

# biotech focus

## Singapore – a global biomedical sciences hub

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Singapore is fast becoming one of the hubs in Asia for biomedical sciences (BMS) research and manufacturing. Although Singapore's involvement in BMS goes way back to the 1970s, the major push started in 2000 as part of the government's effort to diversify the country's economic portfolio. Three agencies were given the task of implementing Singapore's BMS initiative.

They are the Economic Development Board's Biomedical Sciences Group (EDB BMSG), EDB's Bio\*One Capital and the Biomedical Research Council (BMRC) of the Agency for Science, Technology and Research (A\*STAR). EDB BMSG is responsible for formulating the industry development plans and attracting international companies to set up operations in Singapore. Bio\*One Capital makes strategic investments in companies with the aim of generating economic spin-offs in Singapore,

whereas BMRC takes the lead in coordinating and funding public sector and academic research, as well as supporting the training of scientists.

### Biopolis

A vivid icon of Singapore's commitment to support BMS research is the Biopolis. Opened in October 2003 and costing US\$300 million to build, the Biopolis is an integrated R&D complex of two million square feet of space that houses BMRC's five research institutes as well as R&D laboratories of numerous pharmaceutical and biotechnology companies. More than 90% of the space in Biopolis has now been taken up by some 2000 scientists from laboratories in the public and private sectors. As a result of the strong demand, construction of Phase II of Biopolis is set to start in the first half of 2005. This will provide an additional 400,000 square feet of space for industry R&D.

One of the key challenges faced by start-ups and established companies alike is the need to manage R&D costs and bring products to the market as quickly as possible. At Biopolis, companies can take advantage of a 'plug and play' infrastructure. Researchers are able to access state-of-the-art facilities, scientific infrastructure and specialized services. These allow companies to cut R&D costs significantly and accelerate the product development outline. Shared facilities include X-ray crystallography, nuclear magnetic resonance, electron microscopy, DNA sequencing and others. In addition, there are conference

facilities and meeting rooms that companies can use.

### Research in the public sector

The five BMRC research institutes located at the Biopolis are:

- Institute of Molecular and Cell Biology – with research focussed on in cell cycling, cell signalling, cell death, cell motility and protein trafficking.
- Institute of Bioengineering and Nanotechnology – directs its research efforts in nanobiotechnology, delivery of drugs, proteins and genes, tissue engineering, artificial organs and implants, medical devices, and biological and biomedical imaging.
- Genome Institute of Singapore – pursues the integration of cutting-edge technologies with genetics, and biology towards the goal of individualised medicine.
- Bioprocessing Technology Institute – has core expertise in expression engineering, animal cell technology, stem cells, microbial fermentation, product characterization, downstream processing, purification and stability, with supporting proteomics and microarray platform technologies.
- Bioinformatics Institute – focuses its research around knowledge discovery from biological data, exploiting high-end computing in biomedicine, advancing molecular imaging of biological processes, modelling of drug design and delivery, computational proteomics and systems biology.

Apart from the above, BMRC gives out extramural grants to researchers in universities, hospitals and disease centres in Singapore. The latter are clinical centres of excellence in key therapeutic areas such as the National



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## BOX 1

### Local companies

**A-Bio Pharmaceuticals Pte Ltd** was set up to fill Singapore's capability gap in biologics manufacturing. A-Bio aims to be a leading custom manufacturing company that provides manufacturing solutions to pharmaceutical and biotechnology companies worldwide. Its capabilities will be primarily focused on manufacturing biologic products (protein-based therapeutics), in particular, monoclonal antibody products for its customers using mammalian cell culture. In early 2004, A-Bio took over the running of a 200 L pilot mammalian plant from the Biopharmaceutical Manufacturing Technology Centre.

**ES Cell International Pte Ltd** is a spin-off resulting from the collaborative work of three universities: National University of Singapore (NUS), Monash Institute of Reproduction and Development, and Hadassah University of Israel. The company develops and commercializes technologies and products resulting from work on human embryonic stem (hES) cells, with a focus on diabetes. This work has potential applications in the field of biopharmaceuticals, tissue engineering, and transplantation medicine. ESI is today a world leader in the field of stem cell science and cellular therapy.

**Merlion Pharmaceuticals Pte Ltd** was formed in early 2002 as a spin off from the Institute of Molecular and Biology, focusing on natural product discovery. Bio\*One invested in Merlion jointly with pharmaceutical company, GSK, local as well as overseas VC funds. Merlion has since signed partnership agreements with several pharmaceutical and biotechnology companies such as Abbott, Fujisawa, KuDOS, Merck, NovImmune, and Schering-Plough, to screen their targets against Merlion's natural product collections.

