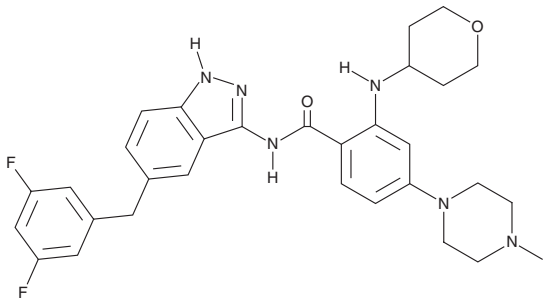
PRODUCT INFORMATION

Entrectinib

Item No. 19476

CAS Registry No.:	1108743-60-7
Formal Name:	N-[5-[(3,5-difluorophenyl)methyl]-1H-indazol-3-yl]-4-(4-methyl-1-piperazinyl)-2-[(tetrahydro-2H-pyran-4-yl)amino]-benzamide
Synonyms:	NMS-E628, RXDX-101
MF:	$C_{31}H_{34}F_2N_6O_2$
FW:	560.6
Purity:	≥98%
UV/Vis.:	λ_{max}: 302, 348 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

Entrectinib is supplied as a crystalline solid. A stock solution may be made by dissolving the entrectinib in the solvent of choice, which should be purged with an inert gas. Entrectinib is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of entrectinib in these solvents is approximately 1, 20, and 30 mg/ml, respectively.

Entrectinib is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, Entrectinib should first be dissolved in DMF and then diluted with the aqueous buffer of choice. Entrectinib has a solubility of approximately 0.2 mg/ml in a 1:4 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

Entrectinib is an inhibitor of TrkA (IC_{50} = 1.7 nM), TrkB (IC_{50} = 0.1 nM), and TrkC (IC_{50} = 0.1 nM), as well as c-ros oncogene 1 (ROS1; IC_{50} = 0.2 nM) and anaplastic lymphoma kinase (ALK; IC_{50} = 1.6 nM).[1,2] Entrectinib blocks proliferation of ALK-dependent cell lines, including those with L1196M or C1156Y resistance mutations, and inhibits ALK-dependent signaling.[2,3] It has been shown to inhibit the growth of a non-small cell lung cancer cell line bearing an EML4-ALK rearrangement.[2,3] In mice bearing various Trk, ROS1, or ALK-driven xenografts, entrectinib has been shown to induce tumor regression.[2,3]

References

1. Siena, S., Drilon, A.E., Ou, S.-H.I., *et al.* Enrectinib (RXDX-101), an oral pan-Trk, ROS1, and ALK inhibitor in patients with advanced solid tumors harboring gene rearrangements, European Cancer Congress, (2015).
2. Ardini, E., Menichincheri, M., De Ponti, C., *et al*. Characterization of NMS-E628, a small molecule inhibitor of anaplastic lymphoma kinase with antitumor efficacy in ALK-dependent lymphoma and non-small cell lung cancer models. *American Association for Cancer Research* **8(12 suppl)**, (2009).
3. Sullivan, I. and Planchard, D. ALK inhibitors in non-small cell lung cancer: The latest evidence and developments. *Ther. Adv. Med. Oncol.* **8(1)**, 32-47 (2016).

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