WNT PATHWAY INHIBITOR: NEW SUBSTANCE CLASS FOR PROMISING NOVEL ANTI-TUMOR AGENT

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HINTERGRUND

The Wnt signalling pathway plays an important role in the regulation of cell proliferation and differentiation. Aberrant activation of the Wnt signalling pathway is known to promote uncontrolled cell growth and survival and can therefore be a major driving force in a broad spectrum of human cancers and diseases such as colon, skin, liver and ovary cancer. For example, the inhibition of aberrant Wnt signalling pathway activity in cancer cell lines effectively blocks their growth1. Other disorders and diseases are considered to be influenced by an aberrant Wnt signaling pathway, too.

The lead compound shows low nM IC50 against colon cancer (stem) cell lines and specificity in epistasis and suppression of double axis formation. PD analyses revealed good CYP/kinase & hERG-profiles, metabolic stability as well as promising t1/2/AUC in mice. Further optimization of in vitro & in vivo ADMET is ongoing.

LÖSUNG

The systematic evaluation of Structure Activity Relationships (SAR) of several 100 hit variants have been investigated to yield a lead structure. Intensive medicinal chemistry on the lead compound improved the pharmacologic profile.
The test compound 80158 inhibits efficiently Wnt-signalling and the viability of the colorectal cancer derived cell lines HCT116 and DLD1.

ANWENDUNGSBEREICHE

Development of a small molecule drug candidate for chemotherapy of cancer types such as colon, skin, liver and ovary cancer.

PUBLIKATIONEN & VERWEISE