# ONO-8430506

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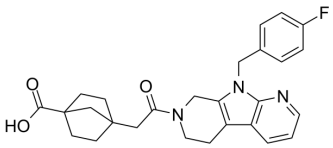
| **Cat. No.:** | HY-145344 |
| **CAS No.:** | 1354805-08-5 |
| **Molecular Formula:** | $C_{27}H_{28}FN_3O_3$ |
| **Molecular Weight:** | 461.53 |
| **Target:** | Phosphodiesterase (PDE) |
| **Pathway:** | Metabolic Enzyme/Protease |
| **Storage:** | 4°C, sealed storage, away from moisture and light<br>* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light) |



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 100 mg/mL (216.67 mM; Need ultrasonic)

| Preparing Stock Solutions | Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 2.1667 mL | 10.8335 mL | 21.6671 mL |
| | 5 mM | 0.4333 mL | 2.1667 mL | 4.3334 mL |
| | 10 mM | 0.2167 mL | 1.0834 mL | 2.1667 mL |

Please refer to the solubility information to select the appropriate solvent.

**In Vivo**

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.42 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.42 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.42 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

ONO-8430506 is an orally bioavailable and potent autotaxin (ATX)/ENPP2 inhibitor with the $IC_{90}$ of 100 nM for ATX activity in mouse plasma[1][2][3].

**In Vitro**

Autotaxin, also known as ectonucleotide pyrophosphatase/phosphodiesterase 2 (ENPP2), is a secreted enzyme that has lysophospholipase D activity. The $IC_{50}$s of ONO-8430506 for the lysophospholipase D (LysoPLD) activity of recombinant human ATX/ENPP2 are 5.1 nM in an assay using synthetic fluorescent substrate (FS-3) and 4.5 nM in an assay using a natural substrate (16:0-LPC)[2].
ONO-8430506 shows efficient inhibition of lysophosphatidic acid (LPA) formation, with $IC_{50}$s of approximately 10 nM with

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| | both recombinant and plasma derived ATX/ENPP2 from various animal species[2].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **In Vivo** | ONO-8430506 (10 mg/kg/day; gavage; for 21 days) slows initial tumor growth and limits lung metastasis[1].<br>ONO-8430506 decreases the initial phase of breast tumor growth and subsequent lung metastases by ~60% in a syngeneic orthotopic mouse model[1].<br>ONO-8430506 (oral; 30 mg/kg) demonstrates good pharmacokinetics and persistently inhibits plasma lysophosphatidic acid formation in rats[2].<br>ONO-8430506 (30 or 100 mg/kg) enhances the antitumor effect of Paclitaxel in a breast cancer model[3].<br>ONO-8430506 exhibits moderate oral bioavailability (rat 51.6%, dog 71.1%, and monkey 30.8%) and $C_{max}$ (rat 261, dog 1670, and monkey 63 ng/mL) following oral administration (rat 1, dog 1, and monkey 1 mg/kg)[3].<br>ONO-8430506 exhibits terminal elimination half-lives (rat 3.4, dog 8.9, and monkey 7.9 h) due to low plasma clearance (8.2, 4.7, and 5.8 mL/min/kg respectively) combined with large volumes of distribution (1474, 1863, and 2275 mL/kg respectively) following intravenous administration (rat 0.3, dog 0.3, and monkey 0.3 mg/kg)[3].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

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| Animal Model: | Female BALB/c mice, 8-10 wk old (BALB/cAnNCrl)[1] |
| Dosage: | 10 mg/kg |
| Administration: | Gavaged daily for 21 days; 10 μL/g |
| Result: | Tumor growth in ONO-8430506-treated mice caught up to the vehicle group by day 13; thereafter, primary tumor size was not significantly different from the vehicle-treated mice. However, treatment with ONO-8430506 decreased the numbers of metastatic nodules in the lungs at day 21 by ~60%. |

## REFERENCES


[1]. Matthew G K Benesch, et al. Inhibition of autotaxin delays breast tumor growth and lung metastasis in mice. FASEB J. 2014 Jun;28(6):2655-66.

[2]. Hiroshi Saga, et al. A novel highly potent autotaxin/ENPP2 inhibitor produces prolonged decreases in plasma lysophosphatidic acid formation in vivo and regulates urethral tension. PLoS One. 2014 Apr 18;9(4):e93230.

[3]. Yuzo Iwaki, et al. ONO-8430506: A Novel Autotaxin Inhibitor That Enhances the Antitumor Effect of Paclitaxel in a Breast Cancer Model. ACS Med Chem Lett. 2020 May 14;11(6):1335-1341.





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