



# LATIN FEVER

**Latin America is shaping up to become a sound region for investment, with benefits for pharma beyond outsourcing their phase II and phase III clinical trials. World Pharmaceutical Frontiers talks to Ernest Egli, Roche Brazil and Latin America, Mahabir P Gupta, University of Panama, and Manuel Fresno, iCON, about what Latin America holds for the future.**

**R**oche is ranked among the top three pharmaceutical companies in Latin America, with double digit growth that has been mainly attributed to their biological products: MabThera, Herceptin, Avastin and Pegasys. The company's decision to shift focus from primary care drugs to biological products meant they were able to concentrate more fully on key franchises such as oncology, rheumatoid arthritis, virology, metabolism and anaemia.

According to Ernest Egli, president of Roche Brazil, Latin American countries have a promising future as their clinical standards become more aligned with European and North American counterparts. Political and economic stability, observed in most Latin American countries over the last ten years, has been key in this trend.

'The pharmaceutical industry has consolidated its presence in Latin America over the last decade after a long period of crises and losses that caused several multinational companies to leave the region,' says Egli. 'Today, all the large multinational companies are re-establishing their presence and the current stability has

motivated further development of the industry, including local and regional players based in Argentina, Brazil and Chile.'

Concerns over the intellectual property (IP) patent violations of the past also seem to be subsiding as an increasing number of Latin American countries attempt to comply with international legislation driven by trade-related aspects of IP rights. 'In spite of this strong alignment tendency, there are some regional differences as well as a clear need for further regulation enforcement,' adds Egli.

In contrast to European countries, Latin America has historically had weaker legislation with regard to approval of follow-on

## ADVANTAGES FOR PHARMA IN LATIN AMERICA

- Established pharma presence
- Improved clinical standards
- Political and economic stability
- Large population for clinical trial participation
- Large opportunities for discovery



### Profiles

Ernest Egli joined Roche in 1972 as product manager in Basel. In 1975, he moved into the company's Latin America business working in various positions until 1998 when he became president of Roche Brazil and Latin America.



Manuel Fresno is vice president Canada and Latin America, clinical operations at iCON. Previously, he was general manager, Latin America for MDS Pharma Services and general manager Spain for Phoenix International Life Sciences.



Mahabir P Gupta, PhD, is research professor of pharmacognosy at the University of Panama. In 2003, he was the recipient of the AAAS Award for International Scientific Cooperation.

products. 'Since biologicals are more complex than chemical products, health authorities need to consolidate their rules for new entrant drugs to guarantee efficacy and safety,' says Egli. 'This can be achieved through powerful trials and pharmaco vigilance.'

Overall, the positive opportunities for Latin American investments outweigh the challenges. For example, Brazil has become the most attractive market in South America due to its large population, positive macroeconomic conditions and political stability. Egli believes a base in Brazil is essential for pharma looking to cement their presence in South America.

'Beyond Brazil, Venezuela, Argentina and Colombia are of particular interest due to their size and growth rates,' he says. 'Together with other smaller countries in South America, they are growing above the regional average, and by having flat, flexible structures in these countries, pharma can mitigate potential risks and boost their regional results.'

### Room for innovation

Competition in the generic drug market remains fierce and production is heavily funded by local governments that offer incentives to regional producers. But Egli believes there is still plenty of scope for introducing innovative drugs into the South American pharmaceutical market. 'This is especially true in therapeutic areas with unmet medical needs such as oncology, rheumatology and diabetes,' he says. 'The "innovation market", which is driven by specialised medicines and developed by multinational pharma, has produced the highest growth rates in the region, despite funding restrictions.'

Local companies have focused their efforts on producing and distributing generics and branded-generics of non-patented products. 'They have invested heavily in new plants, using government incentives, and the quality of their products has increased significantly,' Egli says. 'As a result, these companies have dominated price-driven segments within the market.'

Meanwhile, multinationals have concentrated their efforts on differentiating themselves through innovative drugs. 'Several multinationals, including Roche, have invested in their regional plants in order to become global providers of innovative product lines,' adds Egli. 'These investments bring new technologies to the region and help to improve overall quality standards.'

Looking to the future, Egli believes the direction for other pharmaceutical companies in Latin America may lean further towards biological products. But he warns that this will be a slow process and the costs involved with creating new biotech centres in the region may currently be economically unfeasible.

### CRO opportunities

Manuel Fresno of iCON, the world's fourth largest contract research organisation (CRO), also believes the region holds enormous possibility for pharma, both as an area to conduct clinical trials and as an emerging market for medical therapies.



Latin America contains 50% of the world's biodiversity, which remains largely unexplored by the scientific community.

CROs have seen significant increases in the amount of work flowing in to the Latin American markets. 'The region is attractive for many reasons, but the most important is that it's a good place to source patients for clinical trials,' says Fresno.

Latin America offers the opportunity to test on a wide variety of diseases that affect both developing regions as well as Western countries. As a whole, the region comprises 20 nations and over 550 million people, largely condensed around mega-city centres with populations in excess of 10 or 20 million.

