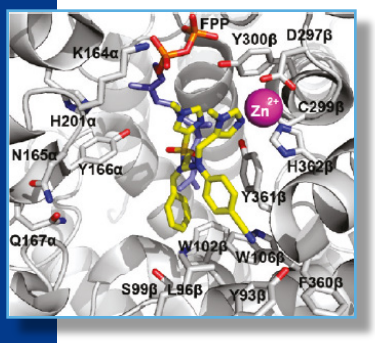
Novel Dual Inhibitor of Farnesyltransferase and Geranylgeranyltransferase-1 as an Anti-Cancer Agent



This technology is a small molecule dual inhibitor of two enzymes necessary for localization and activation of the K-RAS protein, farnesyltransferase and gernaylgeranyltransferase-1. The lead compound has nanomolar IC50 values in vitro against these enzymes. Mutant overactive K-RAS is found in about 25% of all human cancers, making it an attractive target for the development of first-in-class anti-cancer therapeutics. Our lead compound in preclinical development shows promising results for killing pancreatic, lung, and colon cancer cell lines as well as xenografts of fresh tumors derived from pancreatic cancer patients.

COMMERCIAL OPPORTUNITY

- K-RAS is an elusive, yet attractive target for anticancer therapy since on average its overactive mutant forms are present in almost one-quarter of all cancer patients. Mutant K-RAS is found in about 80% of pancreatic cancers, up to 50% each of non-small cell lung and thyroid cancers, over 40% of colorectal cancers.
- The Moffitt lead compound is a dual inhibitor of two enzymes necessary for K-RAS targeting to cell membranes that exhibits promising efficacy in killing several pancreatic, lung, colon and other human cancer cell lines, and shows efficacy in mouse xenograft models as well as patient-derived xenografts.
- The market is attractive as evidenced by Mirati Therapeutics with a market capitalization of about $940M developing a small molecule inhibitor of K-RAS G12C. Mirati has stated that they expect to finalize an IND submission by the fourth quarter of 2018. K-RAS G12C mutations only account for about 50%. In contrast, the Moffitt molecule could potentially treat all K-RAS mutant cancers.

TECHNOLOGY

Our lead compound is an ethylenediamine-based compound that inhibits farnesyltransferase (FT) and geranylgeranyltransferase-1 (GGT-1) with IC50 values of 250-500 nM. The compound inhibits the growth of many human cancer cell lines tested including pancreatic, lung, colon and other human cancer cell lines, and shows efficacy in mouse xenograft models as well as patient-derived xenografts.

PUBLICATION/PATENT

- U.S. patent No. 9,040,563 issued 5/26/2015 from an application filed on 3/11/2013 for Drs. Said Sebti and Andrew Hamilton
- Fletcher, S. et al. *J. Med. Chem.* (2010) 53(19):6867-88.

CONTACT

Haskell Adler PhD MBA
Senior Licensing Manager
Haskell.Adler@Moffitt.org
(813) 745-6596

LICENSING OPPORTUNITY

MOFFITT CANCER CENTER