Product Data Sheet

Product Name: Veledimex racemate (RG-115932 racemate)
Cat. No.: GC33870

Chemical Properties

Cas. No.	755013-59-3		
SMILES	O=C(NN(C(C1=CC(C)=CC(C)=C1)=O)C(C(C)(C)C)CCC)C2=CC=CC(OC)=C2CC		
Formula	$C_{27}H_{38}N_2O_3$	M.Wt	438.6
Solubility	Soluble in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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			

Background

Veledimex racemate is the racemate of veledimex. Veledimex is an orally available, small-molecule activator ligand for the RheoSwitch Therapeutic System.

Interleukin 12 (IL-12) is a pro-inflammatory cytokine critical for stimulating anti-cancer immune responses. Ad-RTS-IL-12 is the adenovirusvector engineered to express hIL-12. Veledimex is an orally active small-molecule diacylhydrazine and controls the expression of the target gene. The amount of gene product produced by the system and the duration of the effect are dependent on veledimex dose level and duration of dosing[1].

Veledimex, combined with Ad-RTS-hIL-12, is in phase I/II clinical trials for the treatment of melanoma and breast cancer. Intratumoral administration of Ad-RTS-mIL-12 along with oral administration of veledimex elicits dose-dependent antitumor effects in murine melanoma, breast cancer, and glioma models, which correlates with increased plasma exposure of veledimex. The increase in tumor veledimex levels in combination with Ad-RTS-mIL-12 results in a dose-related increase in the IL-12 mRNA (switch on) leading to dose-related increases in IL-12p70 in the tumor with minimal increase in serum IL-12.

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The increase in tumor IL-12 correlates with an increase in tumor CD8+ cytotoxic T cells and a concomitant decrease in regulatory T cells in the tumor microenvironment, which leads to Ad-RTS-mIL-12 + veledimex-elicited dose-related decreases in tumor growth rate with no significant change in body weight in both breast and melanoma syngeneic mouse models. Veledimex has moderate to low oral bioavailability after a single oral administration in mice and monkeys (-56% in mice and up to 17.4% in cynomolgus monkeys) with mostly low plasma clearance (1399 and 1170 mL/h per kilogram in mice and monkeys, respectively), high volume of distribution (20271 and 9180 mL/h per kilogram in mice and monkeys, respectively), and long terminal half-lives (-10 hours in mice and -30 hours in monkeys) after intravenous administration[1].

[1]. Cai H, et al. Plasma Pharmacokinetics of Veledimex, a Small-Molecule Activator Ligand for a Proprietary GeneTherapy Promoter System, in Healthy Subjects. Clin Pharmacol Drug Dev. 2017 May;6(3):246-257.

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