Hit To Lead

Tryptanthrins
TB Alliance, Korea Institute of Chemical Technology and Yonsei Univer...

Phenotypic Screening
TB Alliance, University of Illinois

InhA Inhibitors
TB Alliance, GlaxoSmithKline

M. tuberculosis Protein Kinase Inhibitors
Vertex Pharmaceuticals, Incorporated

LeuRS inhibitors
TB Alliance, Anacor Pharmaceuticals

Fungal metabolites
Mycosynthetix, University of Illinois at Chicago

Actinomycete metabolites
University of Illinois at Chicago, Myongji University

DNA metabolism
AstraZeneca R and D Bangalore

Hit to Lead Evaluation of novel compounds
The Lilly TB Drug Discovery Initiative

Phenotype screening
AstraZeneca R and D Bangalore

Lead Optimization

Nitroimidazoles
TB Alliance, University of Auckland, University of Ilinois

New Generation Diarylquinoline
TB Alliance, Tibotec

Riminophenazines
TB Alliance, Institute of Materia Medica, The Beijing Tuberculosis an...

Mycobacterial Gyrase Inhibitors
TB Alliance, GlaxoSmithKline

Bi-functional Molecules
TB Alliance, University of Auckland and Colorado State University

TL1 Inhibitors
Sequella

MTopo
AstraZeneca R and D Bangalore

Pre-Clinical

Quinolone TBK-613
TB Alliance

CPZEN-45
Microbial Chemistry Research Foundation, Tokyo, Japan, Lilly TB Drug ...

New Respiratory Quinolone DC-159a
Japan Anti-Tuberculosis Association, JATA, Daiichi-Sankyo Pharmaceuti...

SQ609
Sequella

SQ641
Sequella

Benzothiozinones
New Medicines For Tuberculosis (NM4TB)

Phase I

Pfizer Oxazolidinone
Pfizer
NCE

Clinical Development of SQ109
Sequella,NIH
NCE

the pipeline overview continues on the next page »

Phase II

PA-824
TB Alliance
NCE

Clinical Development of TMC207 for Multi-Drug Resistant TB
Tibotec BVBA
NCE

Registration of TMC207 for Drug Sensitive TB
TB Alliance, Janssen Pharmaceutica N.V.
NCE

Clinical Development of OPC-67683
Otsuka Pharmaceutical Co., Ltd.
NCE

Low-Dose Linezolid for the Treatment of Multi-Drug Resistant Tuberculosis
TBTC, Pfizer

Rifapentine (TBTC study 29)
Information provided by WGND

LL 3858
Lupin Limited
NCE

TBTC Study 26
CDC, Sanofi-aventis

Phase III

Gatifloxacin
Information provided by WGND

Moxifloxacin in the shortening of Rx for drug sensitive pulmonary TB
University College London

site by darby communications

The Working Group is Supported by Stop TB Partnership

Tryptanthrins

Last Updated: 6-Nov-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

NATURE OF TARGET(S)

NAME OF TARGET(S)
Unknown

NATURE OF LIBRARY OR COMPOUNDS

NUMBER OF COMPOUNDS BEING TESTED
53 compounds are synthesized for proof of concept

TYPE OF LIBRARY OR COMPOUNDS
synthetic compounds (M. wt > 250 Da.)

BRIEF PROJECT DESCRIPTION
Tryptanthrin is a natural product of a Chinese/Taiwanese medicinal plant. This compound and its relatives (collectively known as the tryptanthrins) have been extensively explored as anti-bacterial, anti-malarial and anti-cancer agents. During the 1990s, tryptanthrins emerged as potential anti-tuberculosis therapeutics with the ability to prevent growth of both drug sensitive and drug resistant tuberculosis bacteria. However, due to the inability of the particular compounds tested to kill bacteria in mouse models of TB, tryptanthrins were not pursued. Other challenges to development of tryptanthrins as anti-tuberculosis agents include their insolubility and probable toxicity. In addition, the cellular target of tryptanthrins is not known. The goal of this program is to identify tryptanthrins that combine the ability to kill tuberculosis in mouse models of disease with favorable properties such as low toxicity and thus possess potential for development as TB drugs that are expected to be effective against drug resistant bacteria.

NAME OF COMPOUND OR TARGET
Tryptanthrins analogs

DRUG CLASS
Tryptanthrins antibiotic

SPONSOR OR DEVELOPER NAME(S)
TB Alliance, Korea Institute of Chemical Technology and Yonsei University

PROJECT MANAGER NAME(S)
Gerald J. Siuta

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 3 - 5
- Current Annual Budget: $100,000 - $250,000

LOCATION OF R&D (current and planned)
Korea Institute of Chemical Technology, Yonsei University, CROs and TB Alliance

Phenotypic Screening

Last Updated: 2-Oct-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

TYPE OF SCREEN
whole cell microorganism screen

NATURE OF TARGET(S)

NAME OF TARGET(S)
Whole cell

TARGET(S) DERIVED FROM WHICH ORGANISM
M.tuberculosis

NATURE OF LIBRARY OR COMPOUNDS

NUMBER OF COMPOUNDS BEING TESTED
121,000

TYPE OF LIBRARY OR COMPOUNDS
synthetic compounds (M. wt > 250 Da.)
purified compounds derived from natural products

SPONSOR OR DEVELOPER NAME(S)
TB Alliance, University of Illinois

PROJECT MANAGER NAME(S)
Gerald J. Siuta

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 6 - 10
- Current Annual Budget: $250,000 - $1,000,000

LOCATION OF R&D (current and planned)
University of Illinois, Medicinal Chemistry
CROs and TB Alliance

BRIEF PROJECT DESCRIPTION
Phenotypic screening puts the drug discovery process to work at the level of the whole cell. Antibiotic drugs work by inhibiting specific targets in a bacterial cell. But in phenotypic screening, libraries of small molecules are added not to individual, isolated targets but to whole cells of Mycobacterium tuberculosis (M.tb). Compounds that kill or stop the growth of M.tb - but do not affect the survival or growth of mammalian cells - become potential lead molecules. This approach has proven effective and led to the discovery of all novel anti-mycobacterial agents which are in clinical development today. Adding compounds to whole cells - as in phenotypic screening - makes every pathway in the cell a potential drug target. This greatly increases the likelihood of finding an effective inhibitor. In addition, compounds that cannot get into cells, or that are rapidly effluxed from cells, will never be identified as potential lead molecules and will not result in wasted effort. Phenotypic screening has traditionally been done with a surrogate bacterial species/strain (because of its safety or rapidity) that does not faithfully reproduce the drug susceptibility profile of M.tb. Screening has also been limited to actively replicating cultures and therefore has not necessarily identified or prioritized compounds with the potential to act against persistent populations and thus shorten therapy. The current project is designed to screen directly against M.tb under both replicating and non-replicating conditions. This overcomes the issue of poor predictability associated with the earlier screening approach and enables prioritization of leads with potential for shortening treatment. The assay against non-replicating cells uses low-oxygen cultures of M.tb that may more closely mimic the persistent infection conditions in human. The phenotypic screening project started recently. As a pilot project, the team has completed the screening of two libraries: a diverse scaffold-based library of 50,000 drug-like compounds and a 1,500 compound library of natural products and semi-synthetic natural product derivatives. Several promising and novel compound series have been identified from both synthetic and natural product collections. Some of these series showed potent anti-mycobacterial activity and low cytotoxicity and have moved to the hit-to-lead phase. The project team has completed screening of the third and forth libraries which all together consisted of 66,000 synthetic and natural-product derived compounds. Approximately 1500 hits have been identified and confirmed, and they are currently being triaged.

InhA Inhibitors

Last Updated: 6-Nov-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

PROJECT ADVANCING TO NEXT STAGE
Q12 2010

TYPE OF SCREEN
biochemical target based screen

Purified recombinant enzyme

NATURE OF TARGET(S)

NAME OF TARGET(S)
InhA

TARGET(S) DERIVED FROM WHICH ORGANISM
M. tuberculosis

Rv NUMBER(S)
inhA (Rv1484)

NATURE OF LIBRARY OR COMPOUNDS

NUMBER OF COMPOUNDS BEING TESTED
>2 M

TYPE OF LIBRARY OR COMPOUNDS
synthetic compounds (M. wt > 250 Da.)
synthetic fragments (M. wt < 250 Da.)

