ASIAN PHARMACEUTICAL INDUSTRY ANALYSIS AND MARKET ASSESSMENT FOR CANCER DRUG

by

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ABSTRACT

The project is designed to analyse the Asian pharmaceutical industry and assess the Asian cancer market for Protox's two products: PRX321 and PRX302. First of all, I analysed the Asian pharmaceutical industry in terms of an industry map, development stage, R&D capabilities, IP protection, healthcare systems and regulatory requirements. Next, I took China as a typical example to understand the Asian pharmaceutical market. Then, I evaluated the Asian cancer drug market according to cancer prevalence, current treatments and remuneration systems. Finally, I specifically assessed Asia's brain cancer market, prostate cancer market, and benign prostatic hyperplasia (BPH) market in terms of market capacities, current situations and competitions. The author concluded that the Asian cancer market is lucrative and fast developing. However, it is also challenging due to low per capita healthcare spending, a lack of effective IP protection and transparent regulations, unestablished remuneration systems, and severe market competition.

EXECUTIVE SUMMARY

The project is sponsored by Asia Lifesciences Venture Consulting. Asia Lifesciences Venture Consulting is a venture capital and consulting company that provides financial or consulting services to biotech and medical companies who intend to develop business in the complex and fast growing Asian market. One of its clients, Protox Therapeutics Inc. (TSX-V: PRX) is a Vancouver-based early stage biotech company. The company is dedicated to developing targeted therapeutics for cancers and other proliferative diseases by engineering naturally occurring protein toxins. Currently, Protox is clinically developing its two candidates, PRX321 and PRX302, for the treatment of brain cancer, prostate cancer and BPH. To accomplish the mission of changing the worldwide cancer diseases statistics for the better, Protox would like to explore the potential of entering the Asian cancer drug market. The purpose of the project is to offer background and recommendations for Protox's Asian marketing strategy development. The scope of the project is to analyse Asian pharmaceutical industry and assess Asian cancer market.

In general, Asia's pharmaceutical market is fast growing and lucrative for pharmaceutical companies because of Asia's vast population, aging societies, and rapidly increasing per capita incomes. However, the fast growing drug market is highly fragmented and vulnerable, with thousands of local companies mainly competing on generics. The Asian pharmaceutical market is also challenging due to Asia's extremely low per capita healthcare spending, a lack of effective IP protection, complex regulatory requirements, government interventions on prices and patents, and tough competition from local and international firms.

As for Asia's cancer drug market, it is booming recently due to high cancer incidence, improving remuneration systems, and promoted public healthcare awareness. The market trend

will continue because Asia's high cancer incidence is associated with severe pollutions along with industrialization, improved scanning tools and technologies, and westernized diets and lifestyles. However, the brain cancer market is relatively moderate in Asia because brain cancer is a kind of comparatively low incidence cancer worldwide. With respect to Asia's prostate cancer market, it is much less attractive than stomach, lung, liver, esophagus or colorectal cancers markets due to prostate cancer's extremely low prevalence in Asia, compared with the prevalence in the rest of the world, especially in U.S. and North Europe. The BPH market in Asia is highly lucrative due to BPH's similar high incidence rate around the world and Asia's huge aging population. However, the BPH market is well-established, with tough competition from competing drugs and non-drug treatments.

At present, Protox is testing PRX321 and PRX302 for the treatments of brain cancer, prostate cancer and BPH. If PRX321 and PRX 302, with distinctive modes of action, can be proved to have fewer side effects than existing cancer drugs or other therapies, it should be rewarding for Protox to enter Asia's brain cancer market, prostate cancer market and BPH market. Based on this market study, it may be more promising if Protox could explore Asia's stomach, lung, liver, esophagus, or colorectal cancer markets after testing new indications for PRX321 and PRX302 in clinical trials.

DEDICATION

To my wife, Yihui Geng, my son, Di Wu, and my parents

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I would like to take this opportunity to thank the teaching and administrative staffs of Segal Graduate School of Business, Simon Fraser University, for their excellent and dedicated education and guidance throughout the exciting MBA program. In the past year, I experienced an exciting, colourful, and rewarding life in Vancouver, Canada, which could have impact on my future life and career development.

