

# SINGAPORE'S Strong Economy **CREATES** Pharma Opportunity

With its developed world economy and strong government support for innovation and business, Singapore offers a healthy environment for life-sciences companies to conduct research, development, and manufacturing.

**S**ingapore is a South-East Asian island nation with a population of around 5 million people. The country enjoys a high-standard of living, comparable with many developed nations, and has the highest GDP per capita of all Asian countries.

There are strong government healthcare programs, but unlike programs in many developed countries Singapore has a non-modified universal healthcare system where the government ensures affordability of healthcare within the public health system, largely through a system of compulsory savings in a government-mandated program, subsidies, and price controls.

## Pharma Attraction

Over the past 10 years, the Singaporean government has invested significantly in life sciences in an effort to foster innovation, R&D, future investments, and capabilities, says Carl Firth, Ph.D., CEO and founder of ASLAN Pharmaceuticals, an Asia enabled pharmaceutical company that develops novel medicines for global markets.

The Singapore government has committed to investing S\$16.1 billion (\$13.03 billion) between 2011 and 2015 in support of biomedical research, innovation, and enterprise activities, says Anand Tharmaratnam, M.D., senior VP and head of Asia markets at Quintiles.

“Out of that amount, S\$3.7 billion (US\$2.99 billion) is dedicated to enhancing existing biomedical R&D infrastructure, integrating multi-disciplinary research, and translating basic science into tangible outcomes,” he says.

“The other strand of support Singapore has always been very encouraging of is trying to attract foreign companies, whether those be multinational companies with regional headquarters or multinational companies with manufacturing needs in Singapore,” Dr. Firth says. “And in recent years the focus has been on high-end specialist capabilities and skill sets.”

## Clinical Research: Therapeutic Areas

- » Oncology – 31%
- » Clinical Pharmacology – 17%
- » Cardiology – 7%
- » Pediatric – 6%
- » Ophthalmology – 5%
- » Dermatology – 4%
- » Others – 30%

Source: 2011, Singapore Health Sciences Authority



“ Singapore has one of the highest medical standards across Asia, with medical facilities that are considered among the best in the world ”

DR. ANAND THARMARATNAM / Quintiles



Since the Biomedical Sciences Initiative began in 2000, R&D expenditures by the biomedical sciences industry in Singapore have grown 12-fold, to S\$574 million (\$464.5 million) in 2011 from S\$47 million in 2000, Dr. Tharmaratnam says.

Today, biomedical companies manufacture about S\$21 billion worth of medicines, nutritional products, and medical devices for global markets from Singapore annually, says Steve Robson, managing director of H&T Asia, a healthcare communications business with an office in Singapore servicing southeast Asia and an affiliate member of the inVentiv Health Communications Global Network.

“More than 5,000 researchers across public sector research institutes and the private sector spend in excess of S\$1 billion on biomedical R&D annually,” Mr. Robson says. “Additionally, eight of the top 10 pharmaceutical companies, including AstraZeneca, Bayer, and Sanofi-Aventis, have established international or regional headquarters in Singapore.”

Singapore has built a strong scientific foundation with seven research institutes and five research consortia in key fields that include clinical sciences, genomics, bioengineering, molecular/cell biology, medical biology, bio-imaging and immunology. More than 50 companies are carrying out biomedical sciences R&D that includes drug discovery, translational and clinical research, frequently collaborating with these research institutes.

Dr. Firth says early R&D investments went into building capabilities, and encouraging talent, particularly into the academic sphere in the scientific community.

“We have seen strong academic capabili-

ties and strong science being conducted in Singapore, but perhaps not translating into commercial success in the way originally hoped,” he says.

In recent years, several high-profile companies have either shut down or closed their Singapore facilities. These include ES Cell, a stem cell company, S\*Bio, an oncology company, and Merlion, an anti-infectives organization.

“We are now the largest biotech company conducting drug development in Singapore today,” Dr. Firth says. (For more information, see this issue’s bonus digital content.)

Mr. Robson says more than 30 of the world’s leading biomedical sciences companies, including GlaxoSmithKline, Novartis, and Takeda, are leveraging Singapore as a key home base to drive innovation, growing the nation’s biopharmaceutical industry by more than 30% in 2011.

Leading pharmaceutical, biotechnology, and medical technology companies operate more than 50 commercial-scale manufacturing facilities in Singapore, Mr. Robson says.