BRIEF PROJECT DESCRIPTION
Isoniazid, a first-line drug currently used to treat TB, is activated within the mycobacterial cell by the KatG catalase. The activated molecule is thought to suppress mycolic acid biosynthesis through the inhibition of InhA, an enzyme involved in fatty acid biosynthesis. This makes InhA one of the best validated targets for the treatment of TB. Most isoniazid resistance is mediated through mutations in KatG leading to the inability to activate the drug. Therefore one should be able to attain the same clinical efficacy as isoniazid and avoid much of the current resistance to isoniazid by bypassing the requirement for KatG activation and directly inhibiting InhA, The TB Alliance is working with GlaxoSmithKline (GSK) to identify direct InhA inhibitors with the potential to be developed into a new first-line agent against active TB. GSK has screened its corporate compound library, identified hits compounds that are active on the InhA enzyme and progressed them into leads that have anti-mycobacterial activity. These leads are now the subject of an optimization effort to generate an orally-administered, safe, efficacious new drug. If such a compound proves successful at reducing bacterial load in the intensive phase of TB treatment, it might eventually replace isoniazid in a completely new drug combination regimen.

NAME OF COMPOUND OR TARGET
InhA Inhibitors

DRUG CLASS
Novel structural class

SPONSOR OR DEVELOPER NAME(S)
TB Alliance, GlaxoSmithKline

PROJECT MANAGER NAME(S)
Gerald J. Siuta

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 6 - 10
- Current Annual Budget: $1,000,000 - $3,000,000

LOCATION OF R&D (current and planned)
GSK Diseases of the Developing World drug discovery center in Tres Cantos, Spain and TB Alliance

M. tuberculosis Protein Kinase Inhibitors

Last Updated: 15-Oct-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

PROJECT ADVANCING TO NEXT STAGE
Q4 2011

TYPE OF SCREEN
biochemical target based screen

NATURE OF TARGET(S)

NAME OF TARGET(S)
Protein kinase B

TARGET(S) DERIVED FROM WHICH ORGANISM
M. tuberculosis

Rv NUMBER(S)
Rv0014c

NATURE OF LIBRARY OR COMPOUNDS

NUMBER OF COMPOUNDS BEING TESTED
315,000+

TYPE OF LIBRARY OR COMPOUNDS
synthetic compounds (M. wt > 250 Da.)

BRIEF PROJECT DESCRIPTION
Although PknB is the primary target of interest, there are compounds that also have PknA and PknG activity and the selectivity profile is part of the lead optimization process. The compounds target the ATP binding site. The screening assay uses a basic protein kinase assay and MICs are determined in the Mtb H37Ra strain by reazurin staining. One lead scaffold has pharmacological activity. For the lead compounds, the MICs can range from 0.1 to 10 ug/mL.

NAME OF COMPOUND OR TARGET
Primary target is Protein Kinase (Pkn) B; other targets include PknA and PknG

DRUG CLASS
Several chemical scaffolds with various PknA, PknB and PknG selectivity profiles

SPONSOR OR DEVELOPER NAME(S)
Vertex Pharmaceuticals, Incorporated

PROJECT MANAGER NAME(S)
Christopher Locher

LOCATION OF R&D (current and planned)
Vertex Pharmaceuticals at Cambridge, Massachusetts and Coralville, Iowa. Partners include ChemPartner, Shanghai, China, Central New York Research Center, and Children's Hospital Boston

LeuRS inhibitors

Last Updated: 1-Oct-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

PROJECT ADVANCING TO NEXT STAGE
Q1 2010

TYPE OF SCREEN
biochemical target based screen

Both biochemical assays and ability to inhibit microbial growth are used in this program.

NATURE OF TARGET(S)

NAME OF TARGET(S)
Protein synthesis

TARGET(S) DERIVED FROM WHICH ORGANISM
M. tuberculosis

NATURE OF LIBRARY OR COMPOUNDS

NUMBER OF COMPOUNDS BEING TESTED
>1000

TYPE OF LIBRARY OR COMPOUNDS
synthetic compounds (M. wt > 250 Da.)

BRIEF PROJECT DESCRIPTION
This work will explore whether it is feasible to develop new, novel protein synthesis inhibitor for TB. The starting point is a number of boron-containing compounds developed by Anacor Pharmaceuticals with good ability to inhibit M. tuberculosis growth. The first aim in the program is to attain in vivo efficacy in an animal model of tuberculosis with one of the boron-containing compounds. The second aim is to modify the structure of the compounds in an effort to identify more potent inhibitors that are preferentially active on M. tuberculosis.The final aim is to rigorously test whether the boron-containing compounds kill M. tuberculosis via inhibition of protein synthesis, as is the case in other micro-organisms. If successful, the outcome of this work will be a demonstration of protein synthesis inhibition by boron-containing compounds as a validated approach for TB therapy, and perhaps some promising compounds that could be pursued as leads for further work.

NAME OF COMPOUND OR TARGET
LeuRS inhibitors

DRUG CLASS
Oxaboroles

SPONSOR OR DEVELOPER NAME(S)
TB Alliance, Anacor Pharmaceuticals

PROJECT MANAGER NAME(S)
Eric Easom (Anacor) and Gerald J. Siuta (TB Alliance)

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 3 - 5
- Current Annual Budget: $250,000 - $1,000,000

LOCATION OF R&D (current and planned)
Anacor Pharmaceuticals, Palo Alto, CA and TB Alliance

Fungal metabolites

Last Updated: 20-Oct-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

PROJECT ADVANCING TO NEXT STAGE
Q4 2010

TYPE OF SCREEN
whole cell microorganism screen

NAME OF MICROORGANISM
M. tuberculosis

NATURE OF LIBRARY OR COMPOUNDS

NUMBER OF COMPOUNDS BEING TESTED
15,000 extracts screened

TYPE OF LIBRARY OR COMPOUNDS
extract of natural products

BRIEF PROJECT DESCRIPTION
Extracts with selective toxicity identified. Scale up in progress.

SPONSOR OR DEVELOPER NAME(S)
Mycosynthetix, University of Illinois at Chicago

FUNDERS
NIH

PROJECT MANAGER NAME(S)
Cedric Pearce, Scott Franzblau

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: ≤ 2
- Current Annual Budget: $100,000 - $250,000

LOCATION OF R&D (current and planned)
U.S.

Actinomycete metabolites

Last Updated: 30-Nov-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

PROJECT ADVANCING TO NEXT STAGE
Q2 2010

TYPE OF SCREEN
whole cell microorganism screen

NAME OF MICROORGANISM
M. tuberculosis

NATURE OF LIBRARY OR COMPOUNDS

NUMBER OF COMPOUNDS BEING TESTED
70,000 extracts

TYPE OF LIBRARY OR COMPOUNDS
purified compounds derived from natural products
extract of natural products

BRIEF PROJECT DESCRIPTION
Over 7000 actinomycetes were fermented in 3 different media and extracted with 3 solvents. All were screened against M. tuberculosis for growth inhibition. Actives were profiled for potency and selectivity and 20 were scaled up for primary fractionation. Based on activity on primary fractions, 2 were scaled up for isolation of active principles. Project now in the structure identification stage with several samples showing MIC of less than 0.5 ug/ml.

SPONSOR OR DEVELOPER NAME(S)
University of Illinois at Chicago, Myongji University

PROJECT MANAGER NAME(S)
Scott Franzblau, Sanghyun Cho, Guido Pauli

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 3 - 5
- Current Annual Budget: < $100,000

LOCATION OF R&D (current and planned)
Korea and U.S.

DNA metabolism

Last Updated: 1-Dec-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

PROJECT ADVANCING TO NEXT STAGE
Q2 2010

TYPE OF SCREEN
biochemical target based screen

NATURE OF TARGET(S)

NAME OF TARGET(S)
Enzyme involved in DNA synthesis

TARGET(S) DERIVED FROM WHICH ORGANISM
M.tuberculosis

NATURE OF LIBRARY OR COMPOUNDS

NUMBER OF COMPOUNDS BEING TESTED
~ 500K

TYPE OF LIBRARY OR COMPOUNDS
synthetic compounds (M. wt > 250 Da.)

NAME OF COMPOUND OR TARGET
DNA synthesis enzyme

DRUG CLASS
Novel structural class

SPONSOR OR DEVELOPER NAME(S)
AstraZeneca R and D Bangalore

PROJECT MANAGER NAME(S)
Kaveri Das

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees:
  6 - 10

- Current Annual Budget:

LOCATION OF R&D (current and planned)
AstraZeneca R and D Bangalore

Hit to Lead Evaluation of novel compounds

Last Updated: 15-Nov-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

PROJECT ADVANCING TO NEXT STAGE
Q4 2010

TYPE OF SCREEN
whole cell microorganism screen

n/a

NAME OF MICROORGANISM
M. tuberculosis
BCG

NATURE OF TARGET(S)

NAME OF TARGET(S)
Novel, unknown

NATURE OF LIBRARY OR COMPOUNDS

TYPE OF LIBRARY OR COMPOUNDS
synthetic compounds (M. wt > 250 Da.)

