

Inhibitor of Shp2 Protein Tyrosine Phosphatase

Opportunity Summary: Shp2 is a protein tyrosine phosphatase (PTPase) that mediates growth factor and cytokine signaling. Aberrant Shp2 expression is associated with several types of leukemias and developmental disorders.

Technology Abstract

- Shp2 is a protein tyrosine phosphatase (PTPase) that mediates growth factor and cytokine signaling. It is also involved in cell transformation by oncogenic growth factor receptor kinases and by the oncogenic bacterium *H. pylori*. Mutations of Shp2 are associated with several types of leukemias as well as the developmental disorder Noonan Syndrome.
- Because aberrant Shp2 activation may have a role in cell transformation, Shp2 PTPase is a target for developing oncology therapeutics.
- Scientists at Moffitt Cancer Center have discovered a novel drug-like compound that selectively inhibits the Shp2 PTPase. This compound may be a lead drug for treating a variety of Shp2-associated cancers.

Stage of Development

- The Shp2 inhibitor SPI-112Me is a synthetic isatin compound in pre-clinical development. In cell viability assays SPI-112Me inhibits the survival of human leukemia, as well as breast and colon cell lines.
- SPI-112Me is a prodrug for SPI-112, which preferentially inhibits the PTPase activity of Shp2 over Shp1 and PTP1B by a factor of 20 in cell-free assays. Hence SPI-112Me is selective for its target.

Commercial Opportunity

- SPI-112Me is a novel small molecule that inhibits a specific target. It has drug-like properties of size, solubility and cell permeability.
- Targeted inhibitors of Shp2 represent a new class of drugs that may have uses in treating several diseases including acute myelogenous leukemia (AML).
- Current treatment for AML relies on cytotoxics and antimetabolites, and/or stem cell transplantation. Most patients receive induction chemotherapy with cytarabine and an anthracycline to attempt remission, followed by consolidation therapy that includes more courses of chemotherapy. Many AML patients are elderly and not candidates for intense chemotherapy or cell transplantation.
- Targeted therapies may be a new mode for improving outcomes of this disease, which has relapse rates from 33 to 78%, depending on the type of AML. Elderly patients in particular may benefit from a Shp2-targeted therapy.

Market Summary

- In 2009 there were approximately 13,000 new cases of acute myelogenous leukemia in the US and 9,000 deaths. The initial patient population for Shp2 targeted inhibitors would likely be elderly patients who could not tolerate the toxicities of induction chemotherapy or the risks of stem cell transplantation.
- When AML patients relapse the only potential curative treatment is stem cell transplant, which is not available or appropriate for many patients.

Financial Projections

Gemtuzumab ozogamicin (Mylotarg) is the only targeted therapy used in treating AML. The cost of drug for a course of this monoclonal antibody is approximately \$12,000. Assuming a similar price for a Shp2 inhibitor, annual revenue from treating 10% of new AML patients in the US would be \$16 million.

Intellectual Property and Scientific Publications

- L. Chen et al. (2006) Mol. Pharmacol. 70(2):562-570
- H. Lawrence et al. (2008) J. Med Chem. 51(16):4948-56
- US patent application 11/733,023 filed April 9, 2007
- US patent application 13/055,113 filed July 21, 2009
- PCT application PCT/US09/042305 filed April 30, 2009
- PCT application PCT/US10/031506 filed April 16, 2010
- Provisional application filed March 30, 2011

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