Singapore strengthens position as leading site for biopharmaceutical R&D

Globally, pharmaceutical and biotech companies are confronted by an impending patent cliff, while being challenged with declining research and development (R&D) productivity and the need to integrate multidisciplinary scientific capabilities. Against this backdrop, Asia presents a window of opportunity with an expanding healthcare market which is valued at US$240 billion in 2008 and is expected to grow between 5% to 10% in 2009 (Frost & Sullivan). This growing market may be attributed to the rising demand for more cost-effective and efficacious medicines among the growing middle class and ageing population in Asia. As global pharmaceutical and biotech companies seek to harness Asia's vast markets and resources, they are leveraging Singapore as a strategic beach-head site for regional headquarter functions, research and development and manufacturing.

By Kian-Teik Beh

Singapore may be considered a young entrant in this industry, given that it only embarked on its focused effort in this sector in 2000. However, it was committed to developing the sector as the fourth pillar of its economy when it conceived the biomedical sciences initiative to develop the sector in 2000. Within just one decade, Singapore has emerged as one of the fastest-growing bio-clusters in Asia, with more than 16,000 people in more than 100 biomedical sciences companies and 30 research/medical institutes, and manufactures about S$20 billion worth of medicines and medical devices for global markets.

Accelerating drug discovery and development in Asia

Innovation is key to driving the pharmaceutical and biotech business, as companies seek to expand their pipeline of new therapies to address unmet healthcare needs. However, to do this more effectively and to increase productivity, companies are working with key partners to accelerate their R&D activities.

Over the past few years, Singapore has built up key capabilities from basic science to bedside research and is ready to partner companies to help drive their R&D for Asia. Indeed, the continued stream of R&D announcements in Singapore, despite the challenges in 2009, attest to Singapore's strengths in pharmaceutical and biotech R&D.

Recent pharmaceutical announcements include Schering-Plough's Translational Medicine Research Centre and Abbott's pharmaceutical analytical research lab. Biotech announcements include local biotech S*BIO's licensing agreements with Onyx and Tragara to develop oncology drugs, which will entitle S*BIO to receive more than US$600 million in payment; FORMA Therapeutics' first overseas lab in Nanyang Technological University, Singapore; Inviragen's merger with SingVax, which raised US$15 million

in Series A financing; Cytos and Humalys' collaborations with Singapore Immunology Network to develop antibody-based therapies for infectious diseases that are prevalent in the region.

The key capabilities and resources in Singapore which enable companies to accelerate drug discovery and development in Asia are as follow:

- Ability to establish key infrastructure and capabilities rapidly – Singapore has demonstrated its commitment to developing the sector by building up key infrastructure and capabilities to facilitate innovation as soon as the biomedical sciences initiative was launched. Within the first three years of development, two million square feet of research space at the Biopolis was made available in an integrated campus that is designed to co-locate and promote collaborations among private-sector labs and research institutes. In the past five years, Singapore has established Academic Medical Centres and Investigational Medicine Units dedicated to early-phase trials to facilitate translational and clinical research. In addition, Singapore's research institutes have established capabilities in core areas such as bio-imaging, phenotyping of its pan-Asian patient base, cohort studies, as well as key diseases (eg cancer, neurodegenerative diseases, metabolic diseases, infectious diseases and eye diseases).
- Public sector's openness to partner companies – Singapore's network of 30 public-sector research institutes, academic medical centres, medical institutes and hospitals are open to partnering companies to develop new therapies and address unmet healthcare needs. Leading companies such as AstraZeneca, Bayer, GlaxoSmithKline and Lilly are collaborating with Singapore partners across drug discovery and development activities. On average, more than 250 clinical trials are carried out in Singapore each year.
- Integration of public sector resources – Leveraging its compact locality, Singapore's public-sector resources are connected via an integrated countrywide network that connects research institutes at the Biopolis with Academic Medical Centres, where public hospitals and medical institutes that attend to 80% of Singapore's patients and Investigational Medicine Units are co-located with institutes of higher learning. This integration not only enables an efficient flow of knowledge from the bench to the bedside; equally importantly, it provides a platform for clinician-scientists to address hypotheses derived from the bedside.
- Growing base of supporting services – Complementing Singapore's strengths in early innovation and translational research, the city-state has also established a core base of 20 leading contract research organisations and pharmaceutical companies that manage regional clinical trials from Singapore. Recent announcements in 2009 include ICON's expanded central lab, PPD's new global central lab and Quintiles' expansion of its Asia-Pacific headquarters facility.

