# PRODUCT INFORMATION

## MI-77301

*Item No. 17473*

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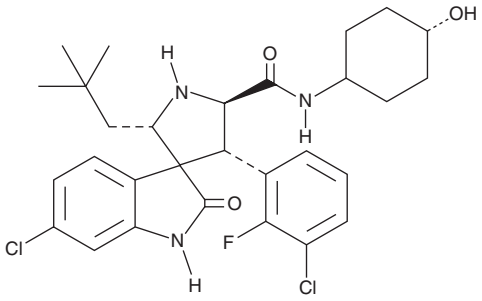
| **CAS Registry No.:** | 1303607-60-4 |
| **Formal Name:** | (2'S,3R,4'S,5'R)-6-chloro-4'-(3-chloro-2-fluorophenyl)-2'-(2,2-dimethylpropyl)-1,2-dihydro-N-(*trans*-4-hydroxycyclohexyl)-2-oxo-spiro[3H-indole-3,3'-pyrrolidine]-5'-carboxamide |
| **Synonym:** | SAR405838 |
| **MF:** | $C_{29}H_{34}Cl_2FN_3O_3$ |
| **FW:** | 562.5 |
| **Purity:** | ≥95% |
| **Supplied as:** | A crystalline solid |
| **Storage:** | -20°C |
| **Stability:** | ≥4 years |




*Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.*

### Laboratory Procedures

MI-77301 is supplied as a crystalline solid. A stock solution may be made by dissolving the MI-77301 in the solvent of choice, which should be purged with an inert gas. MI-77301 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide. The solubility of MI-77301 in these solvents is approximately 25 mg/ml.

MI-77301 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, MI-77301 should first be dissolved in ethanol and then diluted with the aqueous buffer of choice. MI-77301 has a solubility of approximately 0.25 mg/ml in a 1:3 solution of ethanol:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

### Description

The protein p53, often called the 'guardian of the genome,' is a transcription factor that is activated in response to cellular stress (low oxygen levels, heat shock, DNA damage, *etc.*) and acts to prevent further proliferation of the stressed cell by promoting cell cycle arrest or apoptosis. Its role as a tumor suppressor is evident by the observation that approximately 50% of human tumors have mutated or non-functional p53. Mdm2, a key negative regulator of p53, which is over-expressed in many human tumors, functions by binding to and targeting p53 for proteasomal degradation. MI-77301 binds to MDM2 with a $K_i$ value of 0.88 nM and blocks the MDM2-p53 interaction.[1] It activates wild-type p53 *in vitro* and in xenograft tumor tissue of leukemia and solid tumors, leading to p53-dependent cell cycle arrest and/or apoptosis.[1] In an SJSA-1 xenograft model of osteosarcoma, a single dose of 200 mg/kg MI-77301 induces complete tumor regression in mice by upregulating the pro-apoptotic protein PUMA.[1]

### Reference


1. Wang, S., Sun, W., Zhao, Y., *et al.* SAR405838: An optimized inhibitor of MDM2-p53 interaction that induces complete and durable tumor regression. *Cancer Res.* **74(20)**, 5855-5865 (2014).





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