“Besides producing for regional and global markets, many companies continue to enhance their manufacturing activities here through process development, R&D in sustainable manufacturing, and partnering to upgrade their suppliers’ capabilities,” he says.

One recent example is Amgen, which announced in

January that it plans to build a new manufacturing facility in the Tuas Biomedical Park area of Singapore.

## Healthcare Trends

By international standards, Singapore’s state of health is good, Mr. Robson says. Rising standards of living, high standards of education, good housing, safe water supply and sanitation, high-quality medical services, and the active promotion of preventive medicine have all helped to significantly boost the health of Singaporeans.

Healthcare as a proportion of expenditure is on the rise at more than 5% of total expenditure, Mr. Robson notes.

Ethnically, Singapore comprises Chinese, Indian, Malay, and a significant ex-pat population, Dr. Firth says.

“In terms of disease profile, Singapore largely reflects diseases of other developed nations,” he says.

Mr. Robson notes that the leading causes of morbidity and mortality are major non-communicable diseases such as cancer, coronary heart diseases, strokes, pneumonia, diabetes, hypertension, and injuries. In 2009, cancer, ischemic heart disease, and pneumonia together accounted for about 60% of the total causes of death.

In terms of clinical studies in oncology, research has focused on Asia-prevalent types, such as gastric and liver cancer, with strong consortiums in each of those areas, Dr. Firth says.

“There is also a focus on infectious disease, particularly those that have not attracted as much investment internationally, such as

### Principal Causes of Death in Singapore: 2009-2011

	2009	2010	2011
<b>Total No. of Death</b>	<b>17,101</b>	<b>17,610</b>	<b>18,027</b>
<b>% of Total Deaths</b>			
<b>1. Cancer</b>	29.3	28.5	30.0
<b>2. Ischemic Heart Disease</b>	19.2	18.7	16.4
<b>3. Pneumonia</b>	15.3	15.7	16.0
<b>4. Cerebrovascular Disease (including stroke)</b>	8.0	8.4	9.0
<b>5. Accidents, Poisoning, and Violence</b>	5.7	5.5	5.5
<b>6. Other Heart Diseases</b>	4.4	4.8	5.0
<b>7. Urinary Tract Infection</b>	2.5	2.5	2.5
<b>8. Chronic Obstructive Lung Disease</b>	2.4	2.5	2.2
<b>9. Nephritis, Nephrotic Syndrome &amp; Nephrosis</b>	2.3	2.2	2.0
<b>10. Diabetes Mellitus</b>	1.7	1.0	1.7

Source: Singapore Ministry of Health, 2012

**Singapore at a Glance**

**Total Population:** 5,086,600  
**Gross national income per capita (PPP international \$):** 55,790  
**Life expectancy at birth m/f (years):** 79/84  
**Probability of dying under 5 (per 1,000 live births):** 3  
**Probability of dying between 15 and 60 years m/f (per 1,000 population):** 76/42  
**Total expenditure on health per capita (Intl \$, 2010):** 2,273  
**Total expenditure on health as % of GDP (2010):** 4.0%

Figures are for 2009 unless indicated.  
 Source: Global Health Observatory



“Whether companies are expanding in Asia to tap into the region’s fast-growing healthcare markets, or deepening their understanding of the diverse opportunities Asia represents, in Singapore, companies will find a workforce familiar with both Western business practices and Asian culture.”

**STEVE ROBSON / H&T Asia**



“Over the past 10 years, the Singapore government has invested significantly in building a set of capabilities to foster healthcare innovation, R&D, and investments in the country.”

**DR. CARL FIRTH / ASLAN Pharmaceuticals**

dengue fever, as well as diseases of developed countries, such as diabetes,” he says. “The market is very much that of a developed country, and has innovative products, patent protected products, with generics having their place as well. It’s quite different from countries such as Korea or China where branded generics are strong.”

When it comes to patient information, the Internet is gaining traction with patients. A 2009 survey, titled Medical and Health Seeking amongst Singapore Youths, found 54%

agreed that searching for information was a means of staying healthy. Mr. Robson notes, however, that parents and doctors were still felt to be the preference for information. Interestingly, more than one-third read health magazines for information.

**Clinical Research**

In September 2012, the Singapore Health Sciences Authority launched the Clinical Trial Registry to help doctors recruit patients and provide another option for patients not responding to conventional treatment, Dr. Tharmaratnam says. In the same month, an S\$80 million clinical trial grant was also announced to support innovative and high-impact clinical trials and the development of novel therapies, interventions and diagnostics, focusing on healthcare needs.