Accessing global talents

As companies expand their research and business activities into Asia, it will be imperative that their expansion site also draws top-notch talent from both their home-base as well as the rapidly growing Asian populations.

As a cosmopolitan society that remains rooted in Asian culture, Singapore's high quality of life has attracted the world's top scientific and business talent, who find it easy to settle in Singapore.

Singapore provides an enticing environment for professionals, and has been consistently ranked as Asia's top city in terms of quality of life (Mercer HR; ECA International) and offers an excellent education system. The city-state is English-speaking,

cosmopolitan with foreigners making up a quarter of the population, and offers a range of dynamic entertainment and recreation options. Since 2008, Singapore has been hosting Formula One's first night race during Singapore Grand Prix. In 2010, two integrated resorts, which host a world-class hotel, convention centre, entertainment facilities and a casino in one location, will officially open. These resorts are developed by Las Vegas Sands and Genting International. Singapore is also within a seven-hour flight radius from the region's top tourist destinations (eg Angkor Wat in Cambodia, Bali in Indonesia, Hua Hin and Phuket in Thailand and Shangri La in China).

Scientific leaders who have moved to Singapore to head the city-state's research institutes, consortia and laboratories include: Edward Holmes (former Vice Chancellor, University of California, San Diego), Judith Swain (University of California, San Diego), Edison Liu (former director of clinical sciences, National Cancer Institute, US), Neal Copeland and Nancy Jenkins (National Cancer Institute, US), Sir George Radda (former Chief Executive, Medical Research Council), Colin Blakemore (UK Medical Research Council), Axel Ulrich (Max Planck Institute for Biochemistry, Germany), Philippe Kourilsky (College de France, France), Sydney Brenner (Nobel Laureate, Salk Institute of Biological Sciences) and Yoshiaki Ito (University of Kyoto, Japan).

In addition, leading pharmaceutical and biotech companies have teams with an international representation in their Singapore corporate labs. The Novartis Institute for Tropical Diseases, for example, employs more than 100 researchers from 18 nationalities. Singapore is now home to more than 4,300 researchers from across the globe.

Furthermore, Singapore has launched the A*STAR Investigatorship (A*I) award, which was modelled on the prestigious Howard Hughes Medical Institute (HHMI) Investigatorship award, to attract bright young researchers to carry out independent research in Singapore's public-sector research institutes. Bruno Reversade (France) and Prabha Sampath (India) are the first recipients. In September 2009, Reversade led a group of German and Singaporean scientists to publish their findings in genetic mutation that led to premature skin ageing in the prestigious Nature Genetics.

Singapore also recognises the need to nurture the next generation of scientists. Since 2001, Singapore's Agency for Science, Research and Technology (A*STAR) has launched a national scholarship programme that seeks to nurture 1,000 local PhD graduates in the world's top universities. To date, A*STAR has awarded more than 500 biomedical sciences scholarships. More than 100 awardees have completed their PhDs and returned to work in A*STAR research institutes and units. Complementing this pool of researchers is Singapore's annual cohort of more than 8,500 science and engineering graduates. Today, leading pharmaceutical and biotech companies train Singaporean graduates in their headquarters' manufacturing site and hire more than 4,000 skilled workers who are acquainted with the latest manufacturing technologies.

