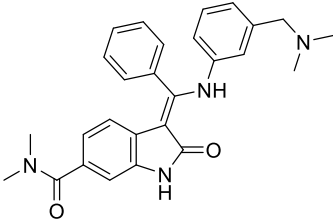


# Product data sheet



|  |   |  |
|--|---|--|
| MedKoo Cat#: 401150<br>Name: BIX 02189<br>CAS#: 1265916-41-3<br>Chemical Formula: C <sub>27</sub> H <sub>28</sub> N <sub>4</sub> O <sub>2</sub><br>Exact Mass: 440.22123<br>Molecular Weight: 440.54 |  |  |
| Product supplied as:   |   | Powder                                     |
| Purity (by HPLC):  |   | ≥ 98%                                      |
| Shipping conditions  |   | Ambient temperature                        |
| Storage conditions:  |   | Powder: -20°C 3 years; 4°C 2 years.        |
|  |   | In solvent: -80°C 3 months; -20°C 2 weeks. |

## 1. Product description:

BIX 02189 is a selective MEK5/ERK5 inhibitor with an IC<sub>50</sub> of 59 nM. BIX02189 was reported to inhibit catalytic function of purified, MEK5 enzyme. BIX02189 blocked phosphorylation of ERK5, without affecting phosphorylation of ERK1/2 in sorbitol-stimulated HeLa cells. BIX02189 also inhibited transcriptional activation of MEF2C, a downstream substrate of the MEK5/ERK5 signaling cascade, in a cellular trans-reporter assay system. BIX02189 may offer novel pharmacological tools to better characterize the role of the MEK5/ERK5 pathway in various biological systems.

## 2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under “QC And Documents” section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

## 3. Solubility data

| Solvent                   | Max Conc. mg/mL | Max Conc. mM |
|---------------------------|-----------------|--------------|
| DMSO                      | 34.48           | 78.27        |
| DMF                       | 15.0            | 34.05        |
| DMF:PBS (pH 7.2)<br>(1:1) | 0.5             | 1.13         |
| Ethanol                   | 10.0            | 22.70        |

## 4. Stock solution preparation table:

| Concentration / Solvent Volume / Mass | 1 mg    | 5 mg     | 10 mg    |
|---------------------------------------|---------|----------|----------|
| 1 mM                                  | 2.27 mL | 11.35 mL | 22.70 mL |
| 5 mM                                  | 0.45 mL | 2.27 mL  | 4.54 mL  |
| 10 mM                                 | 0.23 mL | 1.13 mL  | 2.27 mL  |
| 50 mM                                 | 0.05 mL | 0.23 mL  | 0.45 mL  |

## 5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of “Calculator”

## 6. Recommended literature which reported protocols for in vitro and in vivo study

### In vitro study

1. Amano S, Chang YT, Fukui Y. ERK5 activation is essential for osteoclast differentiation. *PLoS One*. 2015 Apr 17;10(4):e0125054. doi: 10.1371/journal.pone.0125054. PMID: 25885811; PMCID: PMC4401765.
2. Rasmussen SA, Kwon M, Pressly JD, Blumer JB, Regner KR, Park F. Activator of G-protein Signaling 3 Controls Renal Epithelial Cell Survival and ERK5 Activation. *J Mol Signal*. 2015 Nov 27;10:6. doi: 10.5334/1750-2187-10-5. PMID: 27096004; PMCID: PMC4831271.

### In vivo study

1. Chen C, Wu S, Lin X, Wu D, Fischbach S, Xiao X. ERK5 plays an essential role in gestational beta-cell proliferation. *Cell Prolif*. 2018 Jun;51(3):e12410. doi: 10.1111/cpr.12410. Epub 2017 Nov 21. PMID: 29159830; PMCID: PMC6528926.

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2. Nam DH, Han JH, Lim JH, Park KM, Woo CH. CHOP Deficiency Ameliorates ERK5 Inhibition-Mediated Exacerbation of Streptozotocin-Induced Hyperglycemia and Pancreatic  $\beta$ -Cell Apoptosis. *Mol Cells*. 2017 Jul 31;40(7):457-465. doi: 10.14348/molcells.2017.2296. Epub 2017 Jul 6. PMID: 28681594; PMCID: PMC5547215.

## 7. Bioactivity

Biological target:

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BIX02189 is a MEK5 inhibitor with an IC50 of 1.5 nM and also inhibits ERK5 catalytic activity with an IC50 of 59 nM.

### In vitro activity

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Immunoblot analysis using protein lysates from NRK-Ctrl cells treated with increasing doses of BIX02189 (1.5–10  $\mu$ M) demonstrated reduced phosphorylation of ERK5, but not ERK1/2, compared to vehicle (DMSO)-treated cells (Supplemental Figure 1). In the presence of two different doses of BIX02189 within the range used for the immunoblot, a dose-dependent reduction in cell number was calculated at both doses, but reached significance at the higher dose (10  $\mu$ M;  $P < 0.05$  at both time points) compared to the vehicle-treated NRK-Ctrl cells. Treatment of the NRK cells expressing AGS3 shRNA with BIX02189 resulted in poor viability of the cells that could not be maintained beyond 24 hours of incubation (data not shown).

Reference: *J Mol Signal*. 2015; 10: 6. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4831271/>

### In vivo activity

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In order to figure out whether the activation of ERK5 in beta cells may be necessary for the augmentation of beta-cell proliferation during pregnancy, this study injected a specific inhibitor of ERK5 activation, BIX02189, into the pregnant mice to suppress ERK5 signalling. At gestational day 15, mouse islets were isolated and examined for the levels of ERK5 and pERK5. The total ERK5 in islets from the pregnant mice that had received either BIX02189 or control saline did not alter (Figure 3A,B), while the phosphorylated ERK5 was significantly decreased in islets from the pregnant mice that had received BIX02189, compared with those from the pregnant mice that had received saline (Figure 3A,C). Thus, activation of ERK5 in beta cells in pregnant mice is suppressed by BIX02189 injections.

Reference: *Cell Prolif*. 2018 Jun; 51(3): e12410. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6528926/>

*Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.*