Singapore also recently announced additional funding amounting to S\$68 million to enhance its Translational and Clinical Research (TCR) Flagship Program in the areas of diabetes, ophthalmology, gastric cancer, cardiovascular diseases, and non-small cell lung cancer, Dr. Tharmaratnam says.

“This will help support clinical research in these therapeutic areas,” he says. “Two new research programs costing S\$32 million in total have also been launched, one dealing in stratified medicine and the other in rare diseases. One of the programs called POLARIS (PersonalisedOMIC Lattice for Advanced Research and Improving Stratification), aims to identify new technologies that can predict how patients could better respond to medical treatment.”

However, one limiting factor is the coun-

try’s size. With a population of just 5 million, the size of clinical studies that can be conducted is limited, Dr. Firth says. However, he notes that early-phase work, whether Phase I or innovative early-phase development and translational medicine, is a strength.

“There’s been a real focus on greater collaboration between scientists and clinicians, making Singapore a great place to do early-phase work,” he says. “But as soon as there is a need for larger clinical studies — Phase IIb and Phase III — there just aren’t the patients here. So Singapore can certainly participate as part of a larger study but companies would not be able to run those studies in Singapore alone.”

This is something the country is very aware of, and so it has focused on being an attractive place for early-phase innovative research.

“Singapore has a very progressive and sophisticated regulator, the HSA,” Dr. Firth says. “The HSA’s objective is to have INDs approved in 14 days, and while it doesn’t always happen, it’s their target. It’s a great demonstration of what they’re trying to do to be an innovative, drug development friendly country, with the sophistication of a regulator who also understands what makes a safe and ethical trial possible.”

As the secretariat for the APEC Coordinating Centre for Good Clinical Practice (GCP), Singapore plays a strategic role in developing GCP in Asia, steering initiatives such as the training of clinical research personnel and developing a conducive environment for multi-site clinical trials in the region, Mr. Robson notes. <sup>PV</sup>

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# Singapore Supports BIOMEDICAL Sector

There has been significant government investment in research, good tax incentives to encourage R&D, along with world-class facilities, infrastructure, and talent.

**S**ingapore has been hugely supportive of the biomedical sector.

“Singapore has the integrated basic and translational research network needed by biopharma companies to improve R&D productivity and develop innovative medical solutions for Asia,” says Anand Tharmaratnam, M.D., senior VP and head of Asia market, Quintiles. “Such an environment helps position Singapore as a beachhead for global and Asian companies to drive business expansion in Asia.”

One company that has established itself in



“Countries such as Singapore, Korea, and Australia often can offer more innovative environments than the United States or Europe.”

DR. CARL FIRTH / ASLAN Pharmaceuticals

Singapore is ASLAN Pharmaceuticals, which is focused on developing novel medicines in the areas of oncology and inflammation.

Carl Firth, Ph.D., CEO and founder of ASLAN, says the company partners with companies that have preclinical and Phase I compounds, and ASLAN works to develop those through Phase I, II, and deliver Phase III ready compounds that the company will then partner out.

“We look for more creative ways to develop these types of drugs and really leverage Asian clinical centers, recognizing that countries like Singapore, Korea, and Australia often can offer more innovative environments than the United States or Europe,” Dr. Firth says. “Recruitment rates in Asia can also be faster. Several diseases that are significant in this region have been ignored by the industry and represent very significant unmet need. So we focus on those areas trying to develop drugs more creatively, efficiently, and faster than can be done elsewhere.

“For us, early-phase research, translational Phase I is a key part of the process and so we decided to put ourselves in Singapore because that was where we saw some of the strongest capabilities,” he says. “Additionally, we believed that it’s an attractive environment to set up business and easy to attract talent.”

In addition to bringing in talent from overseas, Dr. Firth says there is strong local talent with experience in earlier research, and notes, that in terms of clinical experience there are a number of CROs in Singapore that have strong regional capabilities.

In terms of early-phase research, Dr. Firth says Singapore is a great place to work because the company can collaborate with investigators who are open to creative, innovative ways of working and a regulatory agency that’s experienced in innovative research.

“When we do get into larger Phase II studies we will involve Singapore but we’ll also be working in other countries as well,” he says. “We also don’t do any manufacturing in Singapore today; we do that mostly in China and India. But in terms of having headquarters, the convenience of building a business and attracting talent, Singapore is great.”

