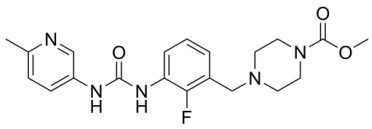
Data Sheet

Product Name:	Omecamtiv mecarbil
Cat. No.:	CS-0460
CAS No.:	873697-71-3
Molecular Formula:	$C_{20}H_{24}FN_5O_3$
Molecular Weight:	401.43
Target:	Myosin
Pathway:	Cytoskeleton
Solubility:	DMSO : 20 mg/mL (ultrasonic;warming;heat to 60°C)



BIOLOGICAL ACTIVITY:

Omecamtiv mecarbil (CK-1827452) is a selective **cardiac myosin** activator. ***In Vitro:*** Omecamtiv mecarbil (10 μM) reduces the maximal ATPase (k_{cat}) 4.5-fold and dramatically reduces the actin concentration at which ATPase is half-maximal (K_{ATPase}) 30-fold. The Omecamtiv mecarbil-induced inhibition of the actin-activated ATPase is evaluated in a concentration-dependent manner to determine the EC_{50} (0.52 ± 0.10 μM). Omecamtiv mecarbil does not change the overall actin affinity. Omecamtiv mecarbil traps a population of myosin heads in a weak actin affinity state with slow product release. Omecamtiv mecarbil can reduce the actin sliding velocity more than 100-fold in the in vitro motility assay[3]. ***In Vivo:*** Omecamtiv mecarbil (100-1000 ng/mL) demonstrates concentration-dependent increases in FS in Sprague−Dawley rats model. Omecamtiv mecarbil demonstrates good PK parameters in both rats (Sprague−Dawley) and dogs (Beagle) with clearances of 22 and 7.2 mL/min/kg, volumes of 3.5 and 3.6 L/kg, and bioavailabilities (F%) of 100 and 80%, respectively[1]. Omecamtiv mecarbil does not affect the phosphorylation status of myofilament proteins in both WT and KO hearts as shown by the absence of significant differences between pre and post Omecamtiv mecarbil samples within WT and KO groups, or affect the force generation at maximal Ca^{2+} activation (pCa 4.5) in any of the groups. Omecamtiv mecarbil increases the responsiveness of the cardiac myofilaments to Ca^{2+} at submaximal Ca^{2+}-activations[2].

References:

[1]. Morgan BP, et al. Discovery of omecamtiv mecarbil the first, selective, small molecule activator of cardiac Myosin. ACS Med Chem Lett. 2010 Aug 20;1(9):472-7.

[2]. Mamidi R, et al. Molecular effects of the myosin activator omecamtiv mecarbil on contractile properties of skinned myocardium lacking cardiac myosin binding protein-C. J Mol Cell Cardiol. 2015 Aug;85:262-72.

[3]. Swenson AM, et al. Omecamtiv Mecarbil Enhances the Duty Ratio of Human β-Cardiac Myosin Resulting in Increased Calcium Sensitivity and Slowed Force Development in Cardiac Muscle. J Biol Chem. 2017 Mar 3;292(9):3768-3778.

CAIndexNames:

1-Piperazinecarboxylic acid, 4-[[2-fluoro-3-[[[(6-methyl-3-pyridinyl)amino]carbonyl]amino]phenyl]methyl]-, methyl ester

SMILES:

O=C(N1CCN(CC1)CC2=C(C(NC(NC3=CC=C(N=C3)C)=O)=CC=C2)F)OC

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

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