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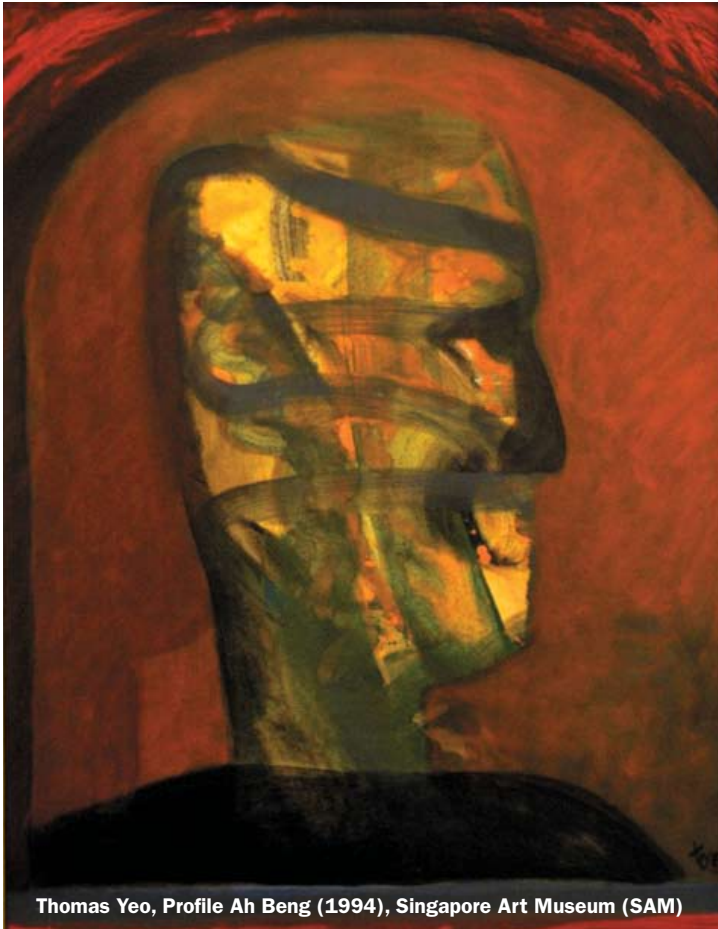
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Thomas Yeo, Profile Ah Beng (1994), Singapore Art Museum (SAM)

SINGAPORE: THE BIOPOLIS OF ASIA

A country with a plan

When Singapore became independent in 1965, the smart money was not on this small South East Asian island with limited natural resources having a prosperous future. However, thanks mainly to appropriate policy making, Singapore went on during the rest of the 20th century to become one of the wealthiest nations in the world, with GDP per capita equal to that of the leading Western European countries.

Singaporeans have always thought that, given the country's tiny size, small population, and lack of resources, it's crucial for them to

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stay one step ahead of their neighbors. Whether building one of the largest airports or creating the planet's largest Ferris wheel, there seems to be a belief in the country that if Singapore is not first in Asia, it will be last.

During the second half of the 20th century, Singapore succeeded in staying one step ahead of the game, becoming a competitive manufacturing hub first for electronics and then for chemicals. Today, as part of a region that has based its extraordinary growth on being a low-cost center for manufacturing, Singaporeans know they need to make a jump into a knowledge-based economy before their neighbors do if they want their economic success story to be sustainable.

The Biomedical Sciences Initiative

Philip Yeo, former chairman of Singapore's Economic Development Board (EDB) and Singapore's Agency for Science, Technology and Research (A*Star), played an important role in the development of the island's electronic and chemical manufacturing capabilities.

Furthermore, In the year 2000 he became part of a team of four mandated by Singapore's prime minister to draft a plan for the development of the country's life sciences industry. "The key to success has

"The key to success has always been to develop the right people."



