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**Product Data Sheet**

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Product Name: AVE-8134

Cat. No.: GC31452

**Chemical Properties**

Cas. No. 304025-09-0

SMILES O=C(O)C1=C(COCCCOCC2=COC(C3=CC=CC=C3)=N2)C=CC=C1CFormula  $C_{22}H_{23}NO_5$  M.Wt 381.42

Solubility Soluble in DMSO Storage Store at -20°C

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**

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

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Address: 10292 Central Ave. #205, Montclair, CA, USA

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### Animal experiment:

Male ZDF rats are treated for 8 weeks. Food consumption and body weight are measured twice a week. The amount of diet for an additional control group is restricted to levels below the estimated consumption of the AVE8134 group: the starting value is 7 g chow/100 g body weight for the first week and then adapted to 8 g/100 g body weight. The chow for that control group is divided into two portions and is offered twice daily when light is switched on and off, all other groups had free access to food, except before measurements of fasted blood glucose, insulin and before oral glucose tolerance test. After two weeks of treatment an oral glucose tolerance test (oGTT) is performed. Briefly, after an overnight fast, the animals are treated with the drugs or vehicle between 06:30 and 07:00, glucose (2 g/kg) is administered orally 2 h later in a volume of 5 mL/kg, blood is drawn from the tip of the tail from using glass capillaries at 0, 30, 60, 90, 120, and 180 min after glucose administration. The glycemic index (GI) is calculated as area under the curve (AUC) of glucose response during oGTT. Blood glucose concentration before oral glucose load (0 min) is defined as baseline of AUC calculation.

### References:

[1]. Schafer HL, et al. AVE8134, a novel potent PPAR $\alpha$  agonist, improves lipid profile and glucose metabolism in dyslipidemic mice and type 2

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diabetic rats.

Acta

Pharmacol

Sin. 2012

Jan;33(1):82-90.

[2]. Linz W,

et al. The

peroxisome

proliferator-

activated

receptor-

alpha (PPAR-

alpha)

agonist,

AVE8134,

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survival in

rats. Acta

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Sin. 2009

Jul;30(7):935-

46.

### Background

AVE-8134 is a potent PPAR $\alpha$  agonist, with EC50 values of 100 and 3000 nM for human and rodent PPAR $\alpha$  receptor, respectively.

AVE8134 is a full PPAR $\alpha$  dominated PPAR agonist, but not active on PPAR $\delta$ [1]. In HUVEC, AVE8134 (1  $\mu$ M) increases Ser-1177-eNOS phosphorylation but not eNOS expression. In

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monocytes, AVE8134 (10  $\mu$ M) increases the expression of CD36 and the macrophage scavenger receptor 1, resulting in enhanced uptake of oxidized LDL[2].

In female hApo A1 mice, AVE8134 (130 mg/kg/d, po for 12 d) dose-dependently lowers the plasma triglycerides, and increases the serum HDL-cholesterol, hApo A1 and mouse Apo E levels. In female ZDF rats, AVE8134 (3-30 mg/kg/d for 2 weeks) improves insulin-sensitivity index. In pre-diabetic male ZDF rats, AVE8134 (10 mg/kg/d for 8 weeks) produces an anti-diabetic action comparable to rosiglitazone, without the PPAR $\gamma$  mediated adverse effects on body weight and heart weight. In male ZDF rats, AVE8134 (20 mg/kg/d for 12 weeks) increases mRNA levels of the target genes LPL and PDK4 about 20 fold in the liver, and there is no relevant effect with rosiglitazone[1]. In post-MI rats, AVE8134 (3 mg/kg and 10 mg/kg) dose-dependently improves cardiac output, myocardial contractility and relaxation and reduces lung and left ventricular weight and fibrosis. Treatment at AVE8134 decreases plasma proBNP and arginine and increases plasma citrulline and urinary NOx/creatinine ratio. In DOCA rats, AVE8134 (3 mg/kg/d) prevents development of high blood pressure, myocardial hypertrophy and cardiac fibrosis, and ameliorates endothelial dysfunction. In old SHR, treatment with a low dose of AVE8134 (0.3 mg/kg/d) improves cardiac and vascular function and increases life expectancy without lowering blood pressure. AVE8134 reduces phenylephrine-induced hypertrophy in adult rat cardiomyocytes[2].

[1]. Schafer HL, et al. AVE8134, a novel potent PPAR $\alpha$  agonist, improves lipid profile and glucose metabolism in dyslipidemic mice and type 2 diabetic rats. *Acta Pharmacol Sin.* 2012 Jan;33(1):82-90. [2]. Linz W, et al. The peroxisome proliferator-activated receptor-alpha (PPAR-alpha) agonist, AVE8134, attenuates the progression of heart failure and increases survival in rats. *Acta Pharmacol Sin.* 2009 Jul;30(7):935-46.

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