

Developing countries can contribute to global health innovation

To the Editor:

Trevor Mundel¹ rightly notes that most pharmaceutical firms are focused on developing lucrative therapies, which has left a vacuum for treating diseases primarily affecting developing countries. However, pharmaceutical firms based in these developing countries are increasingly targeting these large local markets and are investing important sums, now estimated at approximately \$4 billion annually in China and India alone, in drugs and vaccines, including those for neglected diseases².

Take tuberculosis, for example. With incidence rates in 2011 of 1 million in China and 2.2 million in India, together accounting for 55% of the 5.8 million newly diagnosed cases globally, domestic pharmaceutical firms in these countries see a sizable commercial opportunity³. Lupin Pharmaceuticals (India), historically a generic-drug manufacturer, is developing a novel drug for tuberculosis (LL-3858, Sudoterb) that is currently in phase 2 trials; the drug has shown a superior pharmacokinetic and preclinical safety profile compared to the existing front-line therapy isoniazid⁴. Tianjin CanSino Biotechnology (China) has in-licensed a tuberculosis vaccine candidate consisting of an adenoviral vector expressing the mycobacterial protein Ag85A from McMaster University (Canada). This vaccine is in phase 1 trials.

Furthermore, these domestic companies' historic involvement in process innovation to reduce manufacturing costs led to the creation of strong global distribution channels that are encouraging research and development (R&D) inside these same domestic companies in global health disease areas less endemic to their home countries. Early manufacturing R&D efforts in the late 1990s by Shantha Biotechnics (India) using the recombinant vector *Pischia pastoris* reduced the cost of the hepatitis B vaccine from \$15 to \$1 (ref. 5). Shantha has considerable distribution capabilities in many developing countries, generates over \$100 million in revenue annually and uses that revenue to drive R&D in new drugs, including a bivalent inactivated-whole-cell oral cholera vaccine (Shanvac) that launched in 2009 and a rotavirus vaccine, based on VP7 protein from serotypes G1–G4 bovine human reassortment strains, that is in phase 3 trials. A vaccine manufacturer with a similar business model, Bharat Biotech (India) is developing a phase 1 antimalaria vaccine consisting of a recombinant lyophilized receptor-binding domain of *Plasmodium vivax* Duffy binding protein region II (rPvRII) antigen expressed in *Escherichia coli*, as well as neonatal bovine 116E strain rotavirus vaccine. The majority of the cases for rotavirus (>50%), cholera (>50%) and malaria (>80%) are in Africa,

although the incidence is significant in Southeast Asia, as well^{6–8}.

The commercial opportunity in global health disease has also sparked some investor interest. Shantha was acquired by Sanofi-Aventis for \$784 million in 2009, and merger-and-acquisition rumors of Bharat Biotech have abounded ever since. In early 2012, South Korean investors placed \$4 million into Sumagen (Seoul, Korea) to in-license from the University of Western Ontario (Canada) and take into phase 1 trials in the US the first genetically modified killed whole-virus vaccine for HIV. Sumagen received additional grant financing from the Bill & Melinda Gates Foundation.

These domestic pharmaceutical firms are not necessarily looking for the next 'blockbuster drug' and can make an outsized impact in global health because there are so few drugs in development. In addition, their low-cost base can help to improve access to these medicines. Multinational pharmaceutical firms bring large R&D dollars, supporting and engaging domestic pharmaceutical firms with an intrinsic market motivation through equity investments, but grants and inclusion in product development partnerships may be a powerful way of increasing R&D activity. Mundel concludes that "creating and delivering vaccines and drugs for developing world demands new approaches..." that "no single organization alone can accomplish."¹ The pharmaceutical industry in developing countries can play an important part in these new approaches to global health.

COMPETING FINANCIAL INTERESTS

The authors declare competing financial interests: details are available at <http://www.nature.com/doi/10.1038/nm.3086>.

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- Mundel, T. *Nat. Med.* **18**, 1735 (2012).
- Chakma, J. & Sammut, S.M. *Nat. Biotechnol.* (in the press).
- World Health Organization. Global Tuberculosis Report. <http://apps.who.int/iris/bitstream/10665/75938/1/9789241564502_eng.pdf> (2012).
- Palomino, J.C., Ramos, D.F. & da Silva, P.A. *Curr. Med. Chem.* **16**, 1898 (2009).
- Chakma, J., Masum, H., Perampaladas, K., Heys, J. & Singer, P.A. *Nat. Biotechnol.* **28**, 783 (2010).
- World Health Organization. World Malaria Report 2011 <http://www.who.int/malaria/world_malaria_report_2011/en/> (2011).
- Ali, M. *et al. Bull. World Health Organ.* **90**, 209A–218A (2012).
- World Health Organization. <http://www.who.int/immunization_monitoring/burden/rotavirus_estimates/en/> (2012).