Philip Yeo, Chairman of Spring Singapore

always been to develop the right people," explains Yeo, who was also the brain behind Singapore's plan to train 1,000 PhD scholars, who will eventually return to the country and work in areas such as IT, engineering, biochemistry, and medicine.

In mid-2000, Singapore launched its Biomedical Sciences (BMS) initiative with the objective of becoming a leading drug discovery center and making the industry one of the island's main economic pillars, a vision best represented by the initiative's slogan, *Singapore: The Biopolis of Asia*. Since then, EDB and A*Star have worked closely to build state-of-the-art capabilities across the entire value chain of what is known as the BMS cluster: pharmaceuticals, biotech, medical technology, and healthcare services. As part of this policy, Singapore has set up world-class research institutions, built top infrastructure, attracted investment in R&D and manufacturing from MNCs, and seen the birth of a number of local biotech start-ups.

Nevertheless, the BMS industry is significantly different from electronics and chemicals, and it takes more than just investments to become a competitive player in it. With no major local drug company, a limited local talent pool, few private investors to support start-ups, and bigger regional rivals such as China, India, and South Korea also focusing on this sector, this time Singapore will need to overcome unique challenges in order to stay ahead of the game and succeed in becoming the Biopolis of Asia.

"We believe that creative ideas flourish best in conducive environments."



Thomas Teo, CEO of Ascendas Land Singapore



Top infrastructure: Building the Mecca

When the Biomedical Sciences (BMS) initiative was launched in 2000, Singapore already had world-class infrastructure for hosting R&D and manufacturing facilities. In the late 1990s, following the same strategy of clustered development previously applied to electronics and chemicals, Singapore developed the Tuas Biomedical Park a 183-hectare world-class manufacturing hub, which attracted names such as MSD, Novartis, and GlaxoSmithKline Biologicals.

Furthermore, since the 1980s Singapore's Science Park has been one of Asia Pacific's most renowned locations for R&D and technology activities. This techno-park has become a model for many science and IT parks across the region, and today hosts more than 260 MNCs, local companies, and research organizations.

The Singapore Science Park is developed and run by Ascendas, the largest private industrial landlord in Singapore and Asia's leading provider of business space solutions. "Our mission is to create total business environments that inspire people to excel, and the Singapore Science Park is a testimony to the important role Ascendas plays in this regard in the country," explains Thomas Teo, CEO of Ascendas Land Singapore.

Ascendas also played a key role in the development of Singapore's newest, most impressive, state-of-the-art R&D facility: the Biopolis. Conceived as the cornerstone of Singapore's vision to build up the BMS industry, Biopolis is the world's first integrated, purpose-built biomedical research complex, juxtaposing both public and private sector re-

search laboratories. With shared scientific facilities and other services, the idea behind this futuristic complex is to generate interaction and collaboration between industry and public research laboratories. "Every new religion needs its Mecca," says Philip Yeo, who was the main promoter of the Biopolis concept and chairman of A*Star when Phase 1 of the project was completed in 2003.

Ascendas developed Phase 2 of the Biopolis, which officially opened in 2006. With two buildings comprising 37,000 square meters (40,000 square feet), Biopolis II also included "soft" elements such as arts, water features, greenery, and open spaces. According to Teo, "Land is scarce in Singapore. We have always gone against the convention by creating a more open, campus-like environment with lots of greenery in our parks. We believe that creative ideas flourish best in conducive environments."

"We are confident we will succeed, we're proposing a win-win situation."



Dr. Jonathon Sedgwick, Managing Director and Chief Scientific Officer, Lilly-Singapore Center for Drug Discovery

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For his part, Teo expects Ascendas to continue to grow in tandem with the government's focus on developing the BMS industry in Singapore. As a result, the company's next steps will be to redevelop and build new R&D and amenities space in Singapore's Science Park. "We will continue to offer a level of service and quality which stands way above the rest," he states.