NAME OF COMPOUND OR TARGET
Summit PLC compounds

DRUG CLASS
New class

SPONSOR OR DEVELOPER NAME(S)
The Lilly TB Drug Discovery Initiative

PROJECT MANAGER NAME(S)
Professor Tanya Parish

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 6 - 10

- Current Annual Budget:

LOCATION OF R&D (current and planned)
Infectious Disease Research Institute (IDRI), Seattle, Washington, USA. Jubilant Biosys, Bangalore, India. Eli Lilly & Company, Indianapolis, USA

BRIEF PROJECT DESCRIPTION
The Lilly TB Drug Discovery Initiative is conducting medicinal chemistry and pharmacokinetics studies of the Summit PLC compounds to help identify optimized lead compound. This includes exploring structure-activity relationships, conducting pharmaceutical profiling, and generating essential ADME data. The most promising compounds will be selected for animal efficacy, pharmacokinetic and toxicity testing.

Phenotype screening

Last Updated: 1-Dec-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

PROJECT ADVANCING TO NEXT STAGE
Q3 2010

TYPE OF SCREEN
whole cell microorganism screen

Whole cells

NAME OF MICROORGANISM
M. tuberculosis

H37Rv

NATURE OF LIBRARY OR COMPOUNDS

NUMBER OF COMPOUNDS BEING TESTED
200K

TYPE OF LIBRARY OR COMPOUNDS
synthetic compounds (M. wt > 250 Da.)

NAME OF COMPOUND OR TARGET
Whole cells

DRUG CLASS
Novel structural classes

SPONSOR OR DEVELOPER NAME(S)
AstraZeneca R and D Bangalore

PROJECT MANAGER NAME(S)
BheemaRao Ugarkar

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees:
  6 - 10

- Current Annual Budget:

LOCATION OF R&D (current and planned)
AstraZeneca R and D Bangalore India

Nitroimidazoles

Last Updated: 2-Oct-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

NATURE OF TARGET(S)

NAME OF TARGET(S)
Unknown

NATURE OF LIBRARY OR COMPOUNDS

NUMBER OF COMPOUNDS BEING TESTED
>1000 synthesized

BRIEF PROJECT DESCRIPTION
The project team led by Prof. Bill Denny at the University of Auckland has designed and synthesized >800 new analogs, several of which have demonstrated potentcy against Mycobacterium tuberculosis (M.tb) greater than PA-824. Over 30 of the new nitroimidazoles have been evaluated for in vivo efficacy in a mouse TB model and several have shown improved efficacy compared to PA-824. Based on this exciting result, efforts to optimize pharmacokinetics and drug metabolism are continuing in order to select a preclinical development candidate. In parallel to the explorations of new nitroimidazole compounds, a new, commercially viable synthesis of PA-824 has also been developed that will simplify the synthesis of PA-824 and other nitroimidazole analogs and reduce the cost of goods.

NAME OF COMPOUND OR TARGET
Nitroimidazoles

DRUG CLASS
Nitroimidazoles

SPONSOR OR DEVELOPER NAME(S)
TB Alliance
University of Auckland
University of Illinois

PROJECT MANAGER NAME(S)
Gerald J. Siuta

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 6 - 10
- Current Annual Budget: $250,000 - $1,000,000

LOCATION OF R&D (current and planned)
University of Auckland, University of Illinois, Various CROs and TB Alliance

New Generation Diarylquinoline

Last Updated: 12-Oct-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

NATURE OF TARGET(S)

NAME OF TARGET(S)
ATP Synthase

TARGET(S) DERIVED FROM WHICH ORGANISM
M.tuberculosis

Rv NUMBER(S)
Rv1305

NATURE OF LIBRARY OR COMPOUNDS

TYPE OF LIBRARY OR COMPOUNDS
synthetic compounds (M. wt > 250 Da.)

BRIEF PROJECT DESCRIPTION
TMC207 is a member of the Diarylquinoline class of drugs and has a unique mechanism of action, targeting the adenosine triphosphate (ATP) synthase enzyme of the TB mycobacteria.
ATP-synthase is used in the process by which M.tb generates its energy supply. In preclinical studies, TMC207 has been shown to be active against both drug-susceptible and multidrug-resistant strains of M.tb, the bacterium that causes TB. Laboratory studies also have shown it to have strong bactericidal and sterilizing properties. The aim of this project is to develop a back-up Diarylquinoline compound to supplement TMC-207.

NAME OF COMPOUND OR TARGET
ATP Synthase

DRUG CLASS
Diarylquinoline

SPONSOR OR DEVELOPER NAME(S)
TB Alliance, Tibotec

PROJECT MANAGER NAME(S)
Gerald J. Siuta

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 6 - 10
- Current Annual Budget: $1,000,000 - $3,000,000

LOCATION OF R&D (current and planned)
Tibotec locations in Belgium and France, Medicinal and Synthetic Chemistry CROs and TB Alliance

Riminophenazines

Last Updated: 5-Oct-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

NATURE OF LIBRARY OR COMPOUNDS

NUMBER OF COMPOUNDS BEING TESTED
>500

TYPE OF LIBRARY OR COMPOUNDS
synthetic compounds (M. wt > 250 Da.)

BRIEF PROJECT DESCRIPTION
Riminophenazines (Clofazimine) have been effective in treating mycobacterial infections like leprosy, though existing compounds have poor solubility and can cause cosmetic side effects such as pronounced skin discoloration in patients. In 2007 the TB Alliance partnered with the Institute of Materia Medica (IMM) in Beijing to utilize modern techniques to design and synthesize new and more efficacious compounds in this promising class. Riminophenazines are thought to inhibit energy metabolism, which is needed even in slow-growing M.tb persisters. Riminophenazines therefore show promise for treatment shortening. They show no cross-resistance with any other class of TB drugs; their lack of intrinsic P450 interactions means that they should be safe to co-administer with antiretrovirals (ARVs) in patients who are co-infected with TB and HIV. Several series of compounds are now being synthesized under this partnership to explore the potential of this class to treat both drug-susceptible and drug-resistant disease. Riminophenazines are a relatively unexplored series. New science and technology developed in the past two decades has not been used to develop compounds in the series and, therefore, we currently have little knowledge about the structure-activity relationships, which can be used to guide the design of new and better compounds. Over the first year of the program, a large number of novel riminophenazines were prepared and tested tested in vitro for activity against Mycobacterium tuberculosis (M.tb) and in various absorption, distribution, metabolism, elimination and toxicity assays. From this exercise, a number of active analogues have been progressed into mouse in vivo efficacy studies with many demonstrating efficacy comparable or superior to clofazimine. Work has continued this year to optimize the potency, efficacy, pharmacokinetics, and safety profiles for novel riminophenazines with the intent of identifying an appropriate compound for preclinical development.

NAME OF COMPOUND OR TARGET
Riminophenazines

DRUG CLASS
Riminophenazines antibiotic

SPONSOR OR DEVELOPER NAME(S)
TB Alliance, Institute of Materia Medica, The Beijing Tuberculosis and Thoracic Tumor Research Institute and University of Illinois

PROJECT MANAGER NAME(S)
Gerald J. Siuta

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 11 - 20
- Current Annual Budget: $250,000 - $1,000,000

LOCATION OF R&D (current and planned)
Institute of Materia Medica, The Beijing Tuberculosis and Thoracic Tumor Research Institute, Pharmacology and Toxicology CROs and TB Alliance

Mycobacterial Gyrase Inhibitors

Last Updated: 1-Oct-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

PROJECT ADVANCING TO NEXT STAGE
Q10 2009

TYPE OF SCREEN
whole cell microorganism screen

DNA synthesis assay using permeabilised E. coli

NATURE OF TARGET(S)

NAME OF TARGET(S)
DNA Gyrase

TARGET(S) DERIVED FROM WHICH ORGANISM
M.tuberculosis

Rv NUMBER(S)
gyrA (Rv0006) and gyrB (Rv0005)

NATURE OF LIBRARY OR COMPOUNDS

NUMBER OF COMPOUNDS BEING TESTED
>1 M

TYPE OF LIBRARY OR COMPOUNDS
synthetic compounds (M. wt > 250 Da.)