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1 INTRODUCTION

1.1 Objective and Scope of Project

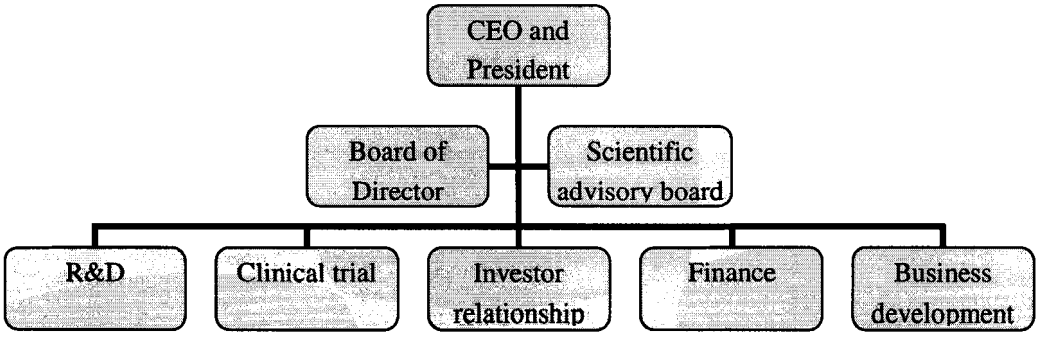
Protox Therapeutics Inc. is a Vancouver-based early stage biotech company, which develops targeted therapeutics for cancers and other proliferative diseases by engineering naturally occurring protein toxins (Protox, 2007n). With a mission "to change the worldwide cancer diseases statistics for the better" (Protox, 2007o), Protox intends to explore Asian cancer market since nearly half of the world's cancer deaths happened in Asia (Asian Medical Forum, 2007). Cancer has been a heavy burden in Asia due to Asia's high cancer incidence rate and Asia's vast population. If Protox can successfully explore Asian cancer market, it will be a great commitment to its mission. The project is designed to analyse the Asian pharmaceutical industry and assess the Asian cancer market in order to provide background and recommendations for Protox's Asian marketing strategy development. Specifically, this project will evaluate Asia's brain cancer, prostate cancer and BPH disease markets, which are Protox's target markets since its two candidates, PRX321 and PRX302, are been testing in clinical trials for the treatments of brain cancer, prostate cancer and BPH disease.

1.2 Company Background

In 2002, Protox Therapeutics Inc. was founded based on Dr. Tom Buckley's research on protein toxins at the University of Victoria. Internationally recognized as an excellent

scientist on channel-forming proteins, Dr. Tom Burckley holds one of the largest NSERC research grants in the biological sciences in Canada (Protox, 2007a). Dr. Tom Buckley received his education at McGill University, Harvard University and the University of Utrecht in Holland in Chemistry and Biochemistry (Protox, 2007b). On July 14, 2004, Protox went public and began trading its stocks on the Toronto Venture Exchange under the ticker of TSX-V: PRX (Protox, 2007p). At present, the company is managed by an experienced team led by Dr. Fahar Merchant, who achieved Ph.D. in Biochemical Engineering from the University of Western Ontario. Dr. Fahar Merchant has over 18 years of progressive experience as a scientist, consultant, entrepreneur and senior biotech executive (Protox, 2007c). The competent management team has proven experience in new drug development, executing clinical trials, and in-licensing or out-licensing technologies. Besides competent management team, Protox also has a convincing Scientific Advisory Board, which is composed of excellent scientists from Harvard Medical School, Johns Hopkins University School of Medicine, and British Columbia Cancer Agency (Protox, 2007d). In summary, Protox's organization is small, efficient, creative, close to leading biotechnology, and staffed by the talented scientists and experienced management team (See Figure 1).

Figure 1 Organization Structure of Protox



Based on author's research

Based on Protox's early stage strategy of developing novel anti-cancer drugs, Protox devotes most of its efforts and resources to new drug research and development, instead of expanding downstream towards the terminal of the industry value chain such as manufacture and marketing. Currently, Protox is developing a product pipeline of clinical trial stage cancer drug candidates, which were derived from its unique PORxin™ and INxin™ technology platforms (See Appendix 1). Through its unique technology platforms, Protox generates its drug candidates by engineering the naturally occurring toxins, Pseudomonas Exotoxin and Proaerolysin. The engineered versions of toxins are expected to have fewer side-effects than current cancer treatments. However, their safety and efficacy have not been certainly testified since the required clinical trials have not been completely finished.

