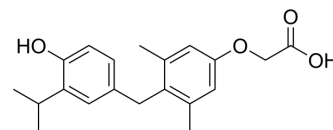


## Sobetirome

Cat. No.:	HY-14823
CAS No.:	211110-63-3
Molecular Formula:	C <sub>20</sub> H <sub>24</sub> O <sub>4</sub>
Molecular Weight:	328.4
Target:	Thyroid Hormone Receptor
Pathway:	Vitamin D Related/Nuclear Receptor
Storage:	Powder    -20°C    3 years 4°C    2 years In solvent   -80°C    2 years -20°C    1 year



### SOLVENT & SOLUBILITY

In Vitro	DMSO : 100 mg/mL (304.51 mM; Need ultrasonic)					
	Preparing Stock Solutions	<div><div>Solvent</div><div>Concentration</div></div>	Mass	1 mg	5 mg	10 mg
		1 mM		3.0451 mL	15.2253 mL	30.4507 mL
		5 mM		0.6090 mL	3.0451 mL	6.0901 mL
		10 mM		0.3045 mL	1.5225 mL	3.0451 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 (7.61 mM); Clear solution					
	2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (7.61 mM); Clear solution					
	3. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (7.61 mM); Clear solution					

### BIOLOGICAL ACTIVITY

Description	Sobetirome (GC-1) is a thyroid hormone receptor β (TRβ)-specific agonist which bind selectively to TRβ-1 with an EC <sub>50</sub> of 0.16 μM <sup>[1]</sup> .
IC <sub>50</sub> & Target	EC <sub>50</sub> : 0.16 μM (TRβ-1), 0.58 μM (TRα-1) <sup>[1]</sup>
In Vivo	Sobetirome (GC-1) is a thyroid hormone receptor β (TRβ)- and liver uptake-selective agonist. Sobetirome (48 nmol/kg) reduces high-density lipoprotein (HDL) cholesterol and very low-density lipoprotein (VLDL) triglyceride levels in euthyroid

Mice. Sobetirome reduces HDL cholesterol and triglyceride Levels in hypercholesterolemic mice. Sobetirome increases hepatic HDL receptors and stimulates bile acid synthesis in hypercholesterolemic mice<sup>[2]</sup>. Treatment with 10× Sobetirome (GC-1) results in a gain of fat mass of only 21% (1.7 g), and treatment with 20× Sobetirome (GC-1) induces a decrease in fat mass of 20% (1.3 g)<sup>[3]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

### Animal

#### Administration <sup>[2][3]</sup>

##### Mice<sup>[2]</sup>

One hundred eighteen male C57BL/6 mice, 3 months old, are kept in standardized conditions with free access to water and normal chow. 3,5,3'-triiodo-L-thyronine (T<sub>3</sub>) or Sobetirome is administered i.p. in 20% DMSO or propylene glycol for 8 days, once daily at 9:00 a.m.; controls receive vehicle. In one experiment, nine groups of six mice are treated with vehicle, or 5.4, 24, 48, and 97 nmol/kg per day of T<sub>3</sub> or Sobetirome. The lowest dose of T<sub>3</sub> induces euthyroidism in hypothyroid mice. In another experiment, one group of seven mice is given no additional supplementation; three groups of seven mice receive 10% corn oil and 2% cholesterol (cholesterol diet); and three groups of seven mice receive 10% corn oil, 2% cholesterol, and 0.5% cholic acid (cholic acid diet). For this experiment, mice are treated with vehicle or 97 nmol/kg per day Sobetirome or T<sub>3</sub>. Food is withdrawn 5 h before kill. Blood is drawn by cardiac puncture under light isoflurane anesthesia. Animals are killed by cervical dislocation. Livers are immediately frozen in liquid nitrogen. For analysis of bile acid excretion, three groups of five chow-fed mice are treated with vehicle, 48 nmol/kg per day of Sobetirome, or T<sub>3</sub> for 5 days. Feces are collected group-wise 24 h before treatment and in the last 24 h of the experiment.

##### Rats<sup>[3]</sup>

Female Wistar rats are randomly divided into five groups (n=8 per group): (i) control, treated with saline; (ii) 10× T<sub>3</sub>, treated with 3 µg T<sub>3</sub>/100 g body weight (BW) per day, which is equivalent to ten times the physiological dose of T<sub>3</sub>; (iii) 20× T<sub>3</sub>, treated with double of the previous T<sub>3</sub> dosage (6 µg T<sub>3</sub>/100 g body weight (BW) per day); (iv) 10× Sobetirome, treated with 1.5 µg Sobetirome/100 g BW per day and (v) 20× Sobetirome, treated with 3 µg Sobetirome/100 g BW per day. The latter two groups are treated with Sobetirome in equimolar doses of 10× T<sub>3</sub> and 20× T<sub>3</sub> respectively. The equimolar doses of Sobetirome are calculated from the molecular mass of T<sub>3</sub> (mol mass=651) and Sobetirome (mol mass=328.4). T<sub>3</sub> is dissolved in 40 mM NaOH, and Sobetirome is dissolved in DMSO to a concentration of 1 mg/mL; either T<sub>3</sub> or Sobetirome are then diluted in saline and administered i.p. every day for 6 weeks. BW is measured thrice a week. Body length (nose to base of the tail) is determined at the end of the experimental period.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## CUSTOMER VALIDATION

- Am J Pathol. 2020 May;190(5):1006-1017.
- Am J Pathol. 2017 Nov;187(11):2473-2485.
- University of Pittsburgh. 21 August 2021
- Patent. US20200375928A1.
- Gene Expr. 2016;17(1):19-34.

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## REFERENCES

- [1]. Gierach I, et al. Bacterial biosensors for screening isoform-selective ligands for human thyroid receptors  $\alpha$ -1 and  $\beta$ -1. FEBS Open Bio. 2012 Aug 15;2:247-53.
- [2]. Johansson L, et al. Selective thyroid receptor modulation by GC-1 reduces serum lipids and stimulates steps of reverse cholesterol transport in euthyroid mice. Proc Natl Acad Sci U S A. 2005 Jul 19;102(29):10297-302.

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[3]. Villicev CM, et al. Thyroid hormone receptor beta-specific agonist GC-1 increases energy expenditure and prevents fat-mass accumulation in rats. J Endocrinol. 2007 Apr;193(1):21-9.

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

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