NAME OF COMPOUND OR TARGET
DNA Gyrase Inhibitors

DRUG CLASS
Novel structural class

SPONSOR OR DEVELOPER NAME(S)
TB Alliance, GlaxoSmithKline

PROJECT MANAGER NAME(S)
Gerald J. Siuta

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 11 - 20
- Current Annual Budget: $1,000,000 - $3,000,000

LOCATION OF R&D (current and planned)
GSK Diseases of the Developing World drug discovery center in Tres Cantos, Spain and TB Alliance

BRIEF PROJECT DESCRIPTION
Quinolone antibiotics, such as moxifloxacin, are highly active against TB, with the potential to significantly reduce the duration of TB treatment. Quinolones inhibit the enzyme DNA gyrase, the only type II topoisomerase so far identified in the Mycobacterium tuberculosis (M.tb) genome, and results in mycobactericidal activity. Therefore DNA gyrase is a highly validated anti-tubercular drug target. Compounds that inhibit DNA gyrase are also active against non-replicating, persistent mycobacteria, which might be important for shortening the duration of TB drug therapy. The TB Alliance has been working with GlaxoSmithKline (GSK) to identify novel DNA gyrase inhibitors that binds to the target enzyme outside the region to which quinolones bind, and thereby retain activity on quinolone-resistant DNA gyrase. Such a compound would be expected to be active against drug-sensitive, MDR and XDR M.tb strains. The mycobacterial gyrase inhibitor program is now in the lead optimization stage. Several lead series were identified. Optimization of one lead class has yielded compounds that are potent in vitro, efficacious in vivo in mouse acute infection models and have pharmacokinetic and toxicological profiles compatible with preclinical development. Work on a second, structurally distinct compound series is following behind the lead compound.

Bi-functional Molecules

Last Updated: 1-Oct-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

NATURE OF LIBRARY OR COMPOUNDS

TYPE OF LIBRARY OR COMPOUNDS
synthetic compounds (M. wt > 250 Da.)

BRIEF PROJECT DESCRIPTION
One of the intrinsic problems associated with chemotherapy of any infectious diseases is the development of drug resistance, as illustrated by the development of multidrug-resistant (MDR) TB and extensively drug-resistant (XDR) TB. In TB, the development of drug resistance is reduced by using combination therapies that consist of three to four individual agents with different mechanisms of action. Resistance to each individual drug arises less readily because of the presence of other co-administered agents. A fundamentally different approach to combination therapy is to develop multifunctional molecules that, as the name suggests, possess multiple functional pharmacophores in the same molecule. A multi-functional molecule can therefore attack several drug targets simultaneously. Once optimized, it will prevent and treat drug resistant disease more effectively, provide synergy for better efficacy, and potentially overcome safety and tolerability issues associated with its parent compounds. The TB Alliance is developing multi-functional molecules that synergize the strengths of pharmacophores from the rifamycin, nitroimidazole, oxazolidinone, quinolone and other classes, while circumventing their resistance development liabilities and some safety and tolerability issues associated with the parent drugs. The rifamycin, nitroimidazole, oxazolidinone and quinolone classes of antibiotics have all shown particular promise as sources of new compounds that could shorten the duration of TB therapy and improve the treatment of drug resistance. Multi-functional antibiotics that utilize compounds from among these classes could prove significantly more effective against TB than any class alone, with the potential to both simplify and shorten TB drug therapy. Stage of Development: Lead optimization The project is currently exploring three bifunctional molecules: the rifamycin-nitroimidazoles, the quinolone-nitroimidazoles, and the nitroimidazole-oxazolidinones. In each case, a single new drug is created by covalently fusing together two existing pharmacophores based on the knowledge of their respective structure-activity relationships. Preliminary results have demonstrated dual functions of these molecules. In each class, promising bifunctional compounds have shown potent antibacterial activity. Optimization of one of these classes (nitroimidazole-oxazolidinones) has continued through 2009. Analogues have been prepared and tested in vitro to verify their multifunctional mode of action, and their improved resistance-development properties

NAME OF COMPOUND OR TARGET
Bi-functional Molecules

DRUG CLASS
Bi-functional Molecules

SPONSOR OR DEVELOPER NAME(S)
TB Alliance, University of Auckland and Colorado State University

PROJECT MANAGER NAME(S)
Gerald J. Siuta

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 3 - 5
- Current Annual Budget: $250,000 - $1,000,000

LOCATION OF R&D (current and planned)
University of Auckland, Colorado State University and TB Alliance

TL1 Inhibitors

Last Updated: 13-Nov-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

PROJECT ADVANCING TO NEXT STAGE
Q2 2011

TYPE OF SCREEN
whole cell microorganism screen

Both whole cell screen and biochemical assays have been used

NAME OF MICROORGANISM
M. tuberculosis
other

NATURE OF TARGET(S)

NAME OF TARGET(S)
Translocase 1 enzyme

NATURE OF LIBRARY OR COMPOUNDS

NUMBER OF COMPOUNDS BEING TESTED
over 7000 compounds

TYPE OF LIBRARY OR COMPOUNDS
synthetic compounds (M. wt > 250 Da.)
purified compounds derived from natural products

BRIEF PROJECT DESCRIPTION
Translocase 1 (TL1) enzyme is a very attractive target for development of new drugs: • essential for biosynthesis of the peptidoglycan layer of the bacterial cell wall • inhibition leads to cell death • unique to bacteria, absent in eukaryotic cells • no antibiotics on the market targeting TL1. The semi-synthetic nucleoside-based Capuramycins inhibit TL1 enzyme. Sequella licensed the Capuramycin class from Daiichi-Sankyo in 2004. SQ641, the lead drug candidate in the class with potent activity against Mycobacterium tuberculosis (Mtb) and non-tuberculous Mycobacteria, undergoes preclinical development at Sequella. Sequella has also initiated a program to develop new TL1 inhibitors with enhanced pharmacological properties and in vivo activity against Mtb. In addition, we are exploring the core structure of Capuramycins to discover modifications that might enable broader spectrum activity.

DRUG CLASS
Capuramycins

SPONSOR OR DEVELOPER NAME(S)
Sequella

FUNDERS
Sequella

PROJECT MANAGER NAME(S)
Venkata Reddy

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 3 - 5
- Current Annual Budget:

LOCATION OF R&D (current and planned)
US

MTopo

Last Updated: 30-Nov-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

PROJECT ADVANCING TO NEXT STAGE
Q3 2010

TYPE OF SCREEN
biochemical target based screen

NATURE OF TARGET(S)

NAME OF TARGET(S)
Mycobacterial Gyrase

NATURE OF LIBRARY OR COMPOUNDS

TYPE OF LIBRARY OR COMPOUNDS
synthetic compounds (M. wt > 250 Da.)

NAME OF COMPOUND OR TARGET
Mycobacterial gyrase inhibitors- MGyrX1

DRUG CLASS
Novel structural class

SPONSOR OR DEVELOPER NAME(S)
AstraZeneca R and D Bangalore

PROJECT MANAGER NAME(S)
Vrinda Nandi

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees:
  11 - 20

- Current Annual Budget:

LOCATION OF R&D (current and planned)
AstraZeneca R and D Bangalore

Quinolone TBK-613

Last Updated: 15-Oct-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

PROJECT ADVANCING TO NEXT STAGE
Q2 2010

PRECLINICAL CANDIDATE
TBK-613

DOES THE PROJECT HAVE A CHEMISTRY BACK-UP ACTIVITY?
NO

HAS THE CANDIDATE ENTERED GLP PHARMACOLOGY / TOXICOLOGY STUDIES IN ANIMALS FOR REGULATORY SUBMISSION?
NO

BRIEF PROJECT DESCRIPTION
Quinolones are one of the few classes of antimicrobial agents that are totally synthetic in origin. The first quinolone, nalidixic acid, was introduced in the 1960s as a narrow-spectrum agent used primarily for the treatment of urinary tract infections. Quinolones possess many desirable attributes for a first-line therapeutic agent against TB. These include potent bactericidal activity against both replicating and non-replicating Mycobacterium tuberculosis (M.tb), favorable long-term safety indicators, oral bioavailability, and an ability to penetrate macrophages. Moxifloxacin, a proven and effective antibacterial agent developed by BayerHealthcare AG, is a third-generation quinolone compound, and has demonstrated effective sterilizing activities against M.tb. The TB Alliance, in collaboration with Bayer, is currently involved in phase III moxifloxacin clinical trials, evaluating the drug as an anti-TB agent with the ability to shorten therapy. However, the quinolone class has not been extensively optimized for a TB indication. In 2003, the TB Alliance initiated a lead identification and optimization project with the goal of identifying a new generation of quinolones with improved efficacy against TB while maintaining safety. Based on data from animal models and the preliminary clinical evaluation of quinolones marketed for other antimicrobial indications, this class of compounds has the potential to be part of a shorter and more effective TB treatment regimen. The objective of the quinolone project is to develop a new generation of DNA gyrase inhibitors that will be effective in shortening TB therapy, while maintaining or improving the safety and tolerability profile. The new agents should also be suitable for the treatment of multidrug-resistant (MDR) TB and TB/HIV co-infections without prohibitive drug-drug interactions with antiretroviral drugs (ARVs) used to treat HIV/AIDS. To achieve these goals, the TB Alliance is collaborating with the Korea Research Institute of Chemical Technology (KRICT) and Yonsei University. Scientists at KRICT have synthesized and tested novel quinolones, and have discovered several promising compounds. Among these, TBK-613 was identified as a preclinical development candidate.