As an early stage R&D biotech company, Protox is dedicated to developing unique technology platforms and novel anti-cancer drugs. Protox has no sales and marketing capabilities therefore does not generate any sales revenue so far. The company is funded by equity investments including seed capital, angel capital, venture capital and IPO. To gain additional capital and build sales and marketing capabilities, Protox is looking for capable partners to either co-develop or out-license the development and commercialization of its potent anti-cancer drug candidates (Protox, 2007e).

In general, Protox is an emerging early stage biotech company. Its strengths stem from its competent management team, convincing scientific advisory board and unique technology platforms. However, a lack of sales and marketing capabilities and extra funding undermines Protox's ability to develop and commercialize its drug candidates. Besides, the

unfinished clinical trials increase the uncertainty of the process of development and commercialization.

1.3 Product Introduction

Protox's leading drug candidates in clinical trial stage include PRX321 and PRX302. PRX321 is been testing for treatment of primary brain cancer, renal cell carcinoma and non-small cell lung cancer (Protox, 2007f). PRX302 is supposed to treat localized prostate cancer and benign prostatic hyperplasia (BPH), which is commonly known as enlarged prostate (Protox, 2007g).

INxin™ drug, PRX321, is an engineered version of Pseudomonas Exotoxin in combination with a ligand that specifically sticks to IL-4 receptors. The engineered version of Pseudomonas Exotoxin is a potent anti-cancer agent after its non-specific toxicity has been reduced by genetic engineering. It is expected that PRX321 has fewer side effects than existing cancer drugs because PRX321 specifically targets cancer cells that create tumor associated IL-4 receptors on their cell surfaces (Protox, 2007h). Once bound to the specific receptors, INxin™ drug enters the cells and inhibits protein synthesis, which ultimately leads to cell deaths (Protox, 2007i). PRX321 has been completed Phase II clinical trials for the treatment of primary brain cancer, specifically recurrent malignant gliomas such as glioblastoma, multiforme and anaplastic astrocytoma. PRX321 is also been conducting Phase I clinical trials to testify safety for the treatment of both renal cell carcinoma and non-small cell lung cancer (Protox, 2007j).

PORxin™ drug, PRX302, is an engineered version of Proaerolysin. The engineered version of toxin contains specific binding and activation sites that make it selective to targeted cells, reducing the likelihood of toxicity to neighbouring healthy cells. PRX302 is a kind of pre-drug that is activated by high level specific proteases created by targeted cancer cells (Protox, 2007k). Once specifically combined with proteases on the surface of targeted cells, PRX302 is activated and then punches holes in cell surfaces, causing cell contents to leak out and ultimately resulting in cell deaths (Protox, 2007l). Protox is currently conducting Phase I clinical trials with PRX302 for the treatment of localized recurrent prostate cancer. PRX302 is also been testing for the treatment of benign prostatic hyperplasia (BPH) in Pre-clinical phase (Protox, 2007m).

Due to their distinctive modes of action, PRX321 and PRX302 are supposed to specifically kill targeted cancer cells without destroying neighbouring normal cells and tissues, so PRX321 and PRX302 are expected to have fewer side-effects than existing anti-cancer drugs and some non-drug cancer treatments.

2 ASIA'S PHARMACEUTICAL INDUSTRY

2.1 Overview

Covering 23.4% of earth's total land area, Asia is world's largest and most populous continent with a population of over 3.8 billon people, which accounts for more than 60% of world's current population, according to United Nations (See Appendix 2). Regarded as one of the fastest developing economies in the world, Asia ranks third for the whole GDP after North America and Europe, with per capita GDP of US$ 2,896.78 and an annual GDP growth rate of 5.23% in 2005 (See Appendix 3 and Appendix 4).

Asia is also one of the most diverse and complex regions in the world with diverse cultures, various political systems, and distinct social and economic development stages. With respect to geography, Asia consists of world's second largest economy: Japan; two biggest developing countries: China and India; several emerging areas: South Korea, Hong Kong, Taiwan, Singapore, Malaysia and Thailand; and some of Middle East and Gulf countries.