**S\*Bio Pte Ltd** is Singapore's first fully integrated drug discovery and development company, which built on its access to Chiron Corporation's state-of-the-art technologies in small molecule drug discovery. The company is a strategic investment for the development of the Biomedical Sciences industry in Singapore. Its fully integrated structure and technology transfer agreement with Chiron enabled the development of capabilities in genomics, combinatorial chemistry, medicinal chemistry, and pharmacology here in Singapore. Since its establishment, S\*Bio has played a key role in helping to attract the setting up of BMS R&D companies in Singapore.

**Attogenix Biosystems Pte Ltd** a spin-off of Defence Science Organization and NTU Ventures Pte Ltd Attogenix Biosystems, based in Singapore, is a developer of novel micro-scale fluidics gene amplification array biochips that can perform hundreds to thousands of simultaneous contamination-free micro-PCRs with integrated DNA- and RNA-extraction capability, together with an accompanying molecular analyser. Attogenix Biosystems is currently developing revolutionary high-throughput integrated genetic bio-analytical solutions. Its products and solutions are for the life sciences and biopharmaceutical research, medical diagnostics, bio-defence, industrial field-test and personalized medicine user markets of high commercial value. The Attogenix solution provides rapid massively parallel genetic analysis capability with on-chip genetic sample preparation to biopharmaceutical researchers, biomedical research institutions, clinical diagnostic laboratories, hospitals and clinics, and the defence industries. The Attogenix solution also enables the diagnoses of a large number of diseases and patients rapidly, reliably and simultaneously.

**Merlin Medical Pte Ltd** was set up by former senior employees of large medical technology companies (such as Boston Scientific Corporation, Guidant Corporation, Cook with extensive domain knowledge and experience in forming start-up companies. The management team has over 60 years of combined experience in medical device field, and in bringing products from R&D phase to the market. The vision of the company is to leverage its strategic location in Singapore to develop, manufacture and market interventional medical devices specifically for cardiology, neurology and other minimum invasive products/accessories. Merlin is dedicated to the development of interventional medical devices that will assist interventional neuroradiologists, neurologists and neurosurgeons in stroke treatment and prevention. Merlin differentiates itself by customising its products to suit the Asian needs with differences in epidemiology and spending patterns. The company has leased 12,000+ sq ft facility in Woodlands Industrial park. Of which, 2000 sq ft of class 100k and class 10K CER for product assembly. The company started pilot production of its proprietary coronary stent, balloons and currently undergoing its ISO audit. Other functions such as purchasing, R&D, Sales/Marketing, QA etc are also being developed and housed at this facility.

**Promatrix Biosciences Pte Ltd** focuses on novel biofunctional and three-dimensional scaffold and related technologies for use in cell therapy and tissue engineering. Promatrix's innovations are licensed from Johns Hopkins Singapore, the international subsidiary of Johns Hopkins University, USA. These technologies enable products that improve *ex vivo* cell culture outcomes or tissue regeneration in combination with appropriate cells.

Cancer Centre, National Neuroscience Institute, Singapore National Eye Centre and the National Heart Centre. Since its first grant call in 2001, BMRC has awarded 214 research grants, which have generated some 240 publications in leading scientific journals and over 20 patents filed to-date. The projects have also led to numerous collaborations with pharmaceutical MNCs, as well as many commercialization opportunities.

### Recruiting and training scientists

In A\*STAR's annual R&D survey for 2003, the gross expenditure on research and development (GERD) was S\$3.4 billion, which represented 2.15% of Singapore's gross domestic product (GDP). The number of research scientists and engineers<sup>1</sup> (RSEs) in

<sup>1</sup>Data include full-time postgraduate research students.

Singapore was 21,139. This works out to 98.3 RSEs per 10,000 labour force in Singapore.

To support Singapore's BMS initiative, A\*STAR has embarked on a programme to increase the number of Singaporeans pursuing PhD studies and post-doctoral fellowships locally as well as in top universities around the world. Since 2001, more than 270 people have received scholarships and fellowships to pursue biomedical sciences related studies.