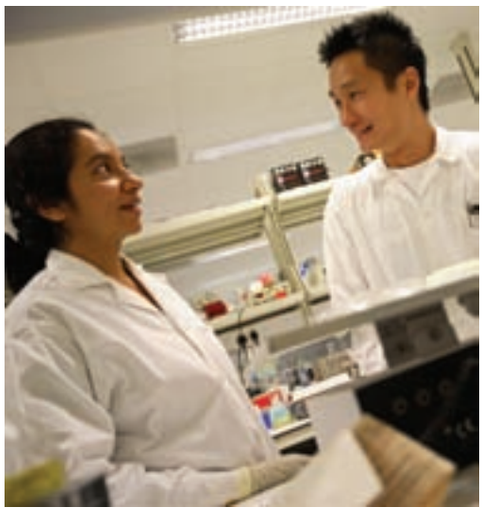
Driving expansion in Asia

Singapore's global business excellence is a strong factor that complements its R&D capabilities. This enables companies to expand their reach in Asia's markets, in addition to developing more effective therapies for Asian patients.

Today, eight of the world's top 10 pharmaceutical companies have located regional headquarters in Singapore to manage and drive their expansion in the region. Most recently, in 2009 Takeda opened its regional headquarters in Singapore to drive its commercial growth and reach in Asia Pacific; Quintiles also doubled the size of its Asia-Pacific headquarters to an 80,000 square-feet facility to meet the region's growing demand.

Key advantages include:

- World's easiest place to do business (World Bank, 2009) – Singapore has established a strong legal system and a stable political system that prides itself on honesty, quality and reliability. At the same time, the city-state offers an international business environment with the world's global industry leaders setting up business activities that include headquarters, R&D and manufacturing. Leveraging its world-class infrastructure and reliable public utilities, Singapore presents a trusted location to manage companies' business expansion while being attuned with global developments.
- Base of leading global professional services companies – Singapore is the world's third leading global financial centre (City of London, 2009) and drawn top-notch professional services companies to Singapore. Today, nine of the top 10 international law firms and all of the top eight human resource consulting firms have established their presence in Singapore. The world's leading third-party logistics service providers is also based in Singapore; DHL and TNT have set up specialised life sciences facilities that offer customised supply chain solutions for pharmaceutical and biotech companies.



- Excellent connectivity – Singapore is well connected with regional markets within a seven-hour flight radius. As a leading aviation hub in Asia, Singapore's Changi Airport serves more than 80 international airlines, with more than 4,500 flights each week, connecting to 200 cities in more than 60 countries. Coupled with its world-class infrastructure, Singapore has been a location of choice for companies to host regional meetings and conferences. Furthermore, Singapore is connected to an extensive network of Free Trade Agreements (FTAs), having concluded 19 FTAs that cover 60% of the world's GDP that include key markets such as China, India, Japan, South Korea, Australia, New Zealand and the European Free Trade Association.
- Ease of relocation – As the city that offers the best quality of life in Asia (Mercer HR, 2009), it has been easy for companies to relocate some of their most talented staff in Singapore. The city-state provides a safe environment and a base of renowned international schools (eg Tanglin Trust, United World College) that cater to the needs of expats' families. In a recent global expats survey (HSBC, 2009), Singapore was ranked the world's fourth most attractive city. At the same time, Singapore remains a cost-competitive location and is ranked 10th against other more expensive cities in Asia (ECA International, 2009).

Manufacturing innovative medicines

As global companies seek to manage their risks by diversifying the geography of their production plants, Singapore presents a reliable manufacturing site where they can effectively transfer technology, efficiently scale-up manufacturing and ensure quality control of their products. Today, leading pharmaceutical and biotechnology companies have invested in 30 commercial-scale facilities, where some of their most innovative medicines are produced. More than 20 of these facilities are in commercial production and have received zero major observations from key international regulatory bodies (eg European Medicines Agency and US Food & Drug Administration).