Table 1 shows Asia's main countries and areas' demographics in terms of population, life expectancy, GDP, growth rate, and per capita income.

Table 1 Asia's Demographics of 2006, US$

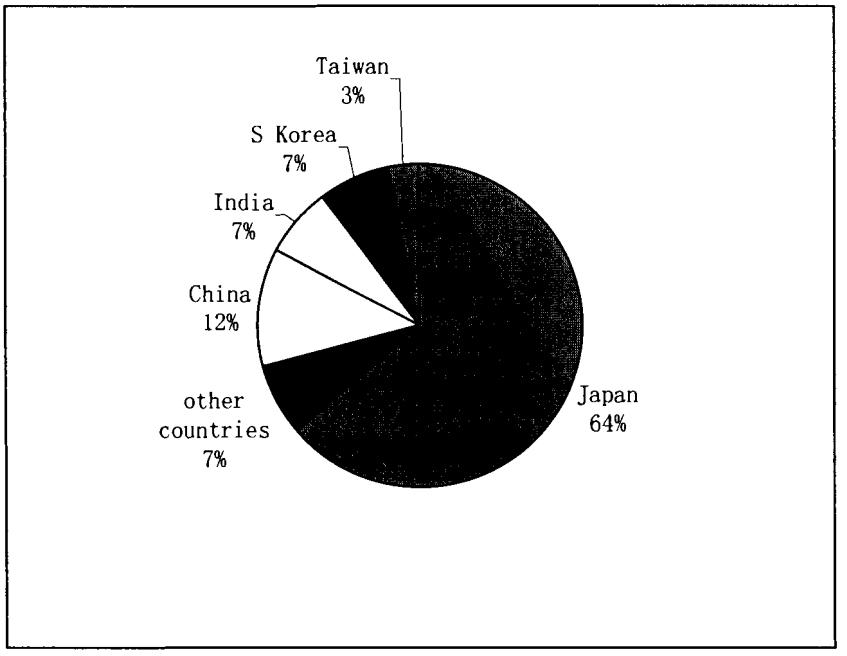
Countries and areas	Population (Million)	Life expect-ancy	GDP (billion)	Growth rate	GDP, PPP (billion)	Per capita, PPP
China	1,321.85	72.88	2,518	10.7%	10,170	7,700
Hong Kong	6.98	81.68	188.7	6.8%	258.8	37,300
Taiwan	22.86	77.56	346.4	4.6%	680.5	29,500
India	1,129.87	68.59	804	9.2%	4,156	3,800
Japan	127.43	82.02	4,883	2.2%	4,218	33,100
S Korea	49.05	77.23	897.4	4.8%	1,196	24,500
Indonesia	234.69	70.16	264.7	5.5%	948.3	3,900
Thailand	65.07	72.55	197.7	4.8%	596.5	9,200
Malaysia	24.82	72.76	132.3	5.9%	313.8	12,900
Singapore	4.35	81.80	122.1	7.9%	141.2	31,400
World	6,602.22	65.82	46,760	5.3%	65,950	10,200

Source: The World Fact Book of CIA, 2007

Due to Asia's vast population, rapidly increasing per capita incomes and gradually aging societies (See Table 1), the Asian pharmaceutical market is supposed to be one of the most lucrative healthcare markets in the world. In 2006, Asia's pharmaceutical market generated total revenue of about US$ 100 billion, which represented a compound annual growth rate (CAGR) of 4.7 % during the five year period from 2001 to 2005 (Datamonitor, 2006a). By comparison, the Japanese and Chinese markets grew at CAGR of 1.9% and 17.3% over the same period, with respective market values of US$ 65.2 billion and US$ 12.6 billion in 2006 (Datamonitor, 2006b). Datamonitor (2006c) argued that Japan, China, South Korea and India were the four biggest pharmaceutical markets in Asia, totally accounting for almost 90% of the whole Asian pharmaceutical market value in 2006 (See Figure 2). As a result of

the world's second biggest pharmaceutical market after U.S., Japan accounted for more than half of the total Asian drug market in 2006, with a market share of 64% (See Figure 2).

