

Product Data Sheet

Product Name: RG3039 (PF-06687859)

Cat. No.: GC30784

Chemical Properties

Cas. No. 1005504-62-0

SMILES NC1=NC(N)=C2C(OCC3CCN(CC4=C(Cl)C=CC=C4Cl)CC3)=CC=CC2=N1

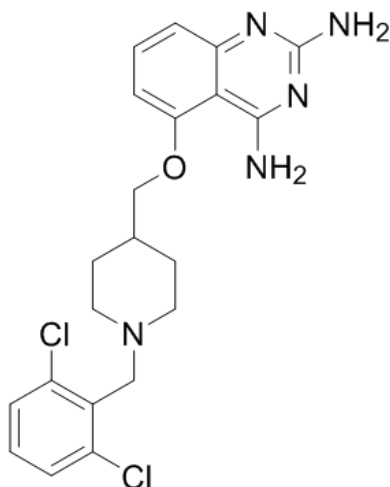
Formula $C_{21}H_{23}Cl_2N_5O$ M.Wt 432.35

Solubility DMSO : 6 mg/mL (13.88 mM); Water : < 0.1 mg/mL (insoluble) 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



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

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Protocol

Animal experiment: Mice: Mice receive intraperitoneal (i.p.) injections of RG3039 starting on post natal day 1 (P1) defined as the day of birth. All treated litters are culled at P4 to a total of six pups. Daily weights and righting-time are determined starting on P1. Ambulation index is performed between P13 and P23. A compilation score is determined during two 60 s trials[3].

References:

- [1]. Gopalsamy A, et al. Design of Potent mRNA Decapping Scavenger Enzyme (DcpS) Inhibitors with Improved Physicochemical Properties To Investigate the Mechanism of Therapeutic Benefit in Spinal Muscular Atrophy (SMA). J Med Chem. 2017 Apr 13;60(7):3094-3108.
- [2]. Gogliotti RG, et al. The DcpS inhibitor RG3039 improves survival, function and motor unit pathologies in two SMA mouse models. Hum Mol Genet. 2013 Oct 15;22(20):4084-101.
- [3]. Van Meerbeke J, et al. The DcpS inhibitor RG3039 improves motor function in SMA mice. Hum Mol Genet. 2013 Oct 15;22(20):4074-83.

Background

RG3039 (PF-06687859) is an orally bioavailable and brain-penetrant DcpS inhibitor with an IC₅₀ of 0.069 nM.

RG3039 is a dibasic lipophilic molecule that is predicted to accumulate in lysosomes[1]. In motor neurons, RG3039 significantly increases both the average number of cells with gems and average number of gems per cell, which is used as an indirect measure of SMN levels[2].

RG3039 can extend survival and improve function in two SMA mouse models of varying disease severity (Taiwanese 5058 Hemi and 2B/- SMA mice), and positively impacts neuromuscular pathologies. In 2B/- SMA mice, RG3039 provides a >600% survival benefit (median 18 days to >112 days) when dosing began at P4, highlighting the importance of early intervention[2]. RG3039 distributes to central nervous system tissues where it robustly inhibits DcpS enzyme activity, but minimally activates SMN expression or the assembly of small nuclear ribonucleoproteins. RG3039 treated SMA mice shows a dose-dependent increase in survival, weight and motor function and it is associated with improved motor neuron somal and neuromuscular junction synaptic innervation and

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function and increased muscle size. RG3039 also enhances survival of conditional SMA mice in which SMN has been genetically restored to motor neurons[3].

[1]. Gopalsamy A, et al. Design of Potent mRNA Decapping Scavenger Enzyme (DcpS) Inhibitors with Improved Physicochemical Properties To Investigate the Mechanism of Therapeutic Benefit in Spinal Muscular Atrophy (SMA). J Med Chem. 2017 Apr 13;60(7):3094-3108. [2]. Gogliotti RG, et al. The DcpS inhibitor RG3039 improves survival, function and motor unit pathologies in two SMA mouse models. Hum Mol Genet. 2013 Oct 15;22(20):4084-101. [3]. Van Meerbeke J, et al. The DcpS inhibitor RG3039 improves motor function in SMA mice. Hum Mol Genet. 2013 Oct 15;22(20):4074-83.

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