Some of the key benefits of manufacturing in Singapore include:

- Rapid set-up and export – Companies setting up in Singapore can construct and validate a manufacturing plant within 24-36 months, given the city-state's quality manpower, world-class infrastructure and reliable supporting services. In addition, Singapore has established a good track record with regulatory authorities, as well as strong trade linkages with major markets. Together with its excellent logistics connectivity, companies can quickly export and distribute their products to global markets.
- Pro-business environment – Singapore is well-known for its business-friendly environment, with its good corporate governance, clear and consistent government guidelines and excellent IP protection. Singapore also offers a politically stable and favourable tax environment. This ease of doing business is complemented by the country's support for the adoption of environmentally-friendly practices and technologies in the manufacturing sector.
- Quality manpower – Singapore offers a base of skilled local talent who are well-trained in science and mathematics. Singapore's workforce is consistently ranked the world's best labour force (BERI). Since the 1970s, the city-state has had zero man-days loss on strikes due to its tripartite system that brings together the government, employers and unions to address manpower issues harmoniously. Manpower costs remain competitive with entry salaries for BEng graduates pegged at US$1,500 each month for about 50 working hours each week.
- Industry's partner in process development – Companies (eg GlaxoSmithKline, Novartis) are extending beyond commercial manufacturing into process development. In addition to setting up their own process development units, companies can also partner our research institutes (eg Institute of Chemical Engineering and Sciences, Bioprocessing Technology Institute) to optimise manufacturing processes and the formulation of new products. The Singapore Institute of Manufacturing Technology has partnered companies to develop automation solutions to streamline operations.

Rapid development within one decade (2000 to 2009)

Prof Edward Holmes, Chairman, National Medical Research Council and Deputy Chairman Biomedical Research Council (Singapore) and former Vice-Chancellor, University of California, San Diego, provides a brief overview of Singapore's rapid development within the last decade.

Singapore made a strategic decision in 2000 to include biomedical research as a pillar of its diversified economy, and in the past 10 years Singapore has developed a robust and comprehensive biomedical research community.

This effort was initiated by the development of the Biopolis complex within the Agency for Science, Technology and Research (A*STAR). The Biopolis colocates both publicly-funded research institutes and private sector R&D organisations, and is home to 2,000 research scientists. The Biopolis has attracted leading basic academic scientists from around the world to Singapore and established Singapore as a leading site in Asia for biomedical research. A*STAR has also developed a training programme for the next generation of Singapore basic scientists and more than 500 outstanding young Singaporeans are receiving PhD training in biomedical research institutions around the world. This effort has been an unqualified success and it has served to jump-start the biomedical research programmes across Singapore.

In conjunction with the launch of the Biopolis initiative, Singapore undertook a vigorous effort to enhance the scope and quality of the basic research programmes in its two major universities, ie National University of Singapore (NUS) and Nanyang Technological University. This effort has led to the transition of these two institutions into strong research universities in a very short period of time and both are now recognised as leading research universities in Asia. Major new programmes have been developed in areas such as cancer biology through the Research Centers of Excellence funded by the National Research Foundation (NRF) and the Ministry of Education. As a consequence of these investments both institutions now host internationally-recognised research scientists and they are training excellent PhD scientists locally.

In 2005, the Singapore Government launched the second phase of its biomedical sciences initiative with the development of a national Translational and Clinical Research (TCR) programme jointly funded by the Ministry of Health, A*STAR and NRF. This effort has centred on three strategic initiatives.

First is a series of programmes aimed at developing the human capital needed to support a robust TCR effort. While still in the early stages, this effort has recruited a number of outstanding clinician scientists from abroad through the Singapore Translational Research Investigator Award open to international competition and through a companion programme, the Clinician Scientist Award, to support clinician scientists from Singapore. These programmes and the companion MD/PhD programmes are on a trajectory to produce a critical mass of clinician scientists by 2015 who will be the thought leaders supporting the TCR effort.

Second is a series of TCR Flagship programmes focused on diseases of relevance to Singapore and the region. These programmes bring together basic, translational and clinical scientists to study in-depth targeted disease cohorts with the goal of bringing basic discovery from the bench through investigational medicine into clinical trials. The areas targeted for study in the flagship programmes thus far are gastric cancer, a common cancer throughout Asia, eye diseases such as myopia and glaucoma common in Asian populations, developmental control of the metabolic syndrome as represented in Asian populations, severe mental disorders relevant to Asia, and dengue fever. Each takes advantage of unique patient populations represented in Singapore.