Figure 2 Asian Pharmaceutical Market Share, 2006



Source: Datamonitor, 2006

Economist Intelligence Unit (2005a) estimated that the Asian countries, except Japan, spent an average percentage of 5.8 of their GDP on healthcare in 2004, which was much lower than international standard of 9.6%. With respect to specific countries, Japan only spent 7.8% of its GDP on healthcare in 2004 (Word Health Organization, 2007a), while most other countries in Asia spent much less than Japan (See Table 2). In contrast, 15.4% of GDP was spent on healthcare in the U.S. in 2004, representing per capita spending of US$6,096.2 (WHO, 2007a). Relatively low percentage of GDP spent on healthcare, in addition to vast population and small GDP of Asian countries, results in extremely low per capita healthcare

spending in Asian countries. For example, Indonesia and India respectively spent as low as US$32.5 and US$31.4 on healthcare per head in 2004 (See Table 2).

Table 2 Healthcare Profile of Asian Countries in 2004 in US$

Countries and areas	Spending, % of GDP	Spending, per head	Pharmaceutical Sales (million)
World (EIU)	9.6	797.8	442,500
Japan	7.8	2,823.2	63,564
China	4.7	70.1	11,500
Malaysia	3.8	180.1	336
India	5.0	31.4	7,000
S Korea	5.5	776.9	7,100
Hong Kong	5.3	1,356	406
Taiwan	6.3	854	3,063
Singapore	3.7	942.9	295
Indonesia	2.8	32.5	2,074

Source: WHO, Economist Intelligence Unit, 2005, and Datemoniter, 2006

In spite of Asia's extremely low per capita healthcare spending, the Asian pharmaceutical market is still fast growing. Datamonitor (2006d) forecasted that Asia's pharmaceutical market would grow rapidly to a market value of US$130.6 billion in 2011, an increase of 27.2% since 2006, representing a compound annual growth rate (CAGR) of 4.9% during the period from 2006 to 2011. Based on Asia's huge population of more than 3.8 billion (See Appendix 1), increasing per capita healthcare expenditure, and rapidly growing market value, Asia's pharmaceutical market is really attractive not only to domestic drug manufacturers, but also to multinational pharmaceutical giants.

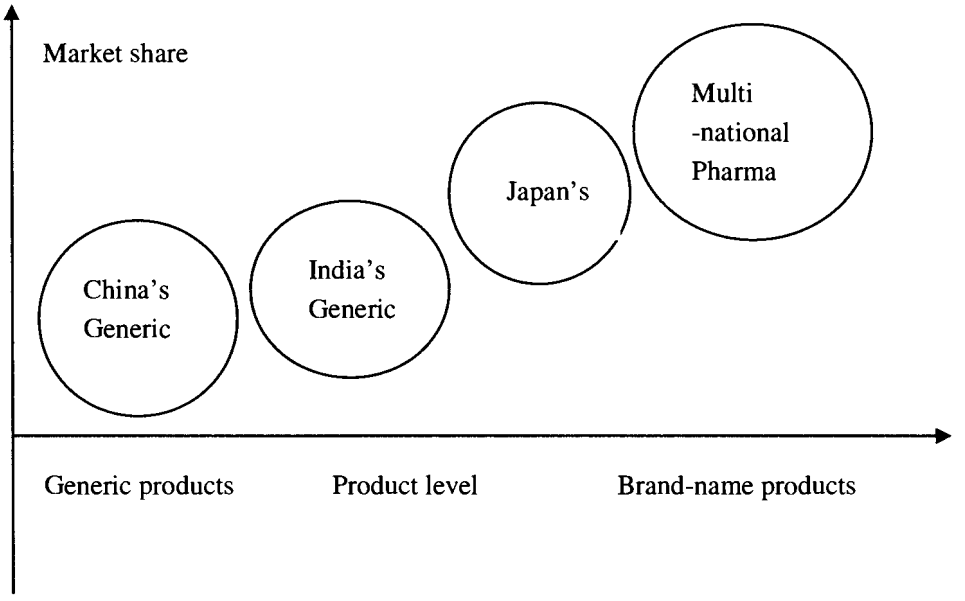
2.2 Industry Map

In general, Asia's pharmaceutical industry is extremely fragmented without a dominating winner in the emerging market, while foreign pharmaceutical companies play a critical role in this market, especially in R&D field. China, for example, has nearly 3,500 drug manufacturers and almost 12,000 medicine distributors scattering around the country to compete the US$12 billion worth market by providing generic drugs or copies of off-patented drugs, without a nationwide champion (State Food and Drug Administration, 2006a). Consisting of nearly 10,000 healthcare firms, India's pharmaceutical industry is also highly fragmented, where the top ten firms control only about 30% of its total US$ 7.0 billon worth market (Economist Intelligence Unit, 2005b).

