SQ109

A New Small Molecule Antibiotic to Treat Helicobacter pylori-related Gastric Diseases

SQ109 is an orally active antibiotic currently in Phase 2 clinical trials for treatment of pulmonary tuberculosis (TB). Sequella filed a U.S. IND in Oct 2010 to expand SQ109’s therapeutic range to a second infectious disease, duodenal ulcers caused by infection with Helicobacter pylori. SQ109 has potential to be used as monotherapy to eradicate H. pylori and reduce ulcer treatment time and cost.

Market

Helicobacter pylori related infections are part of the $24 Billion worldwide gastrointestinal (GI) treatment market.

In the U.S.:

1. Fourteen (14) million people have ulcers
2. H. pylori causes 95% of duodenal and 85% of gastric ulcers
3. Resistance to antibiotics in H. pylori ulcer therapy (proton pump inhibitor/ antibiotic/ bismuth) is increasing
4. H. pylori is implicated in a variety of GI disorders
5. A new H. pylori biomarker (Urea Breath Test, UBT) will increase diagnosis and increase a more effective therapy market

The worldwide market potential is >$650M for H. pylori related duodenal and gastric ulcers.

Overview

SQ109 is an oral NCE in Phase 2 clinical development for treatment of pulmonary TB. In January 2007, Sequella received Fast Track designation from the U.S. Food and Drug Administration (FDA) for SQ109 based on the drug’s potential to fulfill an unmet need in treating TB, a serious, life-threatening medical condition. In October 2007, Sequella received Orphan Drug Status from the FDA, and the European Medicines Agency (EMEA).

In vitro experiments show that SQ109 kills over 99.99% of H. pylori, the bacteria identified as the cause of 95% of duodenal ulcers, in just 4 hours (see Figure 1).

SQ109 is orally bioavailable, stable in stomach acid, has a long half-life, and readily enters cells such as macrophages (specialized cells of our immune system that kill and eliminate bacteria from the body), and gastric cells. In animals, safe and well-tolerated oral doses of SQ109 produced stomach drug concentrations that exceed the 99.99% kill concentration by >3 fold for several hours (see Figure 2).

SQ109’s unique physical and chemical characteristics and broad activity suggest that SQ109 may be an effective antibiotic against H. pylori-related infections, including duodenal ulcer disease.
**H. pylori Pathophysiology**

In sentinel work that was recognized by the 2005 Nobel Prize in Medicine, Barry Marshall and Robin Warren demonstrated that the development of duodenal and gastric ulcers were strongly linked to infection by *H. pylori*. *H. pylori* infection is implicated in a variety of gastric diseases including: chronic gastritis, non-ulcer dyspepsia (NUD), duodenal and stomach ulcers, gastric mucosa-associated lymphoid tissue (MALT), and gastric cancer. In Japan, *H. pylori* is considered to be the second most preventable cause of cancer, behind smoking.

Recent evidence suggests that *H. pylori*, like tuberculosis, may be a facultatively intracellular pathogen, and this may explain why current antibiotics are not very effective in eradicating this pathogen. In contrast, SQ109, which achieves high concentrations in stomach epithelial cells is positioned to be the first antibiotic to completely eradicate *H. pylori* while reducing treatment regimen time and cost.

**Regulatory and Development Background**

**Regulatory**
The October 2009 FDA Draft “Guidance for Industry *Helicobacter pylori*-Associated Duodenal Ulcer Disease in Adults: Developing Drugs for Treatment” provides a straightforward pathway to regulatory approval using the $^{13}$C-urea breath test as a primary efficacy endpoint in 2 pivotal clinical trials.

**Development/Technical Background**
Since 2000, Sequella has applied its scientific expertise in TB research to identify, characterize, and complete preclinical evaluation of SQ109. SQ109 was developed in partnership with the National Institutes of Health (NIH), with several grants from the National Institute of Allergy and Infectious Diseases (NIAID) and the assistance of the NIAID and the National Cancer Institute Inter-Institute Program (NCI IIP) for IND-enabling studies.

More than 63,000 compounds were synthesized and screened in 1999. SQ109 was selected as a lead compound. After a series of integrated studies designed to narrow the field of potential drug candidates, SQ109 completed preclinical toxicology and pharmacokinetic studies prior to entering clinical trials in 2006.

Peer-reviewed scientific articles are available; please contact us for details.

**Manufacturing**
Sequella has collaborated with API manufacturers to develop the chemical process for manufacture of SQ109. Chemical synthesis has been successfully scaled to commercial scale manufacturing. Three registration batches of SQ109 API have been manufactured using a robust, chemical synthesis that produces a highly pure (99.7%) API.

**Intellectual Property**
Sequella has 10 or more issued patents and additional patent filings, including a U.S. patent for compositions of matter and uses of diamine anti-infectives. These patents provide broad coverage for compositions, methods and use claims for treatment of tuberculosis, *H. pylori* related ulcers, systemic fungal agents and other infectious pathogens.

**Alliance Opportunity**
SQ109 is available for partnering worldwide.