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## BOX 2

### Websites of interest

**Economic Development Board Biomedical Sciences Group (EDB BMSG) and information on Singapore's Biomedical Sciences Industry**

[www.biomed-singapore.com](http://www.biomed-singapore.com)

**Bio\*One Capital**

[www.bio1capital.com](http://www.bio1capital.com)

**Agency for Science, Technology and Research (A\*STAR)**

[www.a-star.edu.sg](http://www.a-star.edu.sg)

(The five Research Institutes can be found here too)

**Biopolis**

[www.one-north.com](http://www.one-north.com)

**Biopolis Shared Facilities**

<http://bsf.a-star.edu.sg/bsf/index.do>

**Tuas Biomedical Park**

[www.jtc.gov.sg](http://www.jtc.gov.sg)

**BioSingapore**

[www.biosingapore.org.sg](http://www.biosingapore.org.sg)

**A-BIO Pharma**

[www.a-bio.com](http://www.a-bio.com)

**S\*Bio**

[www.sbio.com](http://www.sbio.com)

**MerLion Pharmaceuticals**

[www.merlionpharma.com](http://www.merlionpharma.com)

**ES Cell International**

[www.escellinternational.com](http://www.escellinternational.com)

**Bioethics Advisory Committee (BAC)**

[www.bioethics-singapore.org](http://www.bioethics-singapore.org)

**Attogenix Biosystems**

[www.attogenix.net](http://www.attogenix.net)

**Merlin Medical**

[www.merlinmedical.com](http://www.merlinmedical.com)

**Promatrix Biosciences**

[www.promatrix-bio.com](http://www.promatrix-bio.com)

- Dr Axel Ullrich heads the molecular biology department at Germany's Max Planck Institute and is also with the Singapore Onco Genome Laboratory
- Dr Alan Colman, formerly from UK-based PPL Therapeutics, is Chief Scientific Officer of ES Cell International
- Dr Edison Liu, former Director of Clinical Sciences at the US National Cancer Institute, is Executive Director of Genome Institute of Singapore
- Dr Jackie Ying, from the Massachusetts Institute of Technology, is Executive Director of the Institute of Bioengineering and Nanotechnology
- Dr Yoshi Ito, from the University of Kyoto in Japan, is Principal Investigator at the Institute of Molecular and Cell Biology

### Growing base of drug discovery and development activities

The scientific capabilities and expertise being built up in Singapore, as well as Biopolis have attracted many pharmaceutical and biotechnology companies to establish R&D operations in Singapore (Box 1). The momentum of new projects by BMS companies was sustained in 2004 with GSK establishing a preclinical research facility for neurodegenerative diseases in Singapore. This was GSK's first such facility in Asia Pacific and Singapore's third pharmaceutical corporate R&D centre, the others being the Novartis Institute of Tropical Diseases (NITD) and Eli Lilly's Systems Biology Centre (LSB).

Also significant was the decision by Albany Molecular Research (AMRI), the world's leading contract chemistry development company, to establish a research centre in Singapore. The facility, AMRI's first outside the USA, will provide fee-for-service chemistry technologies and services, including medicinal and combinatorial chemistry, process research and scale-up chemistry, analytical services and the manufacture of active pharmaceutical ingredients.

Equally importantly, Singapore is the Asian hub for many of the leading pharmaceutical companies and contract research organizations to direct and coordinate their regional clinical development activities, from Phase I to Phase III. This is due to Singapore's excellent infrastructure and geographic location, which



facilitates access to patient populations across Asia. These companies include AstraZeneca, Bristol-Myers Squibb, Covance, Eli Lilly, GSK, Icon Clinical Research, Merck and Co., Novartis, Novo Nordisk, Pfizer, PPD, Quintiles, Sanofi-Aventis and Schering-Plough.

### Manufacturing – exceptional performance in 2004

In manufacturing, Singapore's BMS industry posted a record output of S\$15.8 billion in 2004, a 33.2% increase over the year before. When Singapore started the BMS initiative in mid-2000, the goal was to double the industry's manufacturing output to S\$12 billion by 2005. The industry's strong performance in 2004 meant that the target was comfortably exceeded by a third and achieved one year ahead of schedule.

Singapore also continued to strengthen its position as a strategic manufacturing base for global pharmaceutical companies. In 2004, Novartis Pharma AG started construction of a new production facility to provide needed capacity within its global manufacturing network. In addition, GSK completed an expansion to its existing manufacturing facility in Singapore, while Pfizer opened a multi-purpose facility, making Singapore home to its first large-scale manufacturing plant in Asia.

There were also significant new investments in medical technology. Ciba Vision, a Novartis

By 2010, >1000 Singaporean PhDs will be added to the research community.