NAME OF COMPOUND OR TARGET
TBK-613

DRUG CLASS
Fluoroquinolone antibiotic

SPONSOR OR DEVELOPER NAME(S)
TB Alliance

PROJECT MANAGER NAME(S)
Gerald J. Siuta

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 11 - 20
- Current Annual Budget: $1,000,000 - $3,000,000

LOCATION OF R&D (current and planned)
Toxicology and Pharmacology CRO, Research Triangle Institute and TB Alliance

CPZEN-45

Last Updated: 15-Oct-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

PROJECT ADVANCING TO NEXT STAGE
Q4 2010

PRECLINICAL CANDIDATE
CPZEN-45

SYNONYMS
Caprazene, caprazamycin, nucleoside antibiotic

DOES THE PROJECT HAVE A CHEMISTRY BACK-UP ACTIVITY?
NO

HAS THE CANDIDATE ENTERED GLP PHARMACOLOGY / TOXICOLOGY STUDIES IN ANIMALS FOR REGULATORY SUBMISSION?
NO

BRIEF PROJECT DESCRIPTION
CPZEN-45 is a nucleoside antibiotic that is soluble in water at >10 mg/mL as the trifluoroacetate salt. It is a caprazamycin produced by Streptomyces sp. first described in 2003 by investigators at the Microbial Chemistry Research Foundation (MCRF) and Meiji Seika Kaisa, Ltd of Japan. Subsequently, semi-synthetic production of novel antibiotics based on the caprazamycin structure was described in U.S. patent application US2006/017819 (which includes CPZEN-45 - designated compound II-4) and most recently in a presentation at the 235th American Chemical Society National Meeting (2008) during which the structure of CPZEN-45 was first discussed in a public venue. CPZEN-45 has a minimum inhibitory concentration (MIC) of 1.56 µg/mL against Mycobacterium tuberculosis (Mtb) H37Rv and 6.25 µg/mL against a multidrug resistant (MDR) strain of Mtb. This compound is active against both replicating and non-replicating Mtb in vitro, suggesting it could be efficacious against latent organisms in vivo. CPZEN-45 has shown efficacy against both drug sensitive and extremely drug resistant (XDR) Mtb in a mouse model of acute tuberculosis (TB) in which animals were infected by intravenous injection and treated with s.c. administration of CPZEN-45. Improved efficacy with drug sensitive Mtb was shown when CPZEN-45 was administered in combination with other antitubercular drugs. Recent data generated by NIAID using the gamma interferon gene-disrupted (GKO) mouse model of acute tuberculosis in which infection was achieved by aerosol exposure to Mtb (Erdman) also demonstrated efficacy of CPZEN-45 with 1-1.5 log cfu reduction in lungs of infected mice.

NAME OF COMPOUND OR TARGET
CPZEN-45, Caprazene-45

DRUG CLASS
Caprazene nucleoside

SPONSOR OR DEVELOPER NAME(S)
Microbial Chemistry Research Foundation, Tokyo, Japan
Lilly TB Drug Discovery Initiative
NIAID, IDRI, Lilly, YourEncore

PROJECT MANAGER NAME(S)
Dr. Yuzuru Akamatsu
Dr. Gail Cassell
Dr. Steve Reed
Dr. Barbara Laughon
Dr. Karl Whitney

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 3 - 5
- Current Annual Budget: $100,000 - $250,000

LOCATION OF R&D (current and planned)
IDRI, MCRF, CROs

New Respiratory Quinolone DC-159a

Last Updated: 26-Oct-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

PROJECT ADVANCING TO NEXT STAGE
Q2 2011

PRECLINICAL CANDIDATE
DC-159a

SYNONYMS
New Generation of Respiratory Quinolone

DOES THE PROJECT HAVE A CHEMISTRY BACK-UP ACTIVITY?
NO

HAS THE CANDIDATE ENTERED GLP PHARMACOLOGY / TOXICOLOGY STUDIES IN ANIMALS FOR REGULATORY SUBMISSION?
NO

BRIEF PROJECT DESCRIPTION
DC-159a showed the highest activity against drug-susceptible (DS) TB, quinolone-resistant (QR) MDR-TB and NTM isolates than those of MFLX, GFLX, LVFX and RFP. Activity of DC-159a against QR MDR-TB (MIC90: 0.50 µg/ml) was comparable to that of LVFX against DS-TB isolates. The highest anti-TB activity including MDR strains due to potent inhibitory activity against wild-type and altered DNA gyrase of M. tuberculosis. In the QR MDR-M. tuberculosis infection model, DC-159a treatment groups recorded notable "mean survival days" more than 2~3 times superior to MFLX, LVFX, INH and RFP. In the Drug-Susceptible-M. tuberculosis infection model, DC-159a treatment groups exhibited the best "EBA" and the highest "Log Reduction of CFU in Lungs", which was superior to those of MFLX, LVFX, INH and RFP. Favorable PK ADME profile, high AUC, Cmax, and target distribution. Superior in vivo efficacy of DC-159a in murine TB models might be attributed to its rapid uptake and high concentrations in lungs.

NAME OF COMPOUND OR TARGET
DC-159a

DRUG CLASS
Fluoroquinolone Antibiotics

SPONSOR OR DEVELOPER NAME(S)
Japan Anti-Tuberculosis Association, JATA
Daiichi-Sankyo Pharmaceutical Co.

PROJECT MANAGER NAME(S)
Kazuki Hoshino
Norio Doi

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 11 - 20
- Current Annual Budget: $100,000 - $250,000

LOCATION OF R&D (current and planned)
Japan and US

SQ609

Last Updated: 15-Nov-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

PROJECT ADVANCING TO NEXT STAGE
Q4 2010

PRECLINICAL CANDIDATE
SQ609

SYNONYMS
Dipiperidine

DOES THE PROJECT HAVE A CHEMISTRY BACK-UP ACTIVITY?
NO

HAS THE CANDIDATE ENTERED GLP PHARMACOLOGY / TOXICOLOGY STUDIES IN ANIMALS FOR REGULATORY SUBMISSION?
NO

BRIEF PROJECT DESCRIPTION
Sequella synthesized over 100,000 small molecules to discover new scaffolds with anti-microbacterial activity and identify new leads with sufficient in vitro and in vivo activity against M. tuberculosis (Mtb) appropriate pharmacological properties, and suitable toxicity profiles to warrant taking one or more potential new antitubercular drugs into human clinical trials. The libraries were screened for anti-mycobacterial activity by both direct determination of MIC against Mtb H37Rv and a high-throughput assay with recombinant Mycobacteria containing luciferase (Luc) fused to a promoter, Rv0341, which controls genes that are strongly induced upon treatment by cell wall inhibitors such as ethambutol, isoniazid, and ethionamide. This screen identified a new series of potent cell-wall inhibiting dipiperidines that are structurally unrelated to any existing antitubercular drugs or new drug candidates. After lead optimization studies and extensive analysis of the dipiperidine pharmacophore for antimicrobial activity and drug properties, the compound SQ609 was selected as the most promising in the class. SUMMARY OF ITS ATTRIBUTES INCLUDE: • Potent in vitro activity against laboratory and clinical strains of M.tuberculosis • Inhibition of M. tuberculosis by interfering with cell wall biosynthesis • Moderate in vitro cytotoxicity in cultured mammalian cells • Suitable therapeutic window (in vitro) • Active against intracellular Mtb • High specificity for M. tuberculosis • Good aqueous solubility • Orally bioavailable • Active against M.tuberculosis in two different mouse models of TB upon oral administration • Able to prolong therapeutic effect after the withdrawal of drug therapy in mice • Promising activity against M. tuberculosis when administered in combination with INH, RIF, and PZA • Favorable in vitro safety pharmacology and ADME profile.

