

Strategy

Reaching for the summit in TB

By Peter A. Rittenhouse
Senior Editor

When it comes to deals, it's the larger partner that generally gets the commercialization rights in the major markets. But to get rights to a tuberculosis compound from **Summit plc** for its Lilly TB Drug Discovery Initiative, **Eli Lilly and Co.** let Summit retain rights in the developed world. What the TB Initiative gets is a series of compounds specific to *Mycobacterium tuberculosis* with a novel mechanism of action that the pharma would market in the developing world.

The public-private partnership, which Lilly formed in June 2007, announced the acquisition of its first two compounds last month: an unnamed compound from Summit, and CPZEN-45, which was donated by the non-profit **Microbial Chemistry Research Foundation (MCRF)**.

According to Gail Cassell, VP of scientific affairs at Lilly and chair of the TB Initiative's steering committee, CPZEN-45 is much further along. It has shown efficacy against multi-drug resistant (MDR)- and extensively drug resistant (XDR)-TB in infected mice and has undergone toxicology testing. Nevertheless, she said, the compound could not be considered a clinical candidate for at least another year and a half.

Both MCRF and Summit approached Lilly when they learned of the TB Initiative.

Summit screens compounds from academia and biotech companies using its cell-based and zebrafish platforms, then out-licenses early stage compounds to partners. Jon Tinsley, director of programmes, told BioCentury the company had been screening numerous compounds for antibiotic activity, and a series of compounds with a novel mechanism of action proved to be highly specific for mycobacteria.

"Summit will have access to all data generated on the compounds by the Initiative, and these data will be used as part of any future sub-licensing agreements. Although Summit will remain an active part of the project's scientific steering committee, it will no longer incur any costs associated with further development of the program," Richard Vickers, associate director at Summit, told BioCentury.

"It is only through deal structures of this nature that companies will have any incentive to develop drugs for TB and other neglected diseases," said Vickers.

Tinsley agreed: "If Lilly hadn't come along, we would not have moved it — it would have sat on the shelf."

Christopher Earl, president and CEO of the non-profit **BIO Ventures for Global Health**, said this type of deal marks an example of a new trend where technology flows from the private sector back to the public sector, where the not-for profit entity champions the product development process.

"Every one of these PPP arrangements is unique, and within each deal, there is a lot of thought around the issue of

how to share the value that's created," he noted.

Cassell said the Summit deal could be a model for deals with other biotech companies: "It is absolutely true that the terms might very well be similar in future agreements," she said.

Although Lilly had exited the infectious disease space some years earlier, Cassell, a former director of the **Global Alliance for TB Drug Development**, realized there was room for another non-profit player to work in parallel to get early stage compounds identified and moving toward clinical development.

"This is a total not-for-profit initiative for Lilly," she noted. "We will not receive any income from our investment."

Relative to virtual organizations designed to create new TB drugs, such as the TB Alliance, an advantage of Lilly's TB Initiative is having a cornerstone

pharma that knows how to develop drugs, plus an actual research facility at the non-profit **Infectious Disease Research Institute (IDRI)**. For the Lilly initiative, IDRI serves as the principal coordinator and is providing expertise in microbiology, molecular biology and chemistry, and managing the Initiative's laboratory.

Another key partner in the TB Initiative is NIH's **National Institute of Allergy and Infectious Diseases**. Cassell said NIAID was identified early as a potential member because it is the world's largest funder of drug discovery for infectious diseases.

Cassell hopes this combination will "attract other partners in the effort."

Lilly has provided the TB Initiative with a library of 500,000 compounds plus an upfront commitment of \$15 million, including \$6 million in cash and \$9 million in kind. According to Cassell, **Merck & Co. Inc.** has provided access to its natural products library of several hundred compounds with activity against TB.

Cassell said the criteria for killing compounds at the TB Initiative would be no different than at Lilly. "They will be based on accepted industry criteria," she said. "The go/no-go decision will be very rigorous, with the goal of failing fast."

Steve Reed, founder and head of R&D at IDRI, expects to work very closely with the TB Alliance, noting that Bruce Carter, who sits on TB Alliance's board of directors and is chairman and CEO of **ZymoGenetics Inc.**, also sits on the Lilly TB Initiative's board of advisors. "We want to complement the work of the TB Alliance," Reed said.

Reed said the compounds from Summit and MCRF would require substantial effort to characterize and move through the development process. At most, he envisioned only two to four new compounds, either acquired or identified from libraries, could enter the TB Initiative's development pipeline per year.