Third is an investment in the infrastructure needed to support the TCR effort across Singapore. This includes the formation of two academic medical centres (AMC) that bring together large hospitals and their companion medical schools (NUH and NUS or Duke-NUS graduate medical school and SGH), creation of an investigational medicine unit at each AMC, creation of a national imaging centre dedicated to clinical research, and the formation of a national clinical trials network that brings all the public medical healthcare delivery systems together under one umbrella organisation. This TCR strategy takes advantage of Singapore's diverse population consisting of ethnic Chinese, Malay and Indians; a stable population cared for by a single public health system that enables identification and long-term tracking of individuals with given health problems; and a strong capability to conduct in depth investigational medicine and early in-man clinical trials. Although a small country, Singapore's TCR effort takes advantage of its excellent medical delivery system and diverse population which is reflective of the much larger populations across Southeast Asia to enable in-depth research led by a strong cadre of basic and clinical scientists with a focus on preclinical, investigational medicine, and early in-man clinical trials.

Through these combined and complementary efforts, Singapore has developed in a short period of time a biomedical ecosystem that spans basic, translational and clinical research. In the past few months Singapore has launched a new initiative to bring all the component parts together in a consortium that facilitates access to the various components by external entities such as pharmaceutical, biotechnology and device companies. As the private sector moves to outsource more of its research effort to capture the expertise in the public sector and thereby strengthen its pipeline of new drugs and devices, the Singapore biomedical sciences ecosystem is organising internally to establish itself as a preferred site for this type of new public-private partnership. While still a work in progress, this initiative has seen interest from large multinational pharmaceutical companies to locate translational medicine hubs in Singapore.

Companies' corporate labs are co-located with public-sector research institutes in the 2.4-million sq ft Biopolis campus that advances science and human healthcare via cross-disciplinary, public-private collaborations

- Growing base of supporting industry players to support pharmaceutical and biotechnology companies' engineering and infrastructural needs to implement cutting-edge manufacturing technologies.

Singapore is strengthening its position as Asia's leading site for biopharmaceutical manufacturing. In 2009, leading companies located their first-in-Asia facilities in Singapore – GlaxoSmithKline opened its vaccine plant that will produce purified bulk polysaccharides and conjugates which are used to manufacture GSK's new pneumococcal conjugate vaccine, meningitis and other new innovative vaccines; Baxter commenced construction for its Advate plant; Roche purchased Lonza's mammalian-cell facility to manufacture Avastin and officially opened its microbial-cell facility to manufacture Lucentis. Singapore also made headway in cell therapy with Lonza's first-in-Asia cell therapy plant.

Within five years since the first biologics announcement, leading companies have invested about US$2 billion in six major plants. In 2009, Millipore set up its first regional training centre for biopharmaceutical manufacturing, in response to the growing base of biologics plants in Singapore.

Building on its strong track record for chemical-based pharmaceutical and biologics manufacturing, Singapore is building up capabilities in process development and green manufacturing. In 2009, Bioprocessing Technology Institute partnered GlaxoSmithKline Biologicals for vaccine and process development. GlaxoSmithKline also announced a S$50 million endowment fund, jointly launched with the EDB, to fund graduate studies in green manufacturing and public health policy.

Forging long-standing partnerships

Singapore is committed to be in time for the future and is committed to partnering companies to co-create solutions to address unmet healthcare needs in Asia and the industry's challenges.

Key highlights in 2009 include Lonza's foray into cell therapy after investing in the first biologics plants in Singapore; Baxter's expansion from 30 years of medical device and implantable manufacturing into biopharmaceutical manufacturing; GSK's partnership with EDB in launching the S$50 million endowment fund for graduate studies in green manufacturing and public health policy, on the occasion of its 50th anniversary of doing business in Singapore.

As global pharmaceutical and biotechnology companies seek to locate their key business functions and decision-makers closer to the fast-growing Asian markets, Singapore presents a strategic base as these companies' home-base for the business expansion and innovation in Asia. DDW

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