TB ALLIANCE
GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT

First Tuberculosis Drug Developed by a Non-profit Begins Clinical Trials

Trial is First in TB Alliance's Growing Pipeline of Drugs;
Provides Model for Future Drug Development

NEW YORK CITY (June 14, 2005) – The Global Alliance for TB Drug Development (TB Alliance), a non-profit public-private partnership developing affordable, new drug regimens for tuberculosis, today announced the start of Phase I clinical trials for the lead TB drug in its pipeline, PA-824. The trials begin this month.

The TB Alliance directed and funded the drug's preclinical development, completed through a global network of contractors. The U.S. National Institute of Allergy and Infectious Diseases of the National Institutes of Health also provided in-kind support and technical assistance. The TB Alliance's research and development team established a global development program involving 26 institutions in nine countries managed by Dr. Doris Rouse at RTI International.

"Reaching this milestone greatly enhances the chances of improved TB treatment and is an important advance in the TB community's drive for a faster cure," said Dr. Maria C. Freire, President and CEO, TB Alliance. "We worked creatively and smartly with our partners, donors and contractors. The result is that an extremely promising TB compound moved from lead identification into human trials in near record time."

In a 2002 landmark agreement, the TB Alliance obtained exclusive worldwide rights to PA-824 and its derivatives from the California-based biotechnology firm, Chiron Corporation. Chiron's unprecedented commitment was to make the TB technology available royalty-free in endemic countries.

"We believed this was the best way to move the drug forward to meet a critical public health need when we first reached agreement with the TB Alliance," said Craig Wheeler, President, Chiron Biopharmaceuticals. "Now we're sure. The TB Alliance has moved this extremely rapidly and we are watching the trials with anticipation."

A member of the novel nitroimidazole class, PA-824 was first identified in 1995 by researchers at PathoGenesis, later acquired by Chiron Corporation. Its potential as an anti-tuberculosis agent was described in a 2000 *Nature* magazine article. Recent preclinical studies, directed by the TB Alliance, indicate that it has sterilizing potency and a novel mode of action that could shorten treatment times.

In vitro studies demonstrated that PA-824 has potent activity against both actively and slowly-growing *Mycobacterium tuberculosis (M.tb)*. *In vivo* studies showed that the drug kills *M.tb* effectively in both the initial, intensive phase as well as in the later continuation phase of TB therapy. This demonstrates that the drug has both bactericidal and sterilizing activity, combining in a single compound the most effective attributes of isoniazid and rifampin, which are two of the cornerstones of TB drug therapy today.

"To reach our goal of dramatically shortening TB therapy, we must create novel regimens that incorporate new drugs with different and complementary modes of action," said Dr. Mel Spigelman, Director of Research and Development at the TB Alliance. "PA-824's excellent profile means its introduction into a new regimen could help shorten treatment time dramatically and overcome some of the challenges with TB treatment, such as multi-drug resistance and the treatment of TB-HIV co-infected patients."

Current projections of TB incidence and mortality reflect the need for new, shorter TB therapy. Between 2000 and 2020 it is estimated that nearly 1 billion people will be newly infected from TB, 200 million will become sick and 35 million will die. TB is a leading cause of death among people living with HIV/AIDS. However, treating the two diseases at the same time is extremely difficult because of negative interactions between some ARVs used to treat HIV/AIDS and TB drugs. Early studies of PA-824 indicate that it could be safely used with HIV/AIDS therapies.

The Phase I clinical study, to be conducted by the Nebraska-based MDS Pharma Services, will evaluate the safety, tolerability, and pharmacokinetics of single doses of PA-824 in healthy, male volunteers.

The TB Alliance's scientific goal is to develop safer, more effective drugs and therapeutic regimens to simplify and shorten the current six to eight months of treatment. More than 40 years have elapsed since the last novel compound was introduced for the treatment of TB. The TB Alliance has assembled the first global pipeline of new TB drugs since the 1960s through partnerships with industry, research institutes and academia, and is developing multiple classes of compounds, including quinolones, macrolides and pleuromutilins.

Among the many public health benefits of a shorter TB regimen is improved patient compliance which would increase cure rates and lower toxic side effects. This would limit the rise of new resistant strains caused by people failing to complete treatment. With the backing of thirty-four stakeholder institutions around the world, the TB Alliance embraces a comprehensive strategy to ensure that the TB drugs it develops are affordable, adopted by health practitioners and accessible to the patients who need them most.

About the Global Alliance for TB Drug Development

The Global Alliance for TB Drug Development (TB Alliance) is a not-for-profit, public-private partnership accelerating the discovery and/or development of affordable, new anti-TB drugs. Such drugs promise to shorten treatment, be effective against multi-drug resistant strains, and improve treatment of latent infection. In collaboration with public and private research laboratories worldwide, it is leading the development of the most comprehensive portfolio of TB drug candidates in four decades. The TB Alliance operates with the support of the Bill and Melinda Gates Foundation, the Rockefeller Foundation, the U.S. Agency for International Development, and the Netherlands Ministry for Cooperation Development.

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