NAME OF COMPOUND OR TARGET
SQ609

DRUG CLASS
Dipiperidines

SPONSOR OR DEVELOPER NAME(S)
Sequella

FUNDERS
Sequella, NIAID

PROJECT MANAGER NAME(S)
Marina Protopopova

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 3 - 5
- Current Annual Budget: $100,000 - $250,000

LOCATION OF R&D (current and planned)
US

SQ641

Last Updated: 13-Nov-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

PROJECT ADVANCING TO NEXT STAGE
Q3 2010

PRECLINICAL CANDIDATE
SQ641

DOES THE PROJECT HAVE A CHEMISTRY BACK-UP ACTIVITY?
NO

HAS THE CANDIDATE ENTERED GLP PHARMACOLOGY / TOXICOLOGY STUDIES IN ANIMALS FOR REGULATORY SUBMISSION?
NO

BRIEF PROJECT DESCRIPTION
SQ641 is a chemically-modified analog of nucleoside-based Capuramycin (CM) with a unique mechanism of action and a unique target, the TL-1 enzyme. ATTRIBUTES OF SQ641: • It is bactericidal and kills Mtb faster than any existing antitubercular drugs, including isoniazid and rifampin • It is fast-acting, disintegrating even slow-growing bacteria in 24 hours • 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 • 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 M. avium subspecies paratuberculosis • Acts synergistically with a variety of anti-mycobacterial agents with activity against NTM. Demonstrates efficacy in a mouse model of chronic TB by reducing CFU in lungs of infected mice by 1.0 to 1.5 log. New formulations to improve efficacy of SQ641 have now been explored. Sequella licensed the Capuramycin class of antibacterials from Daiichi-Sankyo in 2004, and has exclusive worldwide rights, excluding the Middle East, for all indications.

NAME OF COMPOUND OR TARGET
SQ641, Inhibitor of translocase I enzyme

DRUG CLASS
Capuramycins

SPONSOR OR DEVELOPER NAME(S)
Sequella

FUNDERS
Sequella, NIH

PROJECT MANAGER NAME(S)
Venkata Reddy

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 6 - 10
- Current Annual Budget: $250,000 - $1,000,000

LOCATION OF R&D (current and planned)
US

Benzothiozinones

Last Updated: 16-Dec-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

PROJECT ADVANCING TO NEXT STAGE
Q2 2010

PRECLINICAL CANDIDATE
2-[(2S)-2-methyl-1,4-dioxa-8-azaspiro[4.5]dec-8-yl]-8-nitro-6-trifluoromethyl-4H-1,3-benzothiazin-4-one

SYNONYMS
BTZ

DOES THE PROJECT HAVE A CHEMISTRY BACK-UP ACTIVITY?
NO

HAS THE CANDIDATE ENTERED GLP PHARMACOLOGY / TOXICOLOGY STUDIES IN ANIMALS FOR REGULATORY SUBMISSION?
NO

NAME OF COMPOUND OR TARGET
2-[(2S)-2-methyl-1,4-dioxa-8-azaspiro[4.5]dec-8-yl]-8-nitro-6-trifluoromethyl-4H-1,3-benzothiazin-4-one / Rv3790

DRUG CLASS
Benzothiozinones

SPONSOR OR DEVELOPER NAME(S)
New Medicines For Tuberculosis (NM4TB)

FUNDERS
European Union

PROJECT MANAGER NAME(S)
Dr Iain G. Old

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 50 - 200
- Current Annual Budget: > $10,000,000

LOCATION OF R&D (current and planned)
EU, Switzerland, Russian Federation, India, South Africa

Pfizer Oxazolidinone

Last Updated: 25-Jan-2010

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

IS THIS A REGISTRATION PROJECT?
Yes

PROJECT ADVANCING TO NEXT STAGE
Q1 2011

PROJECT TYPE
New chemical entity (NCE)

CLINICAL TRIAL INFORMATION
> click to view detailed clinical trial information

CLINICAL PROJECT DESCRIPTION
Standard multiple ascending dose Phase I study evaluating PK and safety

NAME OF COMPOUND OR TARGET
PNU-100480

DRUG CLASS
Oxazolidinone

SPONSOR OR DEVELOPER NAME(S)
Pfizer

PROJECT MANAGER NAME(S)
Paul Miller

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 6 - 10
- Current Annual Budget: $250,000 - $1,000,000

LOCATION OF R&D (current and planned)
Groton, CT, USA

CLINICAL TRIALS

Trial Name: Single Dose Phase I
Primary Sponsor: Pfizer
Trial ID / Reg # / URL:

Study Director	Trial Status	Start Date (First Patient In)	Enrollment as of Last Update	Target Enrollment
Darcy Paige	other	May 2009	Completed	

Trial Name: Multiple Dose Phase I
Primary Sponsor: Pfizer
Trial ID / Reg # / URL:

Study Director	Trial Status	Start Date (First Patient In)	Enrollment as of Last Update	Target Enrollment
Darcy Paige	currently enrolling	November 2009		

Clinical Development of SQ109

Last Updated: 4-Feb-2010

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

IS THIS A REGISTRATION PROJECT?
Yes

PROJECT ADVANCING TO NEXT STAGE
Q3 2010

PROJECT TYPE
New chemical entity (NCE)

CLINICAL TRIAL INFORMATION
> click to view detailed clinical trial information

CLINICAL PROJECT DESCRIPTION
SQ109 is currently being evaluated in a phase 1B study to determine safety and pharmacokinetics of multiple doses of SQ109 in healthy volunteers. Subsequent trials will evaluate safety, efficacy and pharmacokinetics of several dose ranges of SQ109 in combination with other anti-tubercular drugs in patients with drug-susceptible and drug-resistant tuberculosis infection.

NAME OF COMPOUND OR TARGET
SQ109

DRUG CLASS
Ethylenediamines

SPONSOR OR DEVELOPER NAME(S)
Sequella,NIH

PROJECT MANAGER NAME(S)
Dr. Gary Horwith

LOCATION OF R&D (current and planned)
USA, South Africa, Tanzania, Uganda, Kenya

RELATED LINKS
Sequella, Inc.

CLINICAL TRIALS

Trial Name: Dose Escalation Study of SQ109 in Healthy Adult Volunteers
Primary Sponsor: Sequella/NIH
Trial ID / Reg # / URL: NCT 00866190

Study Director	Trial Status	Start Date (First Patient In)	Enrollment as of Last Update	Target Enrollment
David Matthews/Robert Johnson	all patients enrolled	April 2009	30	30

PA-824

Last Updated: 6-Nov-2009

DISCOVERY: HIT-TO-LEAD, LEAD-OPT | PRE-CLINICAL: PRE-CLINICAL | CLINICAL: PHASE I, PHASE II, PHASE III | REGISTRATION: REGISTRATION

IS THIS A REGISTRATION PROJECT?
Yes

PROJECT ADVANCING TO NEXT STAGE
Q4 2010

PROJECT TYPE
New chemical entity (NCE)

CLINICAL TRIAL INFORMATION
> click to view detailed clinical trial information

CLINICAL PROJECT DESCRIPTION
PA-824 is a nitroimidazole, a class of novel anti-bacterial agents. As a potential TB drug, it has many attractive characteristics - most notably its novel mechanism of action, its activity in vitro against all tested drug-resistant clinical isolates, and its activity as both a potent bactericidal and a sterilizing agent in mice. In addition, the compound shows no evidence of mutagenicity in a standard battery of genotoxicity studies, and no significant activity against a broad range of Gram-positive and Gram-negative bacteria. An extensive Phase I program has been successfully conducted, and PA-824 successfully completed its first proof-of-concept study in TB patients, an EBA trial. Results from the initial EBA trial are highly encouraging; suggesting even lower doses than were expected may be efficacious. A low-dose EBA study has been initiated to determine dose(s) to take into later stage development and ultimately clinical use. An update on the clinical development of PA-824 was presented at the Gordon Research Conference (Oxford, UK, August 16-21, 2009).

NAME OF COMPOUND OR TARGET
PA-824

DRUG CLASS
Nitroimidazol-oxazine

SPONSOR OR DEVELOPER NAME(S)
TB Alliance

PROJECT MANAGER NAME(S)
Ngozi Erondu and Erica Egizi

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 6 - 10
- Current Annual Budget: $5,000,000 - $10,000,000

LOCATION OF R&D (current and planned)
Numerous CROs; EBA trial sites: University of Cape Town Lung Institute,South Africa; Intercare Medical and Dental Centre, Cape Town, South Africa; TB Alliance (NYC and Pretoria)

RELATED LINKS
TB Alliance

Safety, tolerability, and Pharmacokinetics of PA-824 in healthy subjects.

Assessment of the Effects of PA-824 on renal function in healthy subjects.

Emerging Drugs for Active Tuberculosis.

Nitroimidazopyran as the Drug Candidate for the Treatment of Tuberculosis.