State-of-the-art developments such as the Tuas Biomedical Park, the Singapore Science Park, and the Biopolis have positioned the country among those with the best infrastructure in the world. This is part of the reason why many people in the industry, just like Yeo, have become firm believers in the country's biomedical aspirations.

The plan is to become an innovator

The most ambitious objective behind the BMS initiative is for Singapore to become a leading player in the drug discovery space. In this regard, the first phase of the initiative (2000–2005) focused on establishing a firm foundation for basic biomedical research.

During this period, the Singaporean government built numerous public research institutes almost from scratch, attracting top research talent from around the world. Furthermore, the

Figure 1

Number of clinical trials conducted in Singapore, by phases

	2000	2001	2002	2003	2004	2005	2006
Phase I	21	19	20	24	31	44	48
Phase II	44	50	52	19	49	50	35
Phase III	63	68	97	91	88	90	116
Phase IV	29	28	26	26	32	17	18
TOTAL	157	165	195	160	200	201	217

Source: Singapore Health Sciences Authority

Singaporean government has been highly active in developing human capital for the industry by promoting the study of life sciences and adapting academic curriculums to fit the industry's needs. "R&D is dependent on the presence of talent," explains Stefan Ziegler, head of Asia Pacific for Novartis. "Singapore has done a great job in shaping the local educational system so as to draw more people into life sciences, as well as in attracting more foreigners to contribute to R&D activities."

A new model for drug discovery

When it comes to private-sector R&D, EDB has invested in local biotechs such as MerLion Pharmaceuticals and S*Bio, which have promising compounds in early clinical trials. It has also been active in luring multinationals to locate their drug discovery facilities in the country.

EDB has established a noteworthy public-private partnership with Novartis. The Novartis Institute for Tropical Diseases (NITD) is a small-molecule drug-discovery institute dedicated to finding new drugs for the treatment of dengue fever, tuberculosis, and malaria. According to NITD director Dr. Alex Matter, Singapore is a great location for the institute—close to both top scientific infrastructure and a large patient pool.

Another MNC conducting R&D in Singapore is Eli Lilly, which opened its marketing and sales office in the 1980, and was the first MNC to establish a clinical trials unit in Singapore in the 1990s. In 2002 the company established the Lilly-Singapore Center for Drug Discovery (LSCDD), which today drives a substantial part of Lilly's cancer biomarker discovery and development. The center has recently expanded its scope to include drug discovery activities in the areas of cancer and diabetes.

Lilly's vision is to use Singa-



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pore as a hub for interacting with the region's many emerging pharmaceutical companies and contract research organizations. As Dr. Michael Schroter, COO of LSCDD, explains, "The FIPCO [fully integrated pharmaceutical company] model is changing, and the current dynamic in the industry is to partner with other companies. It is in this context that Lilly came out with the term FIPNet [fully integrated pharmaceutical network], and Singapore will be at the forefront of this initiative."

The main difference between Lilly's FIPNet model and a typical outsourcing model is that in the latter the activities are centralised in one place, usually the MNCs headquarter. By contrast, in the FIPNet model the objective is to link activities between partners. The vision is that ultimately CROs or other pharma and biotech firms that are working with Lilly will also cooperate among themselves. From a financial point of view, the most innovative concept behind FIPNet is the idea of spreading the risk and reward of drug discovery among the different partners.

Asked why Singapore was chosen as the location for the LSCDD, Dr. Jonathon Sedgwick, the center's managing director and chief scientific officer explains, "Just like when buying a house, the most important factors are location, lo-

cation, location. We plan to develop a very robust network of activities in the region, and Singapore is very well placed for that, being localized centrally to all of our operations and partners around Asia."

Lilly's FIPNet model is still in its early stages, but Dr. Sedgwick is certain of its potential. "We are confident we will succeed, as we are proposing a win-win situation. Lilly wants to leverage the region's talent, while potential regional partners are looking forward to tapping into our company's know-how and experience," he argues.

