Sequella Licensing Opportunity
SQ641 Therapeutic: Pre-clinical
Indication: Broad Spectrum Antibiotic

SEQUELLA Incorporated

SQ641
A Semi-Synthetic Antibiotic

SQ641 is the lead drug candidate selected from a 7000-compound library of semi-synthetic nucleoside-based translocase 1 (TL-1) inhibitors developed as potential treatments for bacterial infections. SQ641 is particularly active against *Mycobacterium tuberculosis* (Mtb, causes tuberculosis [TB]), non-tuberculous *Mycobacteria* (NTM, cause pneumonias and some Crohn's Disease), *Streptococcus pneumoniae* (causes pneumonia) and *Staphylococcus aureus*, including methicillin-resistant *S. aureus* (MRSA, causes skin and soft-tissue infections).

Overview

The Capuramycin class of antibacterial antibiotics inhibits an essential enzyme present only in bacteria, TL-1, that these organisms use to construct their cell walls. Since the TL-I enzyme is absent in eukaryotic cells, it is an attractive target for antibiotic development. Despite the ubiquity of TL-1 in all bacteria, Capuramycin and its analogues, including SQ641, are remarkably specific for *Mycobacteria* and certain gram positive bacteria.

SQ641 possesses exceptional and fast-acting *in vitro* activity against all members of the *Mycobacteria* genus of bacteria, including *M. tuberculosis, M. avium complex*, and *M. avium* subspecies *paratuberculosis*, the potential etiological agent of Crohn's disease.

Sequella is currently developing methods to enhance oral delivery of SQ641 to treat TB and NTM infections in animal models of these diseases. Sequella also collaborates with the University of Wisconsin Veterinary School to assess SQ641 activity against *M. avium* subspecies *paratuberculosis in vitro* and in animal models of Johne's Disease, the veterinary equivalent of Crohn's disease in humans, with an estimated market of $400 million. An oral or parenteral formulation of SQ641 that creates new treatment options for patients suffering from TB, NTM, MRSA, and Crohn's Disease would have wide appeal in the infectious disease community.

Attributes of SQ641 include:

- Kills Mtb faster than any existing antitubercular drugs, including isoniazid and rifampin
- Is active against all strains of multidrug-resistant clinical strains of Mtb tested to date
- Has an exceptional 55 hr post antibiotic effect against Mtb
- Shows strong synergy in TB with Ethambutol, Streptomycin, and SQ109, Sequella's lead antitubercular drug currently completing Phase 1B clinical trials,
- Is highly effective in preventing development of drug resistant mutants in Mtb
- Has excellent *in vitro* activity against NTM: *M. avium* complex (MAC), *M. abscessus*, and *M. kansasii* and the etiologic agent of Johne's Disease (and suspected etiologic agent of Crohn's Disease), *M. avium* subspecies *paratuberculosis*
- Acts synergistically with a variety of anti-mycobacterial agents with activity against NTM.

Alliance and Market Opportunities

Sequella is seeking partners worldwide for development and commercialization of SQ641 and other Capuramycin-derived antibacterials. Based on several independent studies, the drug's worldwide market potential is between $500 million and $1 billion.

Market Need

TB

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 TB disease. Worldwide there are an estimated 2 billion persons infected with *M. tuberculosis* and almost 10 million active cases of TB each year.

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Crohn's Disease

Gastrointestinal diseases represent a large market with unmet medical needs. Inflammatory bowel diseases (IBD) affect approximately 1 million people in the U.S. and 4 million people worldwide. One of the two major IBD diseases is Crohn's Disease, which affects more than 800,000 people in North America, with 20,000 new patients diagnosed each year. The Crohn's Disease market is currently dominated by therapies that address symptoms only, such as anti-inflammatory steroids and expensive biologics that inhibit TNFα. This market is expected to grow to nearly $2 Billion by 2013.

NTM

NTM are important causes of pulmonary disease, resulting in significant morbidity and mortality. NTM infections are not reportable diseases, so numbers of infections that occur each year are difficult to determine. Estimates from Centers for Disease Control (CDC) in Atlanta suggest a NTM prevalence of 1.1 per 100,000 persons in the U.S., with clinicians studying the disease estimating the incidence to be ~5,000 cases per annum. The incidence of NTM disease is rising, and infections are now reported not only in immunocompromised individuals, but also in healthy individuals in the community.

MRSA

Community-associated MRSA has become the most frequent cause of skin and soft tissue infections presenting to emergency departments in the United States. MRSA also can cause severe, sometimes fatal invasive disease. Approximately 20% of bloodstream infections in the hospital setting are caused by *S. aureus*. The CDC estimated number of invasive community-based and healthcare-based MRSA infections annually is 32 per 100,000 persons in the U.S., with an annual incidence of over 94,000 cases.

The market opportunity for Crohn's Disease, community-acquired pneumonias, and MRSA infections rep-resents a substantial opportunity for anti-infective revenues in the U.S. An effective antibiotic to shorten and simplify treatment of NTM pneumonias and cure NTM-associated Crohn's Disease would be able to capture 25% of the projected Crohn's Disease market, or $500 million. Linezolid (marketed as Zyvox), which is used to treat MRSA infections, is on track to eclipse $1 billion in sales in 2009.

Competitive Advantage

Based on nonclinical testing of SQ641, we believe that this compound has extraordinary activity *in vitro* that may translate into a superb antibiotic for select bacteria:

- It has excellent activity against all *Mycobacteria* tested,
- It is bactericidal
- It is fast-acting, disintegrating even slow-growing bacteria in 24 hours
- It has lasting post antibiotic effect
- It synergizes with several antitubercular drugs, including EMB and SQ109
- It is highly effective in suppressing development of drug resistance

Development Status

We are exploring formulations that improve bioavailability of SQ641 and will select the correct formulation for both *in vivo* studies and IND-directed preclinical assessment in the next 9-12 months. We are also exploring the structure of SQ641 to discover modifications that might enable broader spectrum activity.

Intellectual Property

Sequella licensed the Capuramycin class of antibacterials from Daiichi-Sankyo in 2004, and we have exclusive worldwide rights, excluding the Middle East, for all indications.

SQ641 has 124 issued patents and patent applications, including an issued U.S. patent for composition of matter and uses of Capuramycin anti-infectives. These patents provide broad coverage for composition, methods, and use claims for treatment of infectious diseases by Capuramycin compounds, including SQ641.

SQ641 is available for partnering worldwide excluding the Middle East.

For information on alliance opportunities, contact:

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