To complement this, Singapore welcomes talent from all over the world. Good science, a cosmopolitan environment and flexible immigration policies for professionals, help attract research talent. We have been fortunate to have attracted many top names to work in Singapore:

- Dr Sir David Lane, from the University of Dundee, is the Executive Director of the Institute of Molecular and Cell Biology



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subsidiary, started construction of its global contact lens-manufacturing facility during 2004. MDS Sciex, a subsidiary of Canadian-based MDS, announced that it would set up a manufacturing facility to produce its mass spectrometers, its first site outside Canada. A local Singapore company, Forefront Medical Technology, will be expanding its plant to contract manufacture medical devices used in the field of anesthesia.

## Co-Investments by Bio\*One further boosted industry growth

EDB's dedicated BMS investment arm, Bio\*One Capital, manages S\$1.2 billion in several funds. Last year, Bio\*One committed a total of S\$95 million to investments in 16 projects, including new investments as well as follow-on investments in existing portfolio companies. 90% of the investments were made in Singapore-based companies to help build and grow the companies, and in overseas projects with linkages and activities in Singapore. In 2004, Bio\*One's key portfolio companies made significant strides.

- A-Bio Pharma commenced its first major

partnership with leading vaccines company GSK Biologicals (Belgium) to develop and manufacture new generation vaccines.

- S\*Bio has developed a highly competitive oncology program focused on the development of histone deacetylase (HDAC) inhibitors and is on track to deliver its first candidate for clinical development in 2006.
- MerLion Pharmaceuticals (Singapore) entered into further partnerships with international pharmaceutical and biotechnology companies for natural product drug discovery.
- One of the world's leading stem cell company, ES Cell International (Singapore), received a resource infrastructure enhancement award from the US National Institutes of Health (NIH) and a research grant from the Juvenile Diabetes Research Foundation (JDRF) to look into research for the treatment of diabetes.

2004 saw another important milestone for Singapore's BMS industry with the setting up of BioSingapore, a trade association representing the interests of local biosciences enterprises. This signifies a coming of age for the industry. BioSingapore will play an

important role in helping local BMS companies to engage the financial community and other key stakeholders.

## Conclusion

Singapore's vision is to be the Biopolis of Asia (Box 2). To achieve this, Singapore has built up world-class capabilities across the entire value chain from drug discovery and clinical research, to manufacturing and health care delivery. Singapore offers an efficient and comprehensive network of support that enables companies to invest here with ease. Going forward, there will be an increasing emphasis on building up expertise in translational research and on exploring the interface between biomedical sciences and engineering. Singapore will also continue to nurture world-class research talent to further enhance its attractiveness in this sector.

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## Biotechnology in India

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Biotechnology hubs are emerging all over the world. The Americas, Europe, Eurasia, Southeast Asia, Western Asia and the Pacific rim all have hotspots of biotechnology.

India is particularly suited to become the country of choice for biotechnology initiatives and endeavors. The rich human capital in this country of over one billion people is its most valuable asset. India has a large English-speaking base, and the official language of virtually all universities, businesses and research institutes is English. India produces ~2.5 million graduates in the IT, engineering and life sciences, >650,000 postgraduates and 1500 PhDs qualified in the engineering and life sciences each year [1].

The environment for biotechnology in India holds an advantage over other countries for

those ventures that seek to capitalize on the immense biodiversity that is available. The Indian subcontinent occupies only 2.4% of the world's land mass but accounts for 7.6% of all species of mammals, 12.6% of all bird species, 11.7% of all fish species and 6.0% of all higher flowering plant species. For its size, the Indian subcontinent contains a disproportionately large share of the world's biodiversity [1].

**'India produces ca 2.5 million graduates in the IT, engineering and life sciences each year...'**

## The financial opportunity

Today India has more than 200 biotechnology companies. Of these, 75% were incorporated in the past five years, so the industry is young.

The biotechnology industry in India grew by 40% last year, principally in the areas of

pharmaceuticals, agriculture and bioinformatics. Net revenue for this growing industry was US\$705 million, which was the third rank in the Asia-Pacific region, behind Australia at US\$1 billion and China at US\$800 million. India has 60 FDA-approved facilities within its borders, which is second only to the USA [1]. Without question, India has made remarkable progress in a very compressed time frame.

## Sectors of Biotechnology

Biotechnology in India has been categorized in several different ways, and it is instructive to examine these categories. The largest and fastest growing overall segments have been termed as the following:

- medical biotech segment
- agri biotech segment
- services segment

The medical biotech segment is expected to grow to an innovative US\$25 billion industry by 2010, from a 2003 US\$5 billion generic based drug business. The agri biotech segment is very large in India, since this