

## Product Data Sheet

Product Name: CAY10499 (MAGL-IN-5)

Cat. No.: GC14244

### Chemical Properties

Cas. No. 359714-55-9

Chemical Name [4-(5-methoxy-2-oxo-1,3,4-oxadiazol-3(2H)-yl)-2-methylphenyl]-carbamic acid, phenylmethyl ester

SMILES CC1=CC(N(N=C(O2)OC)C2=O)=CC=C1NC(OCC3=CC=CC=C3)=O

Formula  $C_{18}H_{17}N_3O_5$

M.Wt 355.3

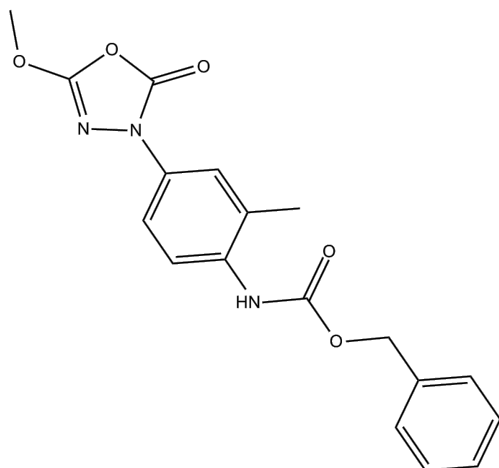
Solubility 20mg/mL in DMSO, 20mg/mL in DMF, 2mg/mL in Ethanol

Storage Store at -20°C, protect from light

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



### Protocol

#### Cell experiment [1]:

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

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|                               |                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|-------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Cell lines                    | OVCAR3 cells                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Preparation Method            | OVCAR3 cells were grown in DMEM medium supplemented with 10% fetal bovine serum and 1% penicillin/streptomycin in 5% CO <sub>2</sub> at 37°C. Cells (5×10 <sup>3</sup> cells/ml) were seeded in 96-well plates and allowed to adhere in a 5% CO <sub>2</sub> incubator at 37°C overnight, and were treated with different concentrations of CAY10499 (0.01, 0.1, 1, 10, and 100μM) for 96h. The cell viability was evaluated.          |
| Reaction Conditions           | 0.01, 0.1, 1, 10, and 100μM; 96h                                                                                                                                                                                                                                                                                                                                                                                                       |
| Applications                  | CAY10499 treatment significantly reduced the cell viability of OVCAR3 cells in a dose-dependent manner.                                                                                                                                                                                                                                                                                                                                |
| <b>Animal experiment [2]:</b> |                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Animal models                 | Female C57BL/6J mice                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Preparation Method            | Female C57BL/6J mice (seven weeks old; 22-25g) were kept under standard conditions (temperature 22±2°C and humidity 50%-60% on a 12h light/dark cycle) with free to food and water ad libitum. After 1 week of acclimatization, the mice were infected with the IAV virus and then received intraperitoneal injections of 10mg/kg dose of CAY10499 twice a day for 4 days. Then, the survival of the mice within 10 days was analyzed. |
| Dosage form                   | 10mg/kg; twice a day; 4 days; p.o.                                                                                                                                                                                                                                                                                                                                                                                                     |
| Applications                  | CAY10499 treatment significantly enhanced the survival of the IAV-challenged mice.                                                                                                                                                                                                                                                                                                                                                     |

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### References:

- [1] Aghazadeh Tabrizi M, Baraldi P G, Baraldi S, et al. Discovery of 1, 5-diphenylpyrazole-3-carboxamide derivatives as potent, reversible, and selective monoacylglycerol lipase (MAGL) inhibitors[J]. Journal of medicinal chemistry, 2018, 61(3): 1340-1354.
- [2] Baek Y B, Kwon H J, Sharif M, et al. Therapeutic strategy targeting host lipolysis limits infection by SARS-CoV-2 and influenza A virus[J]. Signal Transduction and Targeted Therapy, 2022, 7(1): 367.

### Background

CAY10499 (MAGL-IN-5) is a non-selective lipase inhibitor with IC<sub>50</sub> values of 144nM and 14nM for monoacylglycerol lipase (MAGL) and fatty acid amide hydrolase (FAAH), respectively<sup>[1]</sup>. CAY10499 can reduce viral replication and pro-inflammatory cytokine levels by inhibiting lipolysis<sup>[2]</sup>. CAY10499 has been widely used to inhibit the activity of hormone-sensitive lipase (HSL) and to reduce StAR protein expression and progesterone synthesis<sup>[3]</sup>.

In vitro, CAY10499 treatment for 96 hours significantly inhibited the proliferation of OVCAR3, COV318, and CAOV3 cells, with IC<sub>50</sub> values of 43μM, 59μM, and 77μM, respectively<sup>[4]</sup>. The 1-hour pretreatment with 20μM CAY10499 significantly reduced the mRNA expression of IL-6 and IL-8 in adipocytes induced by lipopolysaccharide (LPS)<sup>[5]</sup>. Treatment with 10μM CAY10499 in combination with N-palmitoylethanolamine (PEA) for 72 hours significantly induced cell death in B16 cells<sup>[6]</sup>.

In vivo, intraperitoneal injection of CAY10499 at 10mg/kg (twice a day) for 4 days significantly increased the survival rate of mice infected with influenza A virus (IAV)<sup>[7]</sup>.

### References:

- [1] Granchi C, Rizzolio F, Bordoni V, et al. 4-Aryliden-2-methyloxazol-5 (4 H)-one as a new scaffold for selective reversible MAGL inhibitors[J]. Journal of Enzyme Inhibition and Medicinal Chemistry, 2016, 31(1): 137-146.
- [2] Cesar-Silva D, Pereira-Dutra F S, Giannini A L M, et al. Lipid compartments and lipid metabolism as therapeutic targets against coronavirus[J]. Frontiers in Immunology, 2023, 14: 1268854.
- [3] Manna P R, Cohen-Tannoudji J, Counis R, et al. Mechanisms of action of hormone-sensitive

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lipase in mouse Leydig cells: its role in the regulation of the steroidogenic acute regulatory protein[J]. Journal of Biological Chemistry, 2013, 288(12): 8505-8518.

[4] Aghazadeh Tabrizi M, Baraldi P G, Baraldi S, et al. Discovery of 1, 5-diphenylpyrazole-3-carboxamide derivatives as potent, reversible, and selective monoacylglycerol lipase (MAGL) inhibitors[J]. Journal of medicinal chemistry, 2018, 61(3): 1340-1354.

[5] Aghazadeh Tabrizi M, Baraldi P G, Baraldi S, et al. Discovery of 1, 5-diphenylpyrazole-3-carboxamide derivatives as potent, reversible, and selective monoacylglycerol lipase (MAGL) inhibitors[J]. Journal of medicinal chemistry, 2018, 61(3): 1340-1354.

[6] Hamtiaux L, Masquelier J, Muccioli G G, et al. The association of N-palmitoylethanolamine with the FAAH inhibitor URB597 impairs melanoma growth through a supra-additive action[J]. BMC cancer, 2012, 12(1): 92.

[7] Baek Y B, Kwon H J, Sharif M, et al. Therapeutic strategy targeting host lipolysis limits infection by SARS-CoV-2 and influenza A virus[J]. Signal Transduction and Targeted Therapy, 2022, 7(1): 367.

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