



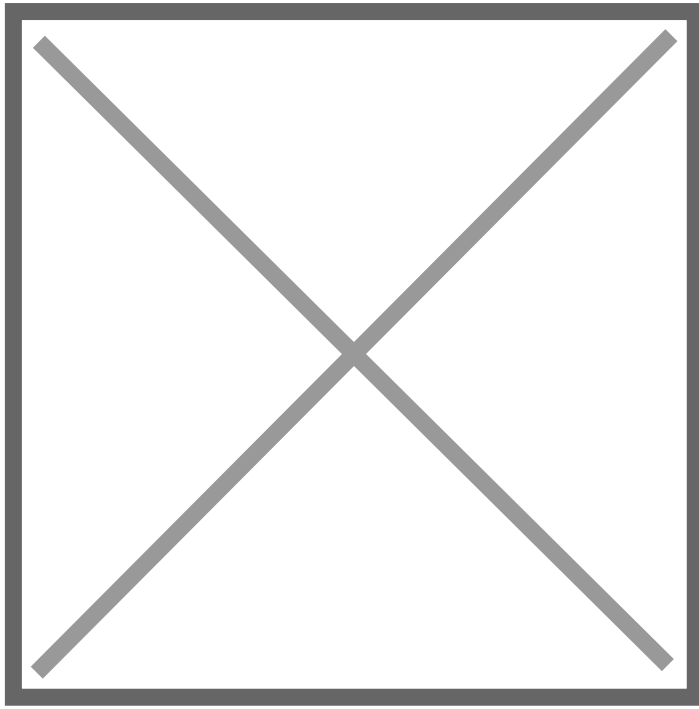
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Early mover advantage

09 February 2006 | News



TAMIFLU

Early mover advantage

The big pharma companies tried hard to get the sub license for manufacturing Oseltamivir (generic "Tamiflu") from Roche. At the end, Hetero Drugs grabbed the bite beating the competition. Its early initiatives well ahead of others served it with the results.

The battle between the leading pharmaceutical companies of India to get the sub license for manufacturing Oseltamivir (generic "Tamiflu") ended on December 21, 2005 as Swiss pharmaceutical company Roche has granted Hetero Drugs Ltd, a sub-license for the production and marketing of Oseltamivir.

Under the sub-licensing agreement, Roche authorizes Hetero to manufacture and market both the active pharmaceutical ingredient (API) and finished product of Oseltamivir for supply to India, least developed countries and developing countries. This agreement focused on providing Oseltamivir for government pandemic use and will have an immediate effect on the availability in India and developing countries both directly and through further agreements with local companies.

Need for licensing

Responding to the heightened demand for Tamiflu and death of nine persons due to avian influenza (including two in China, four in Turkey and three in Indonesia as on January 30, 2006 and 85 deaths since 2003 in countries like Cambodia, China, Indonesia, Thailand, Turkey and Vietnam), Roche's priority is to ensure Tamiflu will be available for seasonal use to patients and to fulfil government pandemic orders. In 2006 Roche has donated another two million treatment courses of Tamiflu to the WHO. This is in addition to previous donations made by Roche in 2004 and 2005, and results in a total of 5.125 million treatment courses being available to the WHO to help people affected by a potential pandemic.

Roche will have increased its own production capacity by the end of 2006. It will then be in a position to potentially produce 300 million treatments of Tamiflu annually. The expansion will be achieved by a further stepwise scale-up of Roche's production network. It means a ten-fold increase over the capacity in 2004. But to meet the present growing need it has decided to work to expand collaborative production network.

In less than two months it has completed the evaluation of around 200 third parties interested in getting involved in the manufacturing of Tamiflu. After systematic screening, Roche production experts zeroed on to twelve companies globally that meet the defined criteria in terms of quality, technical ability, capacity and the speed of bringing that capacity on stream. These companies include major pharmaceutical companies, large generic manufacturers and specialty chemical producers. It

has so far signed agreements with only two companies - one with Hetero Drugs Ltd from India and second with Shanghai Pharmaceutical Group, a Chinese company, the first to sign sub-licensing agreement with Roche for the overall production of Oseltamivir for pandemic use in China.

Roche believes that it is not the patent that is the concern but the production capacities. Roche says the manufacturing of Tamiflu is complex and involves 10 main steps, some of which have been identified as complicated (e.g. azide chemistry). Manufacturing takes approximately 6-8 months once all the raw materials have been sourced. However, Roche's assumption is that for any party starting from scratch it would take 2 to 3 years to produce Tamiflu.



The present status

China

China: Roche and Shanghai Pharmaceutical Group have signed the first sub-licensing agreement for the overall production of Oseltamivir for pandemic use in China.

Taiwan

Taiwan: Roche will be in a position to deliver requested quantities during 2006.

Vietnam

Vietnam: Roche will be providing capsules or active pharmaceutical ingredient for third parties to encapsulate locally.

Korea and Malaysia

Korea and Malaysia: Roche is providing capsules.

India

India: Roche has granted a sub-license to India's Hetero Drugs to make Oseltamivir for India and developing countries.