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Richard Vickers, Summit plc

Strategy**sanofi's malaria gameplan**

By **Erin McCallister**
Senior Writer

sanofi-aventis Group does not expect to make any money from developing drugs to treat tropical diseases in either the developed or the developing world. Rather, the mandate of the company's Access to Medicines unit is to develop malaria and tuberculosis drugs without losing money.

Last month, sanofi announced a memorandum of understanding to work with **Medicines for Malaria Venture (MMV)** in hopes of adding compounds to the pharma's malaria pipeline and offsetting the cost of drug development.

MMV is a public-private partnership that manages and funds discovery, development and delivery of new medicines to treat and prevent malaria. Because of its focus on countries where disease is endemic, each project must fit a strict product profile, including activity against resistant strains, potential to provide complete cure with 3 days of treatment, and a cost per course of therapy below \$1.

The initial focus of sanofi's malaria programs also is the developing world. Although new malaria drugs could be used for travelers and members of the military, Francois Bompert, VP of medical for Access to Medicines, said those markets in the developed world are small and unlikely to provide much profit.

"We must recoup our investment, but the mandate does not go beyond that," Bompert told BioCentury.

The company has a tiered pricing schedule for antimalarials. According to Bompert, the company sells malaria drugs to governments, non-government organizations (NGOs) and not-for-profits at the lowest possible cost. The company also sells the drugs to for-profit pharmacies in Africa where it can charge a higher price.

"We have our mainstream research directed towards money-making drugs; but we know there are very poor populations for malaria drugs, and we do not want price to be an obstacle to giving the drug," he said.

sanofi markets two malaria drugs: Coarsucam, a fixed-dose combination of artesunate and amodiaquine, and Nivaquine chloroquine sulfate syrup. Coarsucam is approved to treat malaria in more than 20 African countries and earlier this month

received approval for the **World Health Organization's** (WHO) Prequalification of Medicines Program. Coarsucam was co-developed with the **Drugs for Neglected Disease initiative (DNDi)**.

Chloroquine, which blocks the asexual phase of the *Plasmodium falciparum* lifecycle, is standard of care. But resistant strains of the protozoan parasite, which causes about 80% of malaria cases, are making it necessary to use combinations of more costly drugs like artemisinin derivatives. For the developing world, cheaper alternatives are necessary.

Thus, sanofi said partnerships with MMV may include co-developing three of the pharma's compounds to treat the

disease. Two of the compounds are in Phase II testing: a chloroquine derivative called ferroquine, and an unnamed bis-thiazolium compound that inhibits phosphatidylcholine synthesis.

The third is trioxaquine, a chimeric compound that contains trioxane and an aminoquinoline. The preclinical testing is partnered with **Palumed S.A.**

Ferroquine has not shown any resistance in animal models, according to Bompert. Trioxaquine is active against chloroquine-resistant malaria parasites, and may act not only during the parasite's asexual phase, but also against its gametophyte forms. The gametophytes are taken up by feeding mosquitos, so a compound that is active against them could reduce disease transmission.

A potential partnership with MMV also may allow the not-for-profit to screen sanofi's libraries to identify new compounds that inhibit parasite proliferation.

MMV provided funding for recently published research in which cultured, malaria-infected red blood cells were used to screen a compound library from **Novartis AG**. That work yielded several hits that would not have been expected to have antimalarial activity (see *SciBX: Science-Business eXchange*, June 26).

Bompert said the partnership with MMV also might provide access to potential financing, which could help sanofi recover its costs.

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Francois Bompert, sanofi-aventis

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Melvin Spigelman, director of R & D at the TB Alliance, told BioCentury he doesn't see the organizations as overlapping because they are each working on separate compounds. Eventually, he noted, "the new drugs may best be used together."

Spigelman added it is important to "figure out the best way to integrate and coordinate drug development efforts. Everyone is careful not to waste resources and leverage the best projects into our pipeline."

COMPANIES AND INSTITUTIONS MENTIONED

BIO Ventures for Global Health (BVGH), Washington, D.C.

Eli Lilly and Co. (NYSE:LLY), Indianapolis, Ind.

Global Alliance for TB Drug Development, New York, N.Y.

Infectious Disease Research Institute (IDRI), Seattle, Wash.

Merck & Co. Inc. (NYSE:MRK), Whitehouse Station, N.J.

Microbial Chemistry Research Foundation, Tokyo, Japan

National Institute of Allergy and Infectious Diseases (NIAID), Bethesda, Md.

Summit plc (LSE:SUMM), Abingdon, U.K.

ZymoGenetics Inc. (NASDAQ:ZGEN), Seattle, Wash.