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(54) Title: 6-(4-AMINO-3-METHYL-2-OXA-8-AZASPIRO[4.5]DECAN-8-YL)-3-(2,3-DICHLOROPHENYL)-2-METHYLPYRIMIDIN-4(3H)-ONE DERIVATIVES AND RELATED COMPOUNDS AS PTPN11 (SHP2) INHIBITORS FOR TREATING CANCER

(57) Abstract: The present invention relates to 6-(4-amino-3-methyl-2-oxa-8-azaspiro[4.5]decan-8-yl)-3-(2,3-dichlorophenyl)-2-methylpyrimidin-4(3H)-one derivatives and related compounds which are useful as inhibitors of PTPN11 (SHP2) for the treatment or prevention of cancer and other PTP-mediated diseases. A preferred compound is e.g. 6-((3S,4S)-4-amino-3-methyl-2-oxa-8-azaspiro[4.5]decan-8-yl)-3-(Ra)-(2,3-dichloro-4-((1-methyl-1H-pyrazol-3-yl)oxy)phenyl)-2,5-dimethylpyrimidin-4(3H)-one (example 18b) with a IC50 of 3 nM in a PTPN11-E76K mutant enzyme inhibition assay.

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