More PPPs for drugs please

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Public–private partnerships (PPP), extensive collaborations between the public and private sectors, have a significant impact on drug development for otherwise neglected diseases, argues the head of an organization that funds and manages the world's largest portfolio of anti-malarial drug discovery and development projects.

Tropical diseases

Most tropical diseases, such as African trypanosomiasis, which kills an estimated 50,000 people annually in the sub-Saharan regions of Africa, come under the definition of neglected diseases, explains Christopher Hentschel, Chief Executive Officer of the non-profit Medicines for Malaria Venture (MMV; http://www.mmv.org) based in Geneva, Switzerland.

These particular diseases suffer from a general lack of global investment, thus leading to a shortage of new drugs and available treatments, says Hentschel, who was speaking at the *Joint International Tropical Medicine* Meeting in Bangkok, Thailand, 2–4 December 2003.

Indeed, of the 1223 new drugs placed on the global market between 1975 and 1996, only 1% were treatments for tropical diseases. Yet tropical diseases kill more people worldwide than anything else with the exception of TB and HIV/AIDS.

Global health and PPPs

The sources and distribution of funding for global health research needs to be re-addressed, says Hentschel, referring to the so-called '10/90 gap'. Only 10% of global health research is dedicated to 90% of global heath problems, according to the Global Forum for Health Research in Geneva, Switzerland, an international foundation that aims to correct the 10/90 gap. In addition, developing a new drug and taking into account product failures can cost the pharmaceutical industry up to US$800 million per approved drug. With such high costs and low potential returns, it is difficult to encourage drug companies to invest in drug discovery and development for the neglected tropical diseases of the developing world.

Hentschel believes that PPPs represent one solution. The MMV, which was set up in November 1999, is one of the first PPPs to be established after discussions between the World Health Organization (WHO; http://www.who.org) and the International Federation of Pharmaceutical Manufacturers Association (IFPMA; http://www.ifpma.org), a non-governmental organization, which represents drug companies. The aim of MMV is to effectively manage drug discovery and development projects undertaken by various members of a PPP.

Antimalarial portfolio

The MMV now manages the world's largest portfolio of antimalarials, with 21 projects investigating different drugs at various stages of clinical development. One of these, DB289, which passed clinical trials for African trypanosomiasis, has also shown promise as an antimalarial. William Petri, Professor of Medicine at the University of Virginia Health System in Virginia, USA (http://hsc.virginia.edu), believes that PPPs are central to the delivery of basic science breakthroughs to the tropics.

'There are many diseases in the tropics for which current therapy is inadequate or non-existent,' said Petri. 'At the same time, new targets for chemotherapy are available in this post-genomic era. Only by partnership of the public with private for-profit companies can these advances in target identification and drug discovery end up in the hands of the people who need them.'

Hentschel recalls the example of a novel antimalarial drug 'LapDap' to illustrate the success of PPPs that work between drug companies and universities in developed and developing countries. LapDap©, which was approved this year, is based on a combination of two antimalarials, chlorproguanil and dapsone. Scientists realized that using a combination of drugs with different activities is one way to tackle the increasing problem of drug resistance. Indeed, LapDap is highly effective against certain drug resistant strains of malaria, and will soon be available in Africa at a price of only US$0.29 per adult treatment.

Success and support

William Watkins, a research fellow based at the University of Liverpool, UK (http://www.liv.ac.uk), who is involved in the LapDap project, told *BioMedNet News* (http://news.bmn.com);

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'Without the PPP between [the] University of Liverpool, Department for International Development, WHO and GlaxoSmithKline, it is very unlikely that LapDap would have been developed as a commercial drug.'

Another keen supporter of the PPP strategy is Carol Sibley, Professor of Genome Sciences at the University of Washington (http://www.washington.edu). 'The public sector supports a wonderful breadth of efforts in drug target identification and antigen definition, a variety that is unlikely to be possible in the private domain,' said Sibley.

'However, these early efforts are often truncated by the dearth in the public sector of expertise and resources required to bring projects of that kind beyond the earliest stages of development,' she said. 'The PPP makes the best of both worlds, and offers real promise for tangible drugs and vaccines for diseases that have for too long been neglected.'

Sea squirt sheds light on advanced soft tissue sarcomas

Paula Moyer, BMN News

Research presented at the 14th joint meeting of the American Association for Cancer Research, the National Cancer Institute, and the European Organization for the Research and Treatment of Cancer (AACR–NCI–EORTC; http://www.aacr.org/2003mtct.asp) Boston, MA, USA, showed that a therapy derived from a marine animal, the tunicate *Ecteinascidia turbinate*, arrests tumour growth in advanced soft tissue sarcomas and shows promise as a third-line therapy, report Spanish researchers.

The humble sea squirt

Tunicates, also known as sea squirts, are marine animals that are surprisingly close relatives of vertebrates. The study of tunicates led to the development of trabectedin (Yondelis), the agent used in the current research.

'This compound has shown promise in patients with disease progression, and therefore [might help] target tumour control and prolong patient survival,' said Luis Flores, a research physician with the company Pharma Mar (http://www.pharmamar.com) based in Madrid, Spain, which manufactures Yondelis. In findings based on several Phase II studies, his team found that the disease stabilized in over a third of patients who had been resistant to at least two previous treatments. The investigators envision using trabectedin as a third therapy in treating soft-tissue sarcoma.

Phase II trials results

In a series of Phase II studies, 183 participating patients received intravenous treatment at a dose of 1.5 mg m^{-2} over 24 hours, with the dose repeated every three weeks. Fifty-nine patients (41%) had previously received at least one line of chemotherapy with a median of two drugs and a range of 1–7. At enrollment, 96% had progressive disease. Prior to treatment, 61% were resistant to anthracyclines, 44% were resistant to ifosfamide and 34% were double-resistant The follow-up period was a median of 33 months.

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