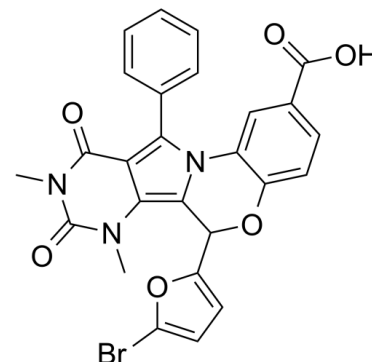


## Data Sheet

<b>Product Name:</b>	BPO-27 (racemate)
<b>Cat. No.:</b>	CS-6271
<b>CAS No.:</b>	1314873-02-3
<b>Molecular Formula:</b>	C <sub>26</sub> H <sub>18</sub> BrN <sub>3</sub> O <sub>6</sub>
<b>Molecular Weight:</b>	548.34
<b>Target:</b>	Autophagy; CFTR
<b>Pathway:</b>	Autophagy; Membrane Transporter/Ion Channel
<b>Solubility:</b>	DMSO : 6 mg/mL (10.94 mM; Need ultrasonic and warming)



### BIOLOGICAL ACTIVITY:

BPO-27 racemate is a potent **CFTR** inhibitor with an **IC<sub>50</sub>** of 8 nM. **IC<sub>50</sub> & Target:** IC<sub>50</sub>: 8 nM<sup>[1]</sup> **In Vitro:** The benzopyrimido-pyrrolo-oxazinedione BPO-27 is an analogue of PPQ-102, which inhibits CFTR with an **IC<sub>50</sub>** of 8 nM. The R enantiomer of BPO-27 inhibits CFTR chloride conductance with an **IC<sub>50</sub>** of 4 nM, while S enantiomer is inactive. In vitro metabolic stability in hepatic microsomes shows both enantiomers as stable, with less than 5% metabolism in 4 h<sup>[1]</sup>. (R)-BPO-27 binds near the canonical ATP binding site. Whole-cell patch-clamp studies shows linear CFTR currents with a voltage-independent (R)-BPO-27 block mechanism. At a concentration of (R)-BPO-27 that inhibits CFTR chloride current by 50%, the **EC<sub>50</sub>** for ATP activation of CFTR increases from 0.27 to 1.77 mM<sup>[2]</sup>. **In Vivo:** Following bolus interperitoneal administration in mice, serum (R)-1 decays with **t<sub>1/2</sub>** ≈ 1.6 h and gives sustained therapeutic concentrations in kidney<sup>[1]</sup>.

### PROTOCOL (Extracted from published papers and Only for reference)

**Cell Assay:** <sup>[2]</sup>Whole-cell recordings are done on CFTR-expressing CHO-K1 cells. After establishing the whole-cell configuration, BPO-27 is added for 5 minutes, and then CFTR is activated by the addition of forskolin (10 μM) in the continued presence of BPO-27 (0.5 or 1 μM). Whole-cell currents are elicited by applying hyperpolarizing and depolarizing voltage pulses from a holding potential of 0 mV to potentials between +80 and -80 mV in steps of 20 mV. Recordings are made at room temperature using an Axopatch-200B. Currents are digitized with a Digidata 1440A converter and filtered at 5 kHz<sup>[2]</sup>. **Animal Administration:** <sup>[1]</sup>Mouse: (R)-BPO-27 is formulated at 1 mg/mL in 5% DMSO, 2.5% Tween-80 and 2.5% PEG400 in water. Male mice in a CD1 genetic background are administered 300 μL of the (R)-BPO-27 formulation by intraperitoneal injection. At specified times, blood samples are collected by eye bleed. At 4 h, kidneys are removed following renal arterial perfusion with PBS. Kidneys are weighed, mixed with acetic acid and homogenized for analysis<sup>[1]</sup>.

### References:

- [1]. Snyder DS, et al. Absolute Configuration And Biological Properties of Enantiomers of CFTR Inhibitor BPO-27. ACS Med Chem Lett. 2013 May 9;4(5):456-459.
- [2]. Kim Y, et al. Benzopyrimido-pyrrolo-oxazine-dione (R)-BPO-27 Inhibits CFTR Chloride Channel Gating by Competition with ATP. Mol Pharmacol. 2015 Oct;88(4):689-96.

### CAIndexNames:

6H-Pyrimido[4',5':3,4]pyrrolo[2,1-c][1,4]benzoxazine-2-carboxylic acid, 6-(5-bromo-2-furanyl)-7,8,9,10-tetrahydro-7,9-dimethyl-8,10-dioxo-11-phenyl-, (6R)-

**SMILES:**

O=C(C1=CC=C(OC(C2=CC=C(Br)O2)C3=C(N(C)C4=O)C(C(N4C)=O)=C(C5=CC=CC=C5)N36)C6=C1)O

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

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