From bench to bedside: Clinical development in Singapore

The second phase of the BMS initiative (2006–2010) focuses on strengthening translational and clinical research. The goal is to realize the full potential of the country's investments by taking discoveries from bench to bedside. In terms of clinical research, although Singapore has top infrastructure and professionals, growth in the number of clinical trials has been unsteady (figure 1), mainly because the island's small population of 4.5 million people presents a ceiling for the industry.

Instead, Singapore has positioned itself as a regional clinical trials management center. Pharmaceutical companies



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The BMS initiative and Healthcare Services: searching for critical mass

As part of the BMS initiative, the Singaporean government is focusing on developing world-class capabilities in the area of healthcare. With this objective in mind, in 2003 the country launched SingaporeMedicine, a program supported by EDB, International Enterprise Singapore and the Singapore Tourism Board to strengthen the country's position as Asia's leading medical hub.

Dr. Jason CH Yap, Director of Healthcare Services at the Singapore Tourism Board, explains that a big difference between Singapore and other countries (such as India and Thailand, which are also trying to position themselves as regional medical hubs) lies in the reasons why the island is concentrating its efforts on attracting international patients. According to him, it is critical for the country to maintain a high quality healthcare system, not only to better serve its population, but also as a key element in what he calls the necessary ecology to keep attracting foreign investment — particularly regional headquarters — into the country. In this regard, although Singapore already has one of the most advanced healthcare systems in the world, given its small population of 4.5 million people, it can prove to be quite a challenge for this city-state to maintain many of its high-end services. "Singapore needs to have patient volumes to maintain the clinical subspecialty expertise, and to gain economies of scale for its technology," he says.

The SingaporeMedicine initiative has proved highly successful with the number of international patients, increasing from 320,000 in 2004 to 410,000 in 2006. For Dr. Yap, while India's main strength for attracting international patients is cost, and Thailand's is customer services, patients come to Singapore mainly because of quality and reliability.

The majority of patients come to Singapore from other countries in the region, looking for quality or for essential healthcare not available in their own countries. Furthermore, in the last years there has been an impressive growth of patients coming from other parts of Asia, the middle East, Russia, and even the US. For American patients, the main motivation for coming to Singapore lies in cost savings.

Singapore's target is to attract at least 1 million medical travelers per year by 2012. Furthermore, Dr. Yap expects not only patients, but also more and more foreign healthcare providers and insurance companies to start taking advantage of opportunities in the country. Today, Western healthcare providers are already establishing themselves in Asia and choosing Singapore as the location for their regional headquarters. Dr. Yap's vision for the coming years is that of Singapore occupying a central position in a regional healthcare network. In the meantime, international patients are set to continue flowing into Singapore from all over the globe in search for world-class capabilities and affordable costs.



Dr. Jason CH Yap, Director of Healthcare Services at the Singapore Tourism Board

such as GlaxoSmithKline, Eli Lilly, and Eisai, together with many of the world's leading contract research organisations (CROs) such as Quintiles, Covance, and ICON have located regional centers in the country.

Growing demand for CROs: A look at the region's leader

In the last years, the CRO industry has been booming in the Asia Pacific region for a number of reasons. First, while the US and European clinical trial markets are getting saturated, Asia offers a large pool of treatment-naive patients. Second, in the last decades Asian data has established a track record of successful registrations with both FDA and EMEA. Third, the growing importance of the main commercial markets in the region has attracted companies to conduct clinical trial activities to best position themselves for future commercial success in those markets.

"Asia is about quality and delivery."



Dr. Anand Tharmaratnam, Head of Clinical Development Asia Pacific & CEO South East Asia for Quintiles

Quintiles, the region's leading CRO, decided to establish its Asian headquarters in Singapore in the early 1990s. "The reasons why it has worked well for us in the last 10 years will be the same reasons why it will work well for us over the next 10 years," explains Dr. Anand Tharmaratnam, Head of Clinical Development Asia Pacific & CEO South East Asia for Quintiles. "Basically, most of our clients have their regional head offices in this country, and Singapore offers a best-in-world infrastructure, legal, regulatory, and corporate framework. The investigators we work with here in Singapore are global and regional key opinion leaders. It is also an excellent transportation and logistics hub allowing us to effectively manage our 24 offices in Asia. All these elements together position Singapore very nicely. While India and China will flourish and drive regional market size, Singapore will always have its place as the location of choice to manage one's operations."