CLINICAL TRIALS

Trial Name: Evaluation of Early Bactericidal Activity in Pulmonary Tuberculosis
Primary Sponsor: TB Alliance
Trial ID / Reg # / URL: NCT00944021

Study Director	Trial Status	Start Date (First Patient In)	Enrollment as of Last Update	Target Enrollment
Andreas Diacon, MD	currently enrolling	August 2009	38	68

Clinical Development of TMC207 for Multi-Drug Resistant TB

Last Updated: 12-Nov-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | **PHASE II** | PHASE III
REGISTRATION: REGISTRATION

IS THIS A REGISTRATION PROJECT?
Yes

PROJECT TYPE
New chemical entity (NCE)

CLINICAL TRIAL INFORMATION
> click to view detailed clinical trial information

CLINICAL PROJECT DESCRIPTION
TMC207 is a member of the Diarylquinoline class of drugs and has a unique mechanism of action, targeting the adenosine triphosphate (ATP) synthase enzyme of the TB mycobacteria. ATP-synthase is used in the process by which M.tb generates its energy supply. In preclinical studies, TMC207 has been shown to be active against both drug-susceptible and multidrug-resistant strains of M. tuberculosis, the bacterium that causes TB. Laboratory studies also have shown it to have strong bactericidal and sterilizing properties. The compound is currently in Phase II testing in patients with pulmonary MDR-TB.

NAME OF COMPOUND OR TARGET
ATP Synthase

DRUG CLASS
Diarylquinoline

SPONSOR OR DEVELOPER NAME(S)
Tibotec BVBA

PROJECT MANAGER NAME(S)
Karel De Beule

LOCATION OF R&D (current and planned)
Tibotec locations in Belgium and USA, Clinical CROs and TB Alliance

RELATED LINKS
Tibotec

TB Alliance

TMC207 for multidrug resistance TB

CLINICAL TRIALS

Trial Name: Anti-bacterial Activity, Safety, and Tolerability of TMC207 in Patients With MDR-TB.
Primary Sponsor: Tibotec BVBA
Trial ID / Reg # / URL: http://clinicaltrials.gov/ct2/show/NCT00449644?term=tmc+207&rank=5

Study Director	Trial Status	Start Date (First Patient In)	Enrollment as of Last Update	Target Enrollment
Tibotec BVBA	all patients enrolled	May 2007	208	

Trial Name: Trial to Evaluate the Safety, Tolerability, and Efficacy of TMC207 as Part of an Individualized MDR-TB treatment Regimen in Patients With Sputum Smear-positive Pulmonary MDR-TB.
Primary Sponsor: Tibotec BVBA
Trial ID / Reg # / URL: http://clinicaltrials.gov/ct2/show/NCT00910871?term=tmc+207&rank=2

Study Director	Trial Status	Start Date (First Patient In)	Enrollment as of Last Update	Target Enrollment
Tibotec BVBA	currently enrolling	July 2009		225

Registration of TMC207 for Drug Sensitive TB

Last Updated: 29-Oct-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

IS THIS A REGISTRATION PROJECT?
Yes

PROJECT ADVANCING TO NEXT STAGE
Q4 2009

PROJECT TYPE
New chemical entity (NCE)

CLINICAL TRIAL INFORMATION
> click to view detailed clinical trial information

CLINICAL PROJECT DESCRIPTION
TMC207 is a diarylquinoline drug active with a novel mechanism of action. It inhibits the ATP Synthase of Mycobacterium tuberculosis and has high in vitro activity against wild-type and drug-resistant strains of M. tuberculosis. Several Phase I studies and a 7-day EBA study have been completed. A Phase II study in MDR patients is ongoing. An EBA study is being planned to evaluate the efficacy of TMC207 over a 14 day treatment period. Subsequent development would include testing TMC207 in combination with other TB drugs to evaluate its potential to improve TB treatment.

NAME OF COMPOUND OR TARGET
ATP Synthase

DRUG CLASS
Diarylquinoline

SPONSOR OR DEVELOPER NAME(S)
TB Alliance
Janssen Pharmaceutica N.V.

PROJECT MANAGER NAME(S)
Gerald J. Siuta

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 11 - 20
- Current Annual Budget: $250,000 - $1,000,000

RELATED LINKS
TB Alliance

Tibotec

Antimycobacterial properties of the diarylquinolines

A once-weekly regimen of TMC207

EBA and Pharmacokinetics of TMC207

TMC207 for multidrug resistance tuberculosis.

CLINICAL TRIALS

Trial Name: Registration of TMC207 for Drug Sensitive TB
Primary Sponsor: TB Alliance
Trial ID / Reg # / URL:

Study Director	Trial Status	Start Date (First Patient In)	Enrollment as of Last Update	Target Enrollment
Ngozi Erondu	study in development			

Clinical Development of OPC-67683

Last Updated: 2-Nov-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

IS THIS A REGISTRATION PROJECT?
Yes

PROJECT TYPE
New chemical entity (NCE)

CLINICAL TRIAL INFORMATION
> click to view detailed clinical trial information

CLINICAL PROJECT DESCRIPTION
A Multi Center, Randomized, Double-Blind, Placebo-Controlled Phase 2 Trial to Evaluate the Safety, Efficacy and Pharmacokinetics of Multiple Doses of OPC 67683 in Patients With Pulmonary Sputum Culture-Positive, Multidrug-Resistant Tuberculosis. This is a clinical trial to evaluate the safety and efficacy of OPC-67683 in the treatment of multidrug resistant tuberculosis (MDR TB) for 56 days. In addition to an optimized background regimen (OBR), patients will be randomized to: • 100 mg OPC-67683 BID • 200 mg OPC-67683 BID • placebo BID After 56 days subjects will complete their OBR.

NAME OF COMPOUND OR TARGET
OPC-67683

DRUG CLASS
Nitro-dihydro-imidazooxazole antibiotic

SPONSOR OR DEVELOPER NAME(S)
Otsuka Pharmaceutical Co., Ltd.

PROJECT MANAGER NAME(S)
Lawrence Geiter

LOCATION OF R&D (current and planned)
China, Estonia, Japan, Republic of Korea, Latvia, Philippines

RELATED LINKS
Otsuka Pharmaceutical Co., Ltd.

CLINICAL TRIALS

Trial Name: A Placebo-Controlled, Phase 2 Trial to Evaluate OPC 67683 in Patients With Pulmonary Sputum Culture-Positive, Multidrug-Resistant Tuberculosis (TB)
Primary Sponsor: Otsuka Pharmaceutical Development & Commercialization, Inc.
Trial ID / Reg # / URL: NCT00685360

Study Director	Trial Status	Start Date (First Patient In)	Enrollment as of Last Update	Target Enrollment
Charles D. Wells	currently enrolling	April 2008		

Low-Dose Linezolid for the Treatment of Multi-Drug Resistant Tuberculosis

Last Updated: 12-Nov-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | **PHASE II** | PHASE III
REGISTRATION: REGISTRATION

IS THIS A REGISTRATION PROJECT?
No

PROJECT ADVANCING TO NEXT STAGE
Q4 2010

PROJECT TYPE
Approved drug without a TB indication

CLINICAL TRIAL INFORMATION
> click to view detailed clinical trial information

CLINICAL PROJECT DESCRIPTION
Study of pharmacokinetics of linezolid and other second-line antituberculosis drugs conducted at the University of Cape Town by Dr. Helen McIlleron and colleagues

NAME OF COMPOUND OR TARGET
Linezolid

DRUG CLASS
Oxazolidinones

SPONSOR OR DEVELOPER NAME(S)
TBTC, Pfizer

FUNDERS
TBTC, Pfizer

PROJECT MANAGER NAME(S)
Dr. William Mac Kenzie

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 6 - 10
- Current Annual Budget: $250,000 - $1,000,000

LOCATION OF R&D (current and planned)
Durban, South Africa

CLINICAL TRIALS

Trial Name: TBTC Study 30 of Low Dose Linezolid for MDRTB
Primary Sponsor: TBTC, Pfizer
Trial ID / Reg # / URL: NCT00664313

Study Director	Trial Status	Start Date (First Patient In)	Enrollment as of Last Update	Target Enrollment
Dr. Wafaa El-Sadr, Dr. Nesri Padayatchi	currently enrolling	February 2009	23	45

Trial Name: TBTC Study 30PK Linezolid Pharmacokinetics in Multi-Drug Resistant (MDR)/Extensively-Drug Resistant (XDR) Tuberculosis
Primary Sponsor: TBTC, Pfizer
Trial ID / Reg # / URL: NCT00691392

Study Director	Trial Status	Start Date (First Patient In)	Enrollment as of Last Update	Target Enrollment
Dr. Wafaa El-Sadr, Dr. Nesri Padayatchi	currently enrolling	April 2009	14	36

Rifapentine (TBTC study 29)

Last Updated: 20-Nov-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

IS THIS A REGISTRATION PROJECT?
No

PROJECT ADVANCING TO NEXT STAGE
Q3 2010

PROJECT TYPE
Approved drug without a TB indication

CLINICAL TRIAL INFORMATION
> click to view detailed clinical trial information

CLINICAL PROJECT DESCRIPTION
The goal of this Phase 2 clinical trial is to evaluate the antimicrobial activity and safety of an experimental intensive phase (first 8 weeks of treatment) tuberculosis treatment regimen in which rifapentine is substituted for rifampin.

