

## Product Data Sheet

Product Name: Olcegepant hydrochloride

Cat. No.: GC36795

### Chemical Properties

Cas. No. 586368-06-1

SMILES O=C1N(CC2=C(N1)C=CC=C2)C3CCN(C(N[C@@H](C(N[C@@H](C(N4CCN(C5=CC=NC=C5)CC4)=O)CCCCN)=O)CC6=CC(Br)=C(C(Br)=C6)O)=O)CC3.Cl

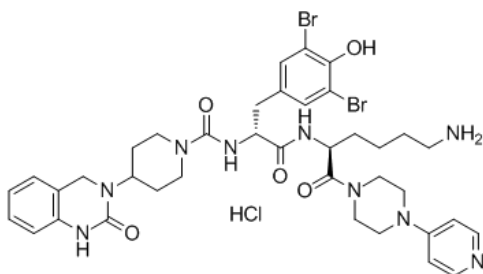
Formula  $C_{38}H_{47}Br_2N_9O_5 \cdot HCl$  M.Wt 906.11

Solubility Water:  $\geq 66.66$  mg/mL (73.57 mM) Storage Store at  $-20^{\circ}C$

General tips For obtaining a higher solubility, please warm the tube at  $37^{\circ}C$  and shake it in the ultrasonic bath for a while. Stock solution can be stored below  $-20^{\circ}C$  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



### Background

Olcegepant hydrochloride is the first potent and selective non-peptide antagonist of the calcitonin gene-related peptide 1 (CGRP1) receptor with  $IC_{50}$  of 0.03 nM and with a  $K_i$  of 14.4 pM for human CGRP.  $IC_{50}$ : 0.03 nM (CGRP1)[1] $K_i$ : 14.4 pM (hCGRP)[2]

Olcegepant possesses higher affinity for the human CGRP receptor than the endogenous ligand

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

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CGRP and 150-fold higher affinity compared to the peptidic antagonist CGRP8-37. Olcegepant reverses CGRP-mediated vasodilation in human cerebral vessels and inhibits neurogenic vasodilation in a surrogate animal model of migraine pathophysiology[1]. Olcegepant (BIBN4096BS) is extremely potent at primate CGRP receptors exhibiting an affinity ( $K_i$ ) for human CGRP receptors of  $14.4 \pm 6.3$  (n=4) pM[2]. Several lines of evidence suggest that a calcitonin-gene related peptide (CGRP) receptor antagonist may serve as a novel abortive migraine treatment. Olcegepant (BIBN4096BS) exhibits competitive antagonism at the CGRP receptor present in SK-N-MC cells. Isolated human cerebral, coronary, and omental arteries are studied with a sensitive myograph technique. CGRP induces a concentration-dependent relaxation that is antagonized by Olcegepant in a competitive manner[3].

Olcegepant (BIBN4096BS) in doses between 1 and 30  $\mu\text{g/kg}$  (i.v.) inhibits the effects of CGRP, released by stimulation of the trigeminal ganglion, on facial blood flow in marmoset monkeys[2]. Pre-treatment with Olcegepant (900  $\mu\text{g/kg}$ ) inhibits the capsaicin-induced expression of Fos throughout the spinal trigeminal nucleus by 57%. In contrast, the expression of phosphorylated extracellular signal-regulated kinase in the trigeminal ganglion is not changed by Olcegepant pre-treatment[4]. Olcegepant (0.3 to 0.9 mg/kg, i.v.) markedly reduces mechanical allodynia in CCI-ION rats. Olcegepant (0.6 mg/kg, i.v.) significantly reduces the number of c-Fos immunolabeled cells in spinal nucleus of the trigeminal nerve and upregulation of ATF3 transcript (a marker of neuron injury) but not that of interleukin-6 in trigeminal ganglion of CCI-ION rats[5].

[1]. Rudolf K, et al. Development of human calcitonin gene-related peptide (CGRP) receptor antagonists. 1. Potent and selective small molecule CGRP antagonists. 1-[N2-[3,5-dibromo-N-[[4-(3,4-dihydro-2(1H)-oxoquinazolin-3-yl)-1-piperidinyl]carbonyl]-D-tyrosyl]-L-lysyl]-4-(4-pyridinyl)piperazine: the first CGRP antagonist for clinical trials in acute migraine. J Med Chem. 2005 Sep 22;48(19):5921-31. [2]. Doods H, et al. Pharmacological profile of BIBN4096BS, the first selective small molecule CGRP antagonist. Br J Pharmacol. 2000 Feb;129(3):420-3. [3]. Edvinsson L, et al. Effect of the CGRP receptor antagonist BIBN4096BS in human cerebral, coronary and omental arteries and in SK-N-MC cells. Eur J Pharmacol. 2002 Jan 2;434(1-2):49-53. [4]. Sixt ML, et al. Calcitonin gene-related peptide receptor antagonist Olcegepant acts in the spinal trigeminal nucleus. Brain. 2009 Nov;132(Pt 11):3134-41. [5]. Michot B, et al. Differential effects of calcitonin gene-related peptide receptor blockade by Olcegepant on mechanical allodynia induced by ligation of the infraorbital nerve vs the sciatic nerve in the rat. Pain. 2012 Sep;153(9):1939-48.

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