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Figure 2

Singapore Biomedical Sciences Industry evolution 2000-2007

	2000	2001	2002	2003	2004	2005	2006	2007
Manufacturing output (\$mil)	6,307	6,599	9,778	11,884	16,432	17,669	23,309	24,035
Value added (\$mil) *	3,820	3,702	5,886	6,808	9,812	9,226	12,773	13,420
Employment	5,880	6,885	7,723	8,642	9,393	10,171	10,581	11,518

Source: Singapore Economic Development Board (EDB)

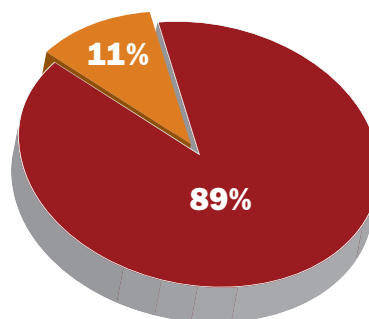
*Value added: Labour cost + Depreciation + Interest cost + Profit before tax + Land cost

Figure 3

Breakdown biomedical sciences industry manufacturing output 2007

Pharmaceuticals	89%
Medical technology	11%

Source: Singapore Economic Development Board (EDB)



Since Dr. Tharmaratnam joined Quintiles Asia Pacific four years ago, the company's operations in the region have more than doubled. Furthermore, in Southeast Asia, the company is growing at 50 to 70 percent, depending on the country, while China and Korea are growing at 100 percent a year. "We hire more people in clinical development than any other pharmaceutical company or CRO in Asia," says Tharmaratnam. "In some of the markets where we operate like Thailand and New Zealand, we actually employ over 50 percent of the entire clinical development talent pool."

Despite challenges regarding talent availability and cultural and regulatory diversity, Dr. Tharmaratnam sees a bright future for CROs in Asia Pacific. "We truly believe Asia has a very prominent role to play in drug development, and we want to be at the very front of that move" he says. According to him, Asia's strengths lie not only in its vast patient pool but also in its excellent investigators. "Asia is not a cost place," he stresses. "Asia is about quality and delivery!"



Dr. Yap Kok Wei, CEO of GleneaglesCRC

The local connection

GleneaglesCRC is a perfect example of how Singapore is developing local capabilities across the whole industry's value-chain. Currently the only Southeast Asian CRO, GleneaglesCRC is the subsidiary of Parkway Holdings, which owns and manages hospitals across Asia—a major advantage, given the challenges CROs in the region face in finding talent.

"We have 3,000 doctors who are specialists in their areas!" explains Dr. Yap Kok Wei, CEO of GleneaglesCRC. "Any medical expertise is just a phone call away. It also means we have access to top-notch labs, diagnostics, radiology, and ancillary services."

Yap says GleneaglesCRC is uniquely positioned, thanks to the long-rooted networks the CRO and Parkway Holdings have developed. Today, the industry is reacting to the opening up of Indonesia, a country in which Gleneagles has been present since 2000.

"The number of trials back in 2000 was minimal, but now it is skyrocketing," says Yap. "Gleneagles was the first CRO to go to Indonesia, and our first comer status gives us an advantage today; if you need 10,000 patients for a trial we can get them!"