Genetically, Latin Americans are relatively homogenous and share strong similarities with Hispanics in the US (representing 13% of the US population and expected to rise to 25% within the next ten years) and offers the potential to conduct relevant clinical trials that target this growing demographic group.

'A lot of pharma are looking for "treatment-naive" patients and the patient population in Latin America is large, especially in metropolitan centres,' says Fresno. 'Patients are often treated in large speciality hospitals, which is another advantage for pharma because they'll need fewer sites compared with other regions where recruiting a large number of sites is not uncommon.'

At the same time, patients are motivated to participate in clinical trials. 'Trial recruitment is both closely monitored and carefully regulated and advantages for patients going into clinical trials can include access to university hospitals and avoiding waiting lists,' he adds.

Compared with Western Europe or the US, Latin American clinical trial drop-out rates can be as much as 60% lower. This is largely attributed to strong doctor-patient relationships. Holding clinical trials in both the northern and southern hemispheres offers pharma the benefit of year-round recruitment and treatment study, thereby halving the number of years it would take to complete clinical trials in one hemisphere.

'On one hand, the cost of running clinical trials in Latin America can be as much as 30-40% lower than the same trial in the US or Europe,' says Fresno. 'This is a clear advantage when companies are considering branching out into other regions. On the other hand, there are also problems.'



Regulatory approval timelines are probably the biggest challenge for clinical trials in the region. Though there has been some improvement in recent years, timelines remain longer than in other countries. Another challenge is the import and export processes, as well as shipping costs to the US and Europe are more expensive.'

### Research challenges

Mahabir Gupta, research professor of Pharmacognosy at the University of Panama, believes there are missed opportunities in Latin America. The region contains nearly 50% of the world's biodiversity, which remains largely unexplored by the scientific community.

'The marine area alone is impressive from the point of view of new molecules that can be identified through concerted effort,' says Gupta. 'But pharmaceutical industries in Latin America are mostly branches of multinational companies that only manufacture products from existing formulations, so very little research and development is being conducted in this region and the pharmaceutical industry is not investing much into R&D.'

Despite this situation, Gupta believes there is a need for investment since Latin America represents around 10% of the world's market for drugs. 'Some companies, such as ATSE, have started R&D programmes in Brazil and have put drugs to market from a Brazilian lab,' he says. 'I understand that Brazil has other projects in the pipeline designed to put local biodiversity into the pharmaceutical market and phytomedicine.'

But these are exceptions, and the reasons may be down to a lack of high quality local scientists and geographic distance from pharmaceutical corporate bases, which can drive up costs. Another factor is that local government cooperation has been notoriously difficult, as new discoveries are frequently detained in their country of origin. Currently, many researchers face challenging bureaucratic processes when trying to obtain permission to study a plant or compound in larger or better equipped labs abroad.

'If the pharmaceutical company wants to own the intellectual property – they will have to make an agreement with local governments over the distribution of royalties,' says Gupta. 'This is why some companies shy away from Latin American R&D. But if

pharma decided to move more into the area of discovery, tapping into the biodiversity of Latin America could be an important step.'

The biggest challenge for researchers in Panama tends to be a lack of funding and a lack of national resources to properly invest in areas of research,' according to Gupta. 'The government has established grant programmes for scientists and have been sending local scientists abroad, currently 115, to obtain degrees at educational centres around the world. Panama has decided to invest in scientific knowledge for development, which is a key area, and over the last three years it has increased five-fold.'

Latin American researchers also face difficulties in obtaining supplies on time, due to customs regulations, and reagent costs tend to be much higher than in the US. 'We have less money but higher expenditures,' he adds, 'And there are no local industries for the production of scientific and medical products, so we must rely on imports for all of our equipment and supplies.'

The region also tends to appoint researchers, unlike the UK or US where research professionals are accredited. Many researchers in Latin America are former professors who were instructed by the government to change careers. 'As a whole, Latin American countries are slightly behind countries such as Taiwan and India, which have realised the importance of scientific studies and are investing heavily in this area,' explains Gupta. 'But regional governments are now moving in that direction.'

### Trials and tribulations

In contrast to research, clinical trials in Latin America are well established compared with other developing nations. Gupta points out that regulations may not be as stringent in some areas of Latin America, making it easier to obtain clearance to run a study. But this does not diminish the quality or standard of clinical findings.

'More international companies are establishing offices in Latin America to run their clinical trials because they can see the benefits and advantages to conducting those studies there,' says Gupta. 'But it should be kept in mind that populations are different and studies conducted here are based on a relatively homogenous patient pool that may not be genetically similar to other regions of the world. Therefore, this scenario can create the possibility of drug reactions which would not be found during clinical trials.'

Researchers must carefully choose participants and try to avoid recruiting patients who may not understand important contents of the study or what it entails. 'Some studies have recruited types of people who volunteer blindly just for the money,' Gupta adds. 'It is easy to gain approval and recruit patients, and therefore standards need to be regulated and monitored. This is because foreign medication is not readily available in this region. For example, in Bolivia, there is very little drug production and medication choice, and they depend mostly on regional medicine. But of course you cannot run clinical trials that endanger the health of the people.' **WPF**