Dr. Firth also notes that after some disappointing results by biotech companies in Singapore, the trend now has turned to stakeholders investing in medical devices/diagnostics, propelled by Singapore’s strength in cross-functional collaboration and interdisciplinary working.

Going forward, Steve Robson, managing director of H&T Asia, a healthcare communications business with an office in Singapore servicing southeast Asia, and an affiliate member of the inVentiv Health Communications Global Network, says as Singapore builds on its foundation in good science and capabilities in translational and clinical research, the city-state is well-positioned to support the industry in its efforts to accelerate the drug discovery process with next-generation technologies.

“In addition, companies and research are focusing on key diseases such as cancer, metabolic diseases, neurological diseases, infectious diseases, and eye diseases,” he says. **PV**

## Singapore Budget Encourages R&D

On Feb. 17, 2012, the Singapore Government handed down its 2012 budget. The main tax changes announced included enhancements to further encourage automation and R&D and further guidelines to provide clarity on when companies will not be taxed on gains from the disposal of equity investments.

## Productivity and Innovation Credit Scheme

The Productivity and Innovation Credit (PIC) scheme was introduced two years earlier to support small and medium enterprises (SMEs) and other businesses that incur qualifying expenditure in undertaking all or any of the six prescribed activities — training, R&D, investments in automation equipment, investments in approved design projects, and acquisition and registration of IP rights.

Under the scheme, eligible businesses can claim benefits in the form of a 400% tax deduction (up to S\$400,000) of qualifying expenses incurred on each of the qualifying activities and/or a cash payout at a prescribed rate of the qualifying expenditure (up to S\$100,000 per year).

The budget proposed that the prescribed payout rate be increased from 30% to 60% and the frequency of cash payouts be increased to four times a year to help SMEs better manage their cash-flow and liquidity. The Budget also proposed to liberalize existing rules to make it easier for businesses to claim PIC benefits in relation to in-house training and software development (except software to be used for internal business administration).

Expenditure incurred on R&D cost sharing agreements will now qualify as R&D

expenditure for tax purposes, without the need to obtain prior approval from the EDB. The expenditure will also qualify for PIC benefits under the R&D activity. The qualifying expenditure will be deemed to be 60% of the shared costs unless the taxpayer is able to demonstrate that the actual qualifying expenditure is higher. These changes, taken together, result in the Singapore Government effectively funding up to 68% of the costs incurred by a company to enhance its productivity (or alternatively access cash payouts of slightly lesser amount than the benefits accessed through the tax deduction system).

## Integrated Investment Allowance Scheme

The new Integrated Investment Allowance (IIA) scheme introduced during the budget proposes to provide an additional allowance (to capital allowances) on fixed capital expenditure incurred for productive equipment placed overseas with sub-contractor(s) for pre-approved projects.

The additional allowance will certainly give added appeal to the outsourcing model and further enhance Singapore's attractiveness as an entrepreneurial hub.

This scheme is especially relevant to the growing number of large multinational company medical original equipment manufacturers (OEMs) that have located R&D centers or regional HQs in Singapore because of its intellectual property protection, skilled labor pool, and easy access to a variety of emerging consumer markets. The IIA scheme may provide fresh impetus for these OEMs to outsource their manufacturing activities within the region in order to derive cost efficiency.

That being said, this model may create

withholding tax and permanent establishment tax exposures in other countries for them. As such, it is still advisable for companies that are considering placing their plant or machinery with companies outside Singapore for the manufacturing of goods, to evaluate the overall tax benefit.

## Gains on Disposal of Equity Investments

M&A has been active within the pharmaceutical industry due to the need for consolidation, resulting from the continued emergence of new products, increased competition, and regulatory costs that can be more effectively diversified through consolidation. New guidelines have been introduced to determine when a company will not be taxed on gains from the disposal of equity investments. This should give international pharmaceutical companies more certainty and confidence in carrying out M&A in Singapore or using Singapore as a holding company or headquarters location.

The new guidelines announced during the budget provide that, with respect to shares disposed of on or after June 1, 2012, gains derived by companies will not be taxed if:

- » The divesting company holds a minimum shareholding of 20% in the company being sold; and
- » The divesting company has held a 20% shareholding for at least 24 months immediately prior to the disposal.

For share disposals in other scenarios, the tax treatment should continue to be determined on the facts and circumstances of the case. The scheme will be reviewed after five years by the Inland Revenue Authority.