Another country showing significant growth in clinical research is Vietnam. Yap has conducted trials in Vietnam since 1992. "At that time the infrastructure was very poor," he says. "We had to monitor trials almost every two or three days to check on the researchers. But today we can see major improvements. We have been in Vietnam for a long time conducting trials, so we have a very good network and know the stakeholders." A bonus for Gleneagles: Parkway's clinic in Ho Chi Minh City. Korea, after a long isolation caused by its regulatory system, is showing signs of opening up, and Gleneagles has an office in Seoul.

The Singaporean government would like to see more local players like GleneaglesCRC establish a leading presence across the value chain. Dr. Yap, a strong supporter of the country's BMS initiative is confident such players will flourish in years to come. He also predicts GleneaglesCRC will continue its aggressive growth across the region in synergy with Parkway Holdings' overall expansion. In the meantime, Dr. Yap expects to continue practicing his main hobby, walking through the region's hospitals to learn from local doctors and administrators. "I have been to China for many years now and have never seen the Great Wall of China, but I have walked through many of China's hospitals," he says proudly.

A manufacturing hub in a region of giants

Singapore started to build its reputation for pharmaceutical manufacturing in the 1980s. “We started to manufacture in Singapore because of the stability and connectivity of the country,” explains Lawrence Siow, vice president Asia Pacific of Stiefel Laboratories. “It was not only what the government offered in terms of schemes, but the kind of country that Singapore is.”

Since the start of the BMS initiative, pharma manufacturing output has grown from S\$6.4 billion in 2000 to S\$24 billion (US\$17.2 billion) in 2007 (See Figure 2). The companies that have chosen Singapore as a base for regional or global manufacturing include GlaxoSmithKline, Merck, Novartis, Pfizer, Sanofi-Aventis, Schering-Plough, Genentech, and GlaxoSmithKline Biologicals.

Probably the main challenge for Singapore’s manufacturing success story comes from the “big kids on the block” China and India. According to Michael Khor, managing director of Pfizer (Singapore, Malaysia, and Brunei), “Whether Singapore can continue to attract new players to set up shop here will depend on its ability to compete against China and India, and what Singapore is able to put on the table.”

Singapore’s success should continue, says Andrew Howden, president of IMS Health Asia Pacific, because the country is well positioned to attract top-end manufacturing. “These are very specific plants that require large investments, and Singapore is offering good incentives together with a well-educated work force and strong IP protection,” he explains. Siow agrees with this view: “The cost of labor in Singapore is clearly higher than that in other countries in the region,” he says. “Thus, it only makes sense to be based here if we produce high-value products that require high-tech processes and have very specific requirements.” Stiefel Laboratories is today gearing up its Singapore manufacturing facility for higher value products.

Targeting the fast growing Asian markets from Singapore

Although Asia Pacific only represents 5 to 6 percent of the global pharmaceutical market, its fast growth has caught the attention of pharmaceutical companies, which in recent years have significantly expanded their operations in the region. Just like many other of these firms, Stiefel Laboratories decided to use Singapore as a commercial gateway to the region. Despite the small size of the local market, this well established dermatology player chose Singapore as a base for its Asia Pacific operation, which has grown by an average of 20 percent for the last five years. “From Singapore, we can easily access the rest of the region. Singapore will be the launch pad into new markets like Japan and China,” says Siow.

Merck chose Singapore for its regional headquarters in 2007. “We chose to be in Singapore because it is at the forefront in terms of IP protection and promoting trade and investment,” explains Ramesh Subrahmanian, president of Asia Pacific for Merck Human Health. “Furthermore, as we build our business in other countries of the region, Singapore gives us the ability to move around efficiently.” Chris Lee, regional head of Asia Pacific for Bayer Schering Pharma agrees: “Our office covers South Korea to India to Australia and everything in between,” he says. “Singapore has quite a central location and the infrastructure here is very convenient in terms of air travel.”



Lawrence Siow, Vice President Asia Pacific of Stiefel Laboratories

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More than just numbers

Obtaining high quality market data in Asia Pacific can be a challenge, given the region's uneven infrastructure development. For example, data collection in China has traditionally been carried out by teams that go to drugstores and gather information on paper.

