# PRODUCT INFORMATION

## (1S,3R)-RSL3

*Item No. 19288*

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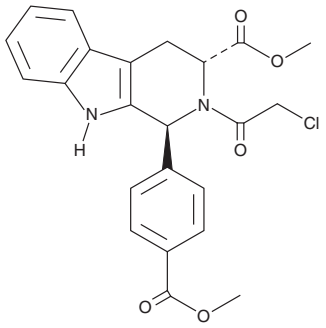
| **CAS Registry No.:** | 1219810-16-8 |
| **Formal Name:** | (1S,3R)-2-(2-chloroacetyl)-2,3,4,9-tetrahydro-1-[4-(methoxycarbonyl) phenyl]-1H-pyrido[3,4-b]indole-3-carboxylic acid, methyl ester |
| **MF:** | $C_{23}H_{21}ClN_2O_5$ |
| **FW:** | 440.9 |
| **Purity:** | ≥98% |
| **UV/Vis.:** | $\lambda_{max}$: 220 nm |
| **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

(1S,3R)-RSL3 is supplied as a crystalline solid. A stock solution may be made by dissolving the (1S,3R)-RSL3 in the solvent of choice, which should be purged with an inert gas. (1S,3R)-RSL3 is soluble in organic solvents such as ethanol, DMSO and dimethyl formamide (DMF). The solubility of (1S,3R)-RSL3 in ethanol is approximately 25 mg/ml and approximately 30 mg/ml in DMSO and DMF.

(1S,3R)-RSL3 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, (1S,3R)-RSL3 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. (1S,3R)-RSL3 has a solubility of approximately 0.33 mg/ml in a 1:2 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

### Description

(1S,3R)-RSL3 is a ferroptosis inducer and is canonically known as an inhibitor of glutathione peroxidase 4 (GPX4).[1-3] It inhibits GPX4 in a context-dependent manner: (1S,3R)-RSL3 inhibits GPX4 in the presence of cell cytosol or recombinant human 14-3-3ε, an adaptor protein, but does not inhibit recombinant human selenocysteine-containing GPX4 or purified rat testis GPX4, when used at a concentration of 100 µM.[4-5] (1S,3R)-RSL3 (50 nM) inhibits peroxidase activity in GPX4-overexpressing COH-BR1 breast cancer cell lysates.[1] It also inhibits thioredoxin reductase 1 (TrxR1; $IC_{50}$ = 7.9 µM in a cell-free assay).[4] (1S,3R)-RSL3 is selectively cytotoxic to H-$Ras^{V12}$-expressing BJeLR cells over wild-type Ras-expressing BJeH cells ($EC_{50}$s = 0.01 and 2 µM, respectively) and induces lipid peroxidation, a hallmark of ferroptosis, in Pfa1 fibroblasts when used at a concentration of 100 nM.[1,2] *In vivo*, (1S,3R)-RSL3 (100 mg/kg) prevents tumor formation and inhibits tumor growth in BJeLR mouse xenograft models.[1]

### References


1. Yang, W.S., SriRamaratnam, R., Welsch, M.E., *et al.* Regulation of ferroptotic cancer cell death by GPX4. *Cell* **156(1-2)**, 317-331 (2015).
2. Kagan, V.E., Mao, G., Qu, F., *et al.* Oxidized arachidonic and adrenic PEs navigate cells to ferroptosis. *Nat. Chem. Biol.* **13(1)**, 81-90 (2017).
3. Yang, W.S. and Stockwell, B.R. Ferroptosis: Death by lipid peroxidation. *Trends Cell Biol.* **26(3)**, 165-176 (2016).
4. Cheff, D.M., Huang, C., Scholzen, K.C., *et al.* The ferroptosis inducing compounds RSL3 and ML162 are not direct inhibitors of GPX4 but of TXNRD1. *Redox Biol.* **62:102703**, (2023).
5. Vučković, A.-M., Travain, V.B., Bordin, L., *et al.* Inactivation of the glutathione peroxidase GPx4 by the ferroptosis-inducing molecule RSL3 requires the adaptor protein 14-3-3ε. *FEBS Lett.* **594(4)**, 611-624 (2020).





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