

## PYZD-4409

Catalog No: tcsc1725



### Available Sizes

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**Size:** 5mg

**Size:** 10mg

**Size:** 50mg

**Size:** 100mg



### Specifications

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**CAS No:**

423148-78-1

**Formula:**

$C_{14}H_7ClFN_3O_5$

**Pathway:**

Metabolic Enzyme/Protease

**Target:**

E1/E2/E3 Enzyme

**Purity / Grade:**

>98%

**Solubility:**

DMSO :  $\geq 35$  mg/mL (99.53 mM)

**Observed Molecular Weight:**

351.67

### Product Description

PYZD-4409 is a novel small molecule inhibitor of Ubiquitin-activating enzyme UBA1/E1 enzyme with an IC50 of 20 uM (cell-free

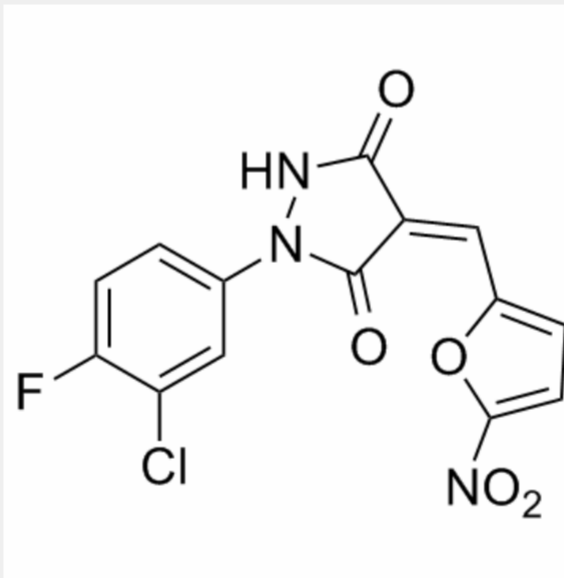
enzymatic assay).

IC50 Value: 20  $\mu$ M (cell-free enzymatic assay) [1]

Target: E1 enzyme (Ubiquitin-activating enzyme)

in vitro: PYZD-4409 inhibited the ATP-dependent activation of ubiquitin and subsequent transfer of the activated ubiquitin from the E1 to the common human E2 enzyme UBE2E2 in a gel-based assay. The IC50 of inhibition was estimated to be 20 $\mu$ M in a cell-free enzymatic assay. Suggesting specificity of PYZD-4409 for the E1 enzyme, the compound had no effect on unrelated enzymes such as  $\alpha$ -Mannosidase II glycosylation enzyme or Luciferase at concentrations up to 100 $\mu$ M (data not shown). It also did not inhibit the summo E1, Uba2, at concentrations up to 100 $\mu$ M. In 5 of 8 leukemia and myeloma cell lines, PYZD-4409 induced cell death with a LD50 less than 10 $\mu$ M. Myeloma cell lines were particularly sensitive to E1 inhibition because PYZD-4409 induced cell death with 3 of 4 myeloma cell lines (ie, LP1, KMS11, and U226) having an LD50 of 3 $\mu$ M or less. In contrast, solid tumor cell lines were less sensitive with an LD50 of approximately 15 to 20 $\mu$ M [1].

in vivo: SCID mice were injected subcutaneously with MDAY-D2 murine leukemia cells and then treated with PYZD-4409 (10 mg/kg) or buffer control intraperitoneally daily on alternate days over 8 days. Sixteen days after tumor implantation, the mice were killed, and the tumors excised and weighed. Compared with control-treated mice, treatment with PYZD-4409 delayed tumor growth and decreased tumor weight without untoward toxicity. Inhibition of the E1 can achieve an antitumor effect in vivo [1].



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