

SQ109

A Small Molecule Antibiotic

SQ109 is an orally active antibiotic for treatment of pulmonary tuberculosis (TB). Currently in Phase I clinical trials, SQ109 could replace one or more drugs in the current first-line TB drug regimen, simplify therapy, and shorten the TB treatment regimen.

Overview

SQ109 is an oral NCE in Phase I 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. Fast Track designation for SQ109 is based on its potential to fulfill an unmet need in treating pulmonary TB, a serious, life-threatening medical condition. In October 2007, Sequella received Orphan Drug Status from the FDA, as well as the European Medicines Agency (EMA). SQ109 preclinical data thus far has demonstrated the potential to enhance the treatment of TB during the first two months of intensive therapy and to treat multi-drug resistant TB. In clinical trials to date, SQ109 was safe up to [a] 300 mg single dose, with linear pK and a long half life.

SQ109 has potent *in vivo* activity against pulmonary TB alone and with other TB drugs. With a mechanism of action distinct from other antibiotics used in TB therapy, SQ109 inhibits cell wall synthesis in a select group of microorganisms with excellent *in vitro* activity against both drug-susceptible and drug-resistant TB bacteria, including XDR-TB. SQ109 also enhances both *in vitro* and *in vivo*, the activity of the anti-tubercular drugs Isoniazid and Rifampin, thereby shortening the time required to cure mice of experimental TB by 30%.

Alliance and Market Opportunities

Sequella is seeking partners worldwide for development and commercialization of SQ109. Based on several independent studies, the drug's worldwide market potential is approximately \$400 million, with over half of expected sales forecast for the Established Market Economies (EME).

Market Need. In the U.S., there are an estimated 15 to 30 million persons suspected to have TB infection; annually there are roughly 15,000 reported new cases of active disease. Worldwide there are an estimated 2 billion persons infected with *M. tuberculosis* and 9+ million active cases of TB.

The total high-risk population for TB in the U.S. casts a wide net and includes the following segments:

- **Opportunistic Infection:** Persons infected with HIV/AIDS, immunosuppressive cancers, or who inject illicit drugs
- **Healthcare:** Hospitals, both staff and patients; Nursing homes and facilities for the elderly
- **Schools and Universities:** Students and faculty in schools ranging from nursery school to colleges
- **Immigrants:** Persons born outside the U.S.
- **Public Welfare:** Employees of prisons and jails, homeless shelter workers and residents
- **Foreign-born:** Persons from developing or TB high-burden countries

Upwards of 450,000 patients are treated or prophylaxed for TB annually in the U.S.

SQ109 also has activity *in vitro* against common nosocomial fungal infections, including *Candida sp.* and *Aspergillus sp.* *Candida* are commensal organisms that colonize the normal GI tract and sometimes the skin. Infections due to *Candida* account for about 70% of all major systemic fungal infections. *Candida* are the fourth most prevalent organisms found in bloodstream infections and the most common cause of fungal infections in immunocompromised people.

Sequella Licensing Opportunity

SQ109 Therapeutic: Phase I

Indication: Treatment of Pulmonary TB

Competitive Advantage. In pre-clinical studies, SQ109 showed efficacy *in vivo* in a murine model of TB by itself, and improved efficacy and time-to-cure compared to the standard regimen for TB when combined with two of the first-line anti-TB drugs. Pharmacokinetic studies indicated that SQ109 has oral bioavailability, concentrates in lung and spleen, has a long half-life, and is effective against profoundly drug-resistant TB *in vitro*. In addition to active TB, SQ109 may have activity in latent TB and is expected to demonstrate improved efficacy, reduced toxicity, and shortened duration of treatment.

Regulatory and Development Background

Regulatory.

- SQ109 is currently in Phase I clinical trials under a U.S. IND.
- SQ109 received FDA Fast Track designation in January 2007.
- Phase Ib clinical trials are anticipated to begin 1Q 2009.

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.

Sequella used combinatorial chemistry to generate a large library of diamine compounds. Working with NIH, Sequella developed a solid-phase method to synthesize hundreds of thousands of diamines and a high throughput screening assay to identify compounds that affect genes activated during cell membrane repair by the tuberculosis bacilli.

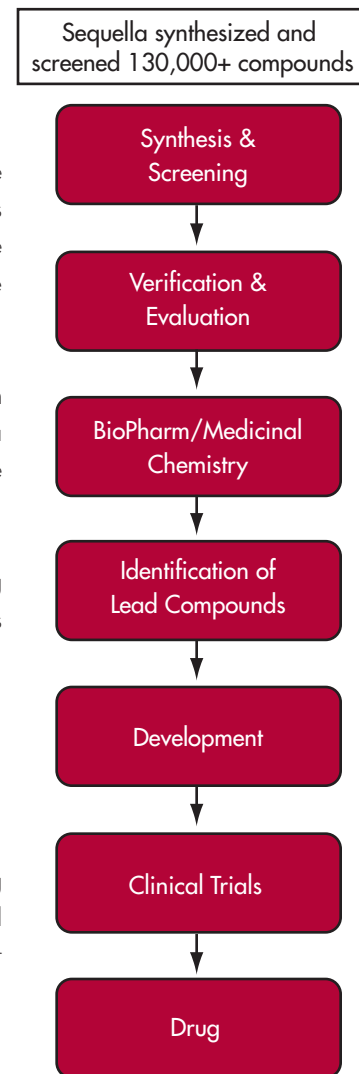
More than 130,000 compounds have been synthesized and screened since 1999 (see Fig 1). Following a series of integrated studies designed to narrow the field of potential drug candidates, SQ109 was selected as a lead compound.

SQ109 completed preclinical toxicology and pharmacokinetic studies prior to entering clinical trials.

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

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 infectious disease, anti-tubercular drugs, and proprietary diamine compounds.

SQ109 is available for partnering worldwide.



For information on
alliance opportunities, contact:

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