Having been a customer of IMS in the past, Andrew Howden, president of IMS Health Asia Pacific, knows where the hotspots are. "We know how to enhance the quality of the data and we are currently investing heavily on this," he says. "We are making large investments, not only in people, but also in acquiring new data sets and collection methodologies and in increasing the efficiency of our systems of data collection." IMS spends more than \$35 million on data in Asia Pacific he says.

In Asia Pacific IMS' revenues have been growing at around 20 percent per year and—like other players in this booming region—Howden sees a bright future for the company. In coming years he expects customers to be able to clearly see the impact of the efforts to enhance quality of data, which has been the core of IMS' business for 50 years. And he expects the company to leverage its regional expertise to consolidate its fast-growing consulting and services practice. "We will become an even closer partner with the industry," he says. Given the challenges posed in fast-growing markets across the region, finding such a partner will prove critical for the success of many MNCs and growing local players.



Andrew Howden, President of IMS Health Asia Pacific

na out of all 6,000 pharmaceutical companies for the past five years," he says. "We no longer talk about China being one of our key markets in the next 10 or 20 years. We are now looking into making China one of the leading sources of revenue for the company in the near future."

Although a highly attractive region thanks to its fast growth, Asia Pacific poses significant challenges for pharma companies. One such challenge is related to the rapid growth itself. With 20- to 30-percent growth every year, most managers say it's a nightmare to find, attract, and retain talent. Other challenges are related to the region's diversity. According to Lee, who was born in Korea and has worked in the US and numerous countries across the region "This is the most complex region in the world. In Asia Pacific everyone speaks a completely different language, with different alphabets, very diverse economic realities, and different histories and religions."

The challenges, however, do not stop MNCs from being optimistic about the region. Lee expects Bayer Schering to maintain growth in the high double digits in every country where it has a presence today. "We are confident we can achieve this, which implies that five years from today we will be the leading pharmaceutical company in Asia Pacific," he says.

The Biopolis of Asia?

Since 2000, Singapore's BMS initiative has shown impressive achievements. By successfully developing internal capabilities and attracting investments in R&D and manufacturing, the country has turned the BMS industry into an undisputed pillar of its economy. Nevertheless, opinions will remain divided regarding the initiative's progress toward making Singapore a leading player in drug discovery—at least until a local start-up is able to take innovation from bench to bedside.

Dr. Edison Liu, a former leading researcher at the National Cancer Institute in the US, who now heads the Singapore Genome Institute, argues that "the local biotech sector is like a canary in a mineshaft. You do not drive an economy by biotech, but its success is an indicator that many good things are happening." Liu thinks that Singapore is on the right track. "If we compare were we stand versus our competition, which is San Francisco, Boston, Cambridge, Paris, and some other cities of the world, we are doing quite well," he claims.

Bearing in mind the relative youth of Singaporean biotech start-ups and the long time frame of innovation cycles, it would be wise to wait for some time before checking again on the canary, and defining whether Singapore has succeeded or not in its ambitious objective of staying one step ahead of its neighbors and becoming the Biopolis of Asia.

From Singapore, Lee runs Bayer Schering's fast-growing operations in Asia Pacific, where the firm ranks seventh in sales volume according to IMS. "This impressive growth is closely related to the disease profile in Asian Pacific," says Lee. "The presence of chronic primary-care diseases that require early detection and life-long treatment is still very significant in this region. This is one of our company's six focus areas, and it represents both the biggest source of revenues for us in Asia and our fastest-growing segment."

Bayer Schering Pharma's leading position in Asia Pacific is best represented by the company's outstanding performance in the region's main markets. Before becoming regional head, Lee ran Bayer Healthcare's operations in China, where the company's revenues grew by a striking 51 percent in 2006. "We have persistently shown one of the best performances in Chi-



Chris Lee, Regional Head Asia Pacific for Bayer Schering Pharma