# PPI-2458

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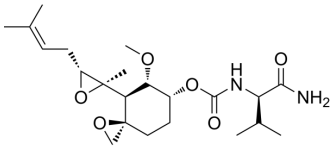
| **Cat. No.:** | HY-13731 |
| **CAS No.:** | 431077-35-9 |
| **Molecular Formula:** | $C_{22}H_{36}N_2O_6$ |
| **Molecular Weight:** | 424.53 |
| **Target:** | MetAP |
| **Pathway:** | Metabolic Enzyme/Protease |
| **Storage:** | Please store the product under the recommended conditions in the Certificate of Analysis. |



## BIOLOGICAL ACTIVITY

**Description**

PPI-2458 is a potent, orally active, selective and irreversible inhibitor of methionine aminopeptidase-2 (MetAP-2). PPI-2458 can be used for arthritis and lymphoma research[1][2].

**In Vitro**

PPI-2458 potently inhibits HUVEC proliferation with a $GI_{50}$ of 0.2 nM and a maximum inhibition of >95% at 1 nM[1].
PPI-2458 (0-100 nM, 6 days) inhibits proliferation and MetAP-2 in SU-DHL-16 cells[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[2]

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| Cell Line: | SU-DHL-16 cells |
| Concentration: | 0, 0.01, 0.1, 1, 10, and 100 nM |
| Incubation Time: | 6 days |
| Result: | Inhibited SU-DHL-16 proliferation in a dose-dependent fashion with maximum inhibition of 60% achieved at the highest concentration (100 nmol/L) and $GI_{50}$ at 1.9 nmol/L. |

**In Vivo**

PPI-2458 (0-50 mg/kg, Orally, qod) reverses joint swelling and inflammation in the PG-PS (25 mg/kg, i.p.)-induced arthritis model[1].
PPI-2458 (0-3 mg/kg, Nasogastric intubation, qod) shows a decrease in germinal center lymphocytes in experimentally naive cynomolgus monkeys[2].
PPI-2458 (0-100 mg/kg, Orally, qod) significantly suppresses tumor growth in a dose-dependent manner in severe combined immunodeficient mice with SR tumor xenografts [2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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| Animal Model: | Female Lewis rats (101–121 g, PG-PS (25 mg/kg, i.p.)-induced arthritis model)[1] |
| Dosage: | 0.25, 1, 5, and 50 mg/kg |
| Administration: | Orally (po), started at day 15 after the chronic destructive phase of the disease was established and terminated on day 31 |
| Result: | Significantly and dose-dependently attenuated the chronic inflammatory response. |

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| | Markedly attenuated paw swelling in a dose-dependent manner with maximal protection at an orally administered dose of 50 mg/kg at day 31. |

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| Animal Model: | Forty-two experimentally naive cynomolgus monkeys[2] |
| Dosage: | 0.1 mg/kg (three males and three females), 0.3 mg/kg (three males and three females), 1.0 mg/kg (five males and five females), and 3.0 mg/kg (five males and five females) |
| Administration: | Nasogastric intubation every other day (QOD) for 13 days (total of seven treatments) |
| Result: | Exhibited a marked decrease in germinal center lymphocytes. |

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| Animal Model: | 60 female Fox Chase severe combined immunodeficient mice (SR lymphoma cells were injected s.c. above the right hind leg)[2] |
| Dosage: | 10, 30, or 100 mg/kg |
| Administration: | oral gavage, QOD |
| Result: | Significantly suppressed tumor growth in a dose-dependent manner. PPI-2458 administered at 100 mg/kg produced the greatest degree of tumor growth inhibition, which was 57% ($P < 0.001$) at the end of the study. |

## REFERENCES

[1]. Bernier SG, et al. A methionine aminopeptidase-2 inhibitor, PPI-2458, for the treatment of rheumatoid arthritis. Proc Natl Acad Sci U S A. 2004 Jul 20;101(29):10768-73.

[2]. Cooper AC, et al. A novel methionine aminopeptidase-2 inhibitor, PPI-2458, inhibits non-Hodgkin's lymphoma cell proliferation in vitro and in vivo. Clin Cancer Res. 2006 Apr 15;12(8):2583-90.



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