Rho Kinase (ROCK) Inhibitors as Anticancer Drugs

Opportunity Summary: Two new compound classes (isoform selective and non-selective) of Rho kinase (ROCK) inhibitors have been discovered for use as anticancer drugs. Lead candidates of both classes have been evaluated in animal models. Potential uses in cardiovascular indications are also possible.

Technology Abstract

Two novel compound classes (Class A and Class B) of Rho kinase (ROCK) inhibitors have been discovered for use as anticancer drugs. Potential uses in cardiovascular indications are also possible. The Rho kinase isoforms, ROCK1 and ROCK2, were initially discovered as downstream targets of the small GTP-binding protein Rho. Because ROCKs mediate various important cellular functions such as cell shape, motility, secretion, proliferation, and gene expression, this pathway plays a pivotal role in the regulation of numerous cellular functions associated with malignant transformation and metastasis.

These two classes encompass compositions and methods for blocking cancer cell growth or proliferation and/or inducing cancer cell death – a central event in the process of metastasis.

Stage of Development

- **Class A Compounds:**
  - Found to inhibit ROCK2 enzymatic activity with IC_{50} values < 3 nM
  - Inhibited ROCK1 with an IC_{50} of 76 ± 55 nM
  - Displayed robust in vitro efficacy

- **Class B Compounds:**
  - No ROCK 1/2 isoform selectivity observed
  - Novel and potent inhibitors of ROCK1 displaying low nanomolar potency *in vitro* biochemical assay and low micromolar in *in vitro* cell-based assay

Lead candidates of both classes have been evaluated in animal models.

Commercial Opportunity

- Rock inhibitors are a promising new class of anticancer agents that has the potential to play a substantial and more effective role in metastatic potential of cells of malignant tumors, particularly of sarcomas.
- A large number of Rho kinase inhibitors have been developed during the past decade, and to our knowledge none of these distinguish between the two ROCK isoforms, ROCKI and ROCKII.

- Currently, surgery is the most common treatment for sarcomas, to remove the cancer and a safe margin of the healthy tissue around it. Depending on the size and location of the sarcoma, it may occasionally be necessary to amputate all or part of an arm or leg.
- Alternatively, ROCK inhibitors have the potential to block cancer cell growth or proliferation and/or induce cancer cell death, which would decrease amoeboid tumor cell invasion and substantially attenuates tumor growth and metastasis. This could significantly improve the effectiveness of sarcoma treatment in the future.

Market Summary

- While one target of ROCK are sarcoma cancers, it has also been linked to ovarian cancer, pancreatic, testicular, breast, gastrointestinal and bladder cancer.
- Approximately 2% of cancer deaths are caused from sarcomas. This is largely due sarcoma's aggressive biological behavior, and attributes to approximately 13,000 who will be diagnosed with soft tissue and bone sarcoma in the US, and that approximately 5,000 will die from the diseases.

Financial Projections

- In 2008, 13 kinase inhibitors had reached the market, and their collective sales were approaching $8 billion.
- Comparing ROCK inhibitors to other drugs used to treat sarcomas, breast cancers, and testicular cancer, such as doxorubicin and ifosfamide, the cost of the chemotherapy drug for a course of treatment is about $1,200 per injection.
- Assuming a 10% use rate in the sarcoma population, and that each patient receives 4- 8 injections during a course of treatment.
- Annual revenues in sarcoma could be between $6,250,000-$12,500,000 per year.

Intellectual Property and Scientific Publications

- Provisional patent filed: April 16, 2010
- AACR poster

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