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产品名称：Olumacostat glasaretil
产品别名：Olumacostat glasaretil

生物活性：

Description	Olumacostat glasaretil is a small molecule inhibitor of acetyl coenzyme A carboxylase (ACC).
In Vitro	Acetyl coenzyme A carboxylase controls the first, rate limiting step in fatty acid biosynthesis. Olumacostat glasaretil inhibits *de novo* lipid synthesis in primary and transformed human sebocytes. At 3 μM, olumacostat glasaretil reduces fatty acid synthesis to at or below baseline levels. ^{14}C-acetate incorporation levels are 85%-90% lower for SEB-1 cultures treated with olumacostat glasaretil at 20 μM compared to control samples. At 3 μM, olumacostat glasaretil reduces sebocyte triacylglycerol, cholesteryl/wax ester, diacylglycerol, cholesterol and phospholipid levels from control values on average by approximately 86%, 57%, 51%, 39% and 37%, respectively[1].
In Vivo	Olumacostat glasaretil is a pro-drug of the ACC inhibitor 5-(tetradecyloxy)-2-furoic acid (TOFA) and is designed to enhance delivery in vivo. Topical application of olumacostat glasaretil but not TOFA significantly reduces hamster ear sebaceous gland size. HPLC analyses of hamster ear extracts shows that olumacostat glasaretil treatment increases ACC levels and the ratio of acetyl-CoA to free CoA in tested animals, indicating increased fatty acid oxidation. These changes are consistent with ACC inhibition. Matrix-assisted laser desorption/ionization (MALDI) imaging reveals that OG applied onto Yorkshire pig ears accumulates in sebaceous glands relative to the surrounding dermis[1]. At week 12, OG treatment shows greater reductions from baseline in inflammatory lesions and noninflammatory lesions, and more patients with greater than or equal to 2-grade improvement in investigator global assessment score than vehicle[2].
Solvent&Solubility	***In Vitro:*** **DMSO : 125 mg/mL** (**259.54 mM;** Need ultrasonic) **H_2O : < 0.1 mg/mL** (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0763 mL	10.3816 mL	20.7633 mL
5 mM	0.4153 mL	2.0763 mL	4.1527 mL
10 mM	0.2076 mL	1.0382 mL	2.0763 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

	Solubility: ≥ 2.08 mg/mL (4.32 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (4.32 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: 2.08 mg/mL (4.32 mM); Suspended solution; Need ultrasonic 此方案可获得 2.08 mg/mL (4.32 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.08 mg/mL (4.32 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (4.32 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Hunt DW, et al. Inhibition of Sebum Production with the Acetyl Coenzyme A Carboxylase Inhibitor OlumacostatGlasaretil. J Invest Dermatol. 2017 Mar 1. pii: S0022-202X(17)30186-0. [2]. Bissonnette R, et al. Olumacostat glasaretil, a novel topical sebum inhibitor, in the treatment of acne vulgaris: A phase IIa, multicenter, randomized, vehicle-controlled study. J Am Acad Dermatol. 2017 Jan;76(1):33-39.

实验参考：

Cell Assay	Primary human sebocytes are grown to confluence in 96-well plates in sebocyte growth medium and stimulated with 1 μM human insulin and 1 μM liver X receptor (LXR) agonist T0901317 in the presence of increasing concentrations of TOFA or olumacostat glasaretil in culture medium containing 0.1% DMSO. After 24 hours, stimulation/treatment medium is removed and test articles are reapplied in labeling medium containing [^{14}C]-acetate. Following an additional 16 hours, cells are harvested using trypsin/EDTA. Lipid extracts are prepared and the amount of [^{14}C]-acetate incorporation is determined by liquid scintillation as a measure of *de novo* fatty acid synthesis[1].
Animal Administration	Hamster: To assess treatment effects on ACC activity, hamsters receive 20 □L of solvent mixture with or without 6% olumacostat glasaretil, once daily onto one ear for 1, 4 or 7 days. Punch biopsies are harvested 24 hours after the final dose. Livers are harvested 24 hours after the 7th application. HPLC CoA ester analysis is adapted[1].
References	[1]. Hunt DW, et al. Inhibition of Sebum Production with the Acetyl Coenzyme A Carboxylase Inhibitor OlumacostatGlasaretil. J Invest Dermatol. 2017 Mar 1. pii: S0022-202X(17)30186-0. [2]. Bissonnette R, et al. Olumacostat glasaretil, a novel topical sebum inhibitor, in the treatment of acne vulgaris: A phase IIa, multicenter, randomized, vehicle-controlled study. J Am Acad Dermatol. 2017 Jan;76(1):33-39.