lower cytotoxicity towards normal cells (MCF10A; $IC_{50}$=20.4 μM), while demonstrating higher inhibitory activity on BC cells (MCF-7; $IC_{50}$=3.4 μM). |

Apoptosis Analysis[1]

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| Cell Line: | MCF-7 cells |
| Concentration: | 10, 30, 50 μM |
| Incubation Time: | 24 h |
| Result: | Increased the ratio of apoptotic cells. |

Cell Cycle Analysis[1]

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|---|---|
| Cell Line: | MCF-7 cells |
| Concentration: | 10, 30, 50 μM |
| Incubation Time: | 24 h |
| Result: | Remained largely in G1 phase. |

Western Blot Analysis[1]

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| Cell Line: | MCF-7 cells |
| Concentration: | 2, 5, 10, 30, 50 μM |
| Incubation Time: | 24 h |
| Result: | Could degrade various proteins (MDM2, Cyclin D1, Her2, ERα) in a dosedependent manner. |

**In Vivo**

LLK203 (20 mg/kg; Intraperitoneal; every day; for 23 days) significantly reduces tumor growth in a 4T1 tumor-bearing mice model[1].

Pharmacokinetic Parameters of LLK203 in male Sprague-Dawley rats[1].

| | Intravenously (5 mg/kg) | Orally (50 mg/kg) |
|---|---|---|
| $T_{max}$ (h) | | 6 |
| $C_{max}$ (ng/mL) | 36630 | 1572 |
| $AUC_{0-t}$ (h⊠ng/mL) | 60824 | 19144 |
| $T_{1/2}$ (h) | 20 | 6.14 |
| CL (mL/h/kg) | 58 | |
| F (%) | | 2.2% |

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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|---|---|
| Animal Model: | BALB/c mice subcutaneously inoculated with 4T1 cells[1] |
| Dosage: | 20 mg/kg |
| Administration: | Intraperitoneal; every day; for 23 days |
| Result: | Significantly reduced tumor growth in a 4T1 tumor-bearing mice model. |

## REFERENCES

[1]. Yucheng Tian, et al. The discovery of potent USP2/USP8 dual-target inhibitors for the treatment of breast cancer via structure guided optimization of ML364. European Journal of Medicinal Chemistry. Volume 268, 15 March 2024, 116275.

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

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