In some countries, e.g. Thailand, Philippines and Indonesia, Tamiflu is not patent protected. These governments are therefore free to purchase or manufacture Oseltamivir at their discretion. Roche

Whilst Roche says it remains on schedule to meet the current orders received from over 50 governments, the collaboration with Hetero will enhance the supply of Oseltamivir in some of the world's poorest countries, resulting in earlier than anticipated delivery timelines and more capacity for further orders. Hetero is the first company that was identified to be able to speed up agreed delivery timelines in the first half of 2006.

"As a result of a period of intense production planning, we are pleased to announce the partnership with Hetero Drugs as the latest step in our scale-up efforts to meet the needs of governments in preparing for the potential public health threat posed by avian influenza. This is another demonstration of Roche's commitment to working as a collaborative and responsible partner with governments and the World Health Organization (WHO) to assist in pandemic planning, " said David Reddy, Roche's Pandemic Taskforce Leader on signing of agreement between Roche and Hetero Drugs.

Dr B Parthasaradhi Reddy, chairman and managing director, Hetero Group of Companies said, "Hetero commends Roche's commitment to increasing the availability of Tamiflu for government pandemic stockpiling. Hetero is capable of fulfilling Roche's objective of addressing the needs of least developed and developing countries in preparing for a pandemic by increasing supplies of Oseltamivir. "

The winner

Hetero Drugs Ltd, the Rs 720-crore pharmaceutical group company based in Hyderabad, is a relatively young company started in 1993. It maintained a low profile during the entire episode but it still bagged the license. It has beaten Indian pharma giants such as Ranbaxy Laboratories Ltd, which has recorded consolidated sales of Rs 5195.60 crore (\$1178 million for December ending 2005) and Cipla that has garnered a 5.5 percent share of the domestic market at the retail level, with sales of Rs 1,128 crore (as on March 31, 2005 and marginally ahead of GlaxoSmithKline). Both these were trying hard to get the license from Roche. At the end it was Hetero Drugs that went with the order.

On December 1, 2005, Ranbaxy Laboratories Ltd said that if called upon by the US Government or by the innovator Roche, the Ranbaxy global organization is well prepared to provide oseltamivir phosphate capsules (generic version of Tamiflu) to the US healthcare system to meet the threat of the avian flu that has now become a global concern. Dr Brian Tempest, then CEO and Managing Director and now the chief mentor of Ranbaxy stated, "In terms of available capacity, within six months, we anticipate being able to produce 22 Tons per Annum (TPA) of the Active Pharmaceutical Ingredient (API) based on Ranbaxy's API process. Within a twelve-month period, we expect to scale up our operations to produce a total of 100 TPA. The 22 TPA translates to a total of approximately 300 million 75mg capsules, and within a year to a total of 1.3 billion 75 mg capsules. The API would be manufactured in Ranbaxy's FDA compliant facilities in India, and the capsules could be manufactured at its US facilities. It is estimated that within the first six months approximately 20 million patients could receive a course of treatment, and within the first year in excess of 100 Million patients could be managed for the avian flu."

Ranbaxy also stated that it would make all efforts to secure the required quantities, the starting material (shikimic acid) that is critical to the entire process from a variety of independent sources. And it will also make all efforts to work with the USFDA to secure approvals to manufacture the API as well as capsules within Ranbaxy facilities in order to reach the projected goals as may be indicated by the US government. "We are prepared and are committed to meet the needs of the US healthcare system, and are able and willing to partner with other organizations, including the innovator, to effectively meet this public health challenge that threatens the US," said Dr Tempest. Similarly Cipla too had said that it could manufacture 100,000-200,000 dosages of the bird flu drug Tamiflu for emergencies.

However, Roche went with Hetero Drugs which has been working on this project for over two and half years. Following approval from the Government of India to manufacture and market a generic version of Oseltamivir, Hetero began investing in the manufacturing of Oseltamivir. Hetero has invested about Rs 76.5 crore on this project. The reports say it had bagged the order given the fact its focus on retroviral products from 1996. Earlier, Generic Product Organisation Thailand had approved for providing necessary inputs for Tamiflu. Since then it was engaged in work related to this project over the last couple of years.

Hetero maintained that it is currently the only company, which is in the advanced stages of the production process for a generic version of Oseltamivir. Hetero with its huge capacities, can fulfil the total requirement of the Indian market. It is committed to deliver one million capsules of Oseltamivir to the Government of India by January 2006. Besides it will start fulfilling orders for least developed and developing countries. Each capsule is likely to be priced at \$12. This has the potential to add Rs 100 crore to its turnover in the first year of marketing.

A release from Hetero adds, "This is the first instance in which a sublicense has been granted since the introduction of India's new patent legislation agreed in 2005. This legislation complies with international patent laws. Roche and Gilead Sciences filed patents for Oseltamivir in India of which some have been granted and the remaining process and product patents are

currently under evaluation by the patent office in India."

Reacting to this, a spokesperson of Ranbaxy said, "Ranbaxy has always demonstrated commitment to support humanitarian efforts by making available quality affordable generic products around the world employing all necessary critical resources. The company is confident of its scientific know-how to produce generic Oseltamivir, the Active Pharmaceutical Ingredient, in large volumes. The company has the capacity to supply Oseltamivir to markets around the world after meeting the required issues relating to Intellectual Property and other regulatory clearances and we are preparing ourselves to begin commercial production. Ranbaxy will be very happy to be a part of the government effort in any part of the world to combat avian-flu."

Narayan Kulkarni