NAME OF COMPOUND OR TARGET
Rifapentine

SPONSOR OR DEVELOPER NAME(S)
Information provided by WGND

CLINICAL TRIALS

Trial Name: TBTC Study 29: Rifapentine During Intensive Phase Tuberculosis (TB) Treatment
Primary Sponsor: Centers for Disease Control and Prevention, Sanofi-Aventis
Trial ID / Reg # / URL: NCT00694629

Study Director	Trial Status	Start Date (First Patient In)	Enrollment as of Last Update	Target Enrollment
Susan Dorman	currently enrolling	December 2008		480

LL 3858

Last Updated: 30-Nov-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

IS THIS A REGISTRATION PROJECT?
No

PROJECT ADVANCING TO NEXT STAGE
Q4 2010

PROJECT TYPE
New chemical entity (NCE)

CLINICAL TRIAL INFORMATION
> click to view detailed clinical trial information

CLINICAL PROJECT DESCRIPTION
This study is a Single Arm open label study and will be conducted at one center to Determine the Early Bactericidal,Extended Early Bactericidal Activity and Pharmacokinetic Study of 400 mg of LL 3858 for the Treatment of Newly Diagnosed Sputum Smear-Positive Pulmonary Tuberculosis. The patients will be admitted for 7 days. The IP Tablet (400mg of LL 3858) will be administered orally once daily for 5 days on empty stomach. The patients will be shifted to the standard ATT from day 7 onwards. Patients receiving the study drug will be evaluated by sputum examination. The primary outcome measures will be to evaluate safety and fall in log10 colony forming units (CFU) of Mycobacterium tuberculosis per ml sputum per day viz.0-2 days (EBA study) and 2-5 days (Extended EBA) The secondary outcome will be to determine the Pharmacokinetic profile of 400mg of LL 3858.

NAME OF COMPOUND OR TARGET
LL 3858

DRUG CLASS
Pyrrole derivative

SPONSOR OR DEVELOPER NAME(S)
Lupin Limited

FUNDERS
- Lupin Limited,CSIR

PROJECT MANAGER NAME(S)
Rajesh Kumawat

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 11 - 20
- Current Annual Budget: $250,000 - $1,000,000

LOCATION OF R&D (current and planned)
46A/47A, Nande Village, Mulshi-Taluka,Pune-411042,Maharashtra(India)

CLINICAL TRIALS

Trial Name: A Phase IIa, Open Label Study to Determine the EBA, Extended EBA and Pharmacokinetic Study of LL3858 for the Treatment of Newly Diagnosed Sputum Smear-Positive Pulmonary TB
Primary Sponsor: Lupin Limited
Trial ID / Reg # / URL: Protocol Number LRP/CTP/022/3858/II/01/TEMP UTRN 105052390-1009200912121142

Study Director	Trial Status	Start Date (First Patient In)	Enrollment as of Last Update	Target Enrollment
Rajender K Kamboj	study in development			

TBTC Study 26

Last Updated: 3-Dec-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | **PHASE II** | PHASE III
REGISTRATION: REGISTRATION

IS THIS A REGISTRATION PROJECT?
No

PROJECT ADVANCING TO NEXT STAGE
Q2 2011

PROJECT TYPE
Approved drug with a TB indication

CLINICAL TRIAL INFORMATION
> click to view detailed clinical trial information

CLINICAL PROJECT DESCRIPTION
Randomized multicenter open-label non-inferiority trial comparing 12 once-weekly doses of Rifapentine 900mg + Isoniazid 900 mg given by DOT vs 9 mo of self-administered daily INH 300 mg in treatment of LTBI in persons at high risk

NAME OF COMPOUND OR TARGET
Rifapentine

DRUG CLASS
Rifamycin

SPONSOR OR DEVELOPER NAME(S)
CDC, Sanofi-aventis

PROJECT MANAGER NAME(S)
M. Elsa Villarino, MD, MPH

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 20 - 50
- Current Annual Budget: $1,000,000 - $3,000,000

LOCATION OF R&D (current and planned)
Multicenter international trial, largely in North America

CLINICAL TRIALS

Trial Name: TBTC Study 26
Primary Sponsor: CDC
Trial ID / Reg # / URL:

Study Director	Trial Status	Start Date (First Patient In)	Enrollment as of Last Update	Target Enrollment
Timothy Sterling, MD	all patients enrolled		8500	8000

Gatifloxacin

Last Updated: 20-Nov-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | PHASE III
REGISTRATION: REGISTRATION

IS THIS A REGISTRATION PROJECT?
Yes

PROJECT TYPE
Approved drug without a TB indication

CLINICAL TRIAL INFORMATION
> click to view detailed clinical trial information

CLINICAL PROJECT DESCRIPTION
Tuberculosis is currently treated with a 6-month course regimen. During this time many patients might fail to adhere to treatment and default, increasing the risk of recurrent disease which might be multidrug resistant. A shorter duration of treatment is expected to provide improved patient compliance and at least equal or better clinical outcome. The aim of the trial is to evaluate the efficacy and safety of a gatifloxacin-containing regimen of four months duration for the treatment of pulmonary tuberculosis.

NAME OF COMPOUND OR TARGET
Gatifloxacin

DRUG CLASS
Fluoroquinolones

SPONSOR OR DEVELOPER NAME(S)
Information provided by WGND

LOCATION OF R&D (current and planned)
Benin, Guinea, Kenya, Senegal, South Africa

CLINICAL TRIALS

Trial Name: A Controlled Trial of a 4-Month Quinolone-Containing Regimen for the Treatment of Pulmonary Tuberculosis.
Primary Sponsor: Institut de Recherche pour le Developpement, World Health Organization, European Commission
Trial ID / Reg # / URL: NCT00216385

Study Director	Trial Status	Start Date (First Patient In)	Enrollment as of Last Update	Target Enrollment
Christian Lienhardt	currently enrolling			2070

Moxifloxacin in the shortening of Rx for drug sensitive pulmonary TB

Last Updated: 19-Oct-2009

DISCOVERY: HIT-TO-LEAD | LEAD-OPT
PRE-CLINICAL: PRE-CLINICAL
CLINICAL: PHASE I | PHASE II | **PHASE III**
REGISTRATION: REGISTRATION

IS THIS A REGISTRATION PROJECT?
Yes

PROJECT ADVANCING TO NEXT STAGE
Q4 2013

PROJECT TYPE
Approved drug without a TB indication

CLINICAL TRIAL INFORMATION
> click to view detailed clinical trial information

CLINICAL PROJECT DESCRIPTION
REMoxTB, is a three-arm randomized, double-blind, controlled study in which moxifloxacin is substituted for either ethambutol or isoniazid and is administered for a total of four months. REMoxTB will determine whether these new, four-month regimens are not inferior to standard six-month therapy in terms of failure and relapse, as well as safety. A shorter TB regimen is needed to ease the burden on patients and health systems and to reduce the development of drug resistance. REMoxTB patient enrollment began in January 2008. A total of 20-30 sites, including sites in Asia (India, China and other Asian countries), Africa and Latin America are being recruited into the study to reach enrollment targets.

NAME OF COMPOUND OR TARGET
Moxifloxacin

DRUG CLASS
Fluoroquinolones

SPONSOR OR DEVELOPER NAME(S)
University College London

FUNDERS
TB Alliance, EDCTP, BMRC

ESTIMATED ANNUAL RESOURCES DEDICATED TO PROJECT
- Current Full-Time Employees: 20 - 50
- Current Annual Budget: > $10,000,000

LOCATION OF R&D (current and planned)
Kenya, South Africa, Tanzania, Zambia, Mexico, Hong Kong, Taiwan, Korea, Peru, Malaysia, Thailand, India, UK

RELATED LINKS
Trial information on clinicaltrials.gov web site

CLINICAL TRIALS

Trial Name: Controlled comparison of two moxifloxacin containing treatment shortening regimens with the standard regimen in pulmonary TB
Primary Sponsor: University College London
Trial ID / Reg # / URL: www.remoxtb.org

Study Director	Trial Status	Start Date (First Patient In)	Enrollment as of Last Update	Target Enrollment
Prof. Stephen Gillespie	currently enrolling	January 2008	451	2400