However, changes are taking place in Asia's drug market due to tough competition and improved R&D capabilities. In India, local pharmaceutical companies such as Ranbaxy, Dr. Reddy's and Cipla have attempted to dominate Indian generic market and start to expand their business around Asia. For example, India's biggest local drug maker, Ranbaxy, has built factory in Guangzhou, China to manufacture and market its high-quality generic drugs out of India (EIU, 2005c). In 2005, Japan-based Takeda accounted for the biggest market share of 5% in Asia, prior to Astellas and Pfizer, which had respective market share of 4.9% and 3.4% (Datemonitor, 2006e). The above three pharmaceutical companies along with other multinational pharmaceuticals in Asia such as Novartis, Merck, AstraZeneca, and GSK, and several leading generic drug manufacturers from India such as Ranxaby and Cipla, as well as some state-owned pharmaceutical enterprises from China such as Shanghai Pharma, Huayuan

Pharma, Huabei Pharma, Guangzhou Pharma and China Pharma, make up of the Asian pharmaceutical industry map (See Figure 3).

Figure 3 Asian Pharmaceutical Industry Map



Based on author's understanding

2.3 Generics and Development Stage

According to Datamonitor (2005a), Asia is the second biggest generic drug market after U.S., accounting for 31.5% of the global generic market. In 2004, Asian generic drug market generated total value of US$ 14.2 billion, representing a compound annual growth rate (CAGR) of 19.2% over the five year period from 2000 to 2004 (Datamonitor, 2005b). By comparison, Asia's whole pharmaceutical market grew at a CAGR of 4.7% over the period 2001-2005 (Datamonitor, 2006f).

As a whole, Asia's pharmaceutical industry is still in early stage development and positions itself a generic drug producer due to a lack of capitals, talents and effective IP

protection. Asia's generic drug suppliers are mainly from India and China, while Japan's pharmaceutical companies, along with many other multinational pharmaceutical giants dominate the Asian brand name drug market (See Figure 3). So far, almost all top 50 pharmaceutical giants have invested in Asia, manufacturing and marketing their brand name products, and most of them chose China as their production bases in Asia. Because of their outstanding R&D capabilities, additional capitals, strong marketing power, and advanced corporate management, Japan's top pharmaceutical companies such as Takeda, Astellas and Daiichi Sankyo are at the same level of development to international big pharmaceuticals. India, long recognized as a leader in generic market, has competitive advantage over other Asian countries at generic manufacture, relying on India's comparatively strong R&D capability and talent pool. China's fragmented pharmaceutical industry generated the biggest generic market value in Asia, with total revenue of US$ 9.4 billion in 2004 (Datamonitor, 2005c).

As an example of conversion from generic to unique, India's leading pharmaceutical companies such as Ranbaxy, Dr. Reddy's and Cipla have recently been on aggressive acquisitions and business expansions in Asia and Europe, in an effort to complement their R&D capabilities in different therapeutic areas and reinforce existing research pipelines (Chaze, 2007, p.91-91). These Indian top pharmaceuticals start to provide new brand name drugs around the world, competing against multinational giants. Like many other Asian countries' pharmaceutical industries, the domestic pharmaceutical industry in South Korea has so far focused on generic drugs as well. However, pioneered by local big firms such as Dong-A and Daewoong, a move towards brand name products has been identified recently in

South Korea. It is estimated that South Korea will soon turn into a source of patented drugs, together with Japan and India in Asia (Datemonitor, 2006g).

2.4 R&D Capability and IP Protection

The main reason why Asian countries' pharmaceutical industries, except Japan's, compete on generic products is that most of the local drug manufacturers lack talents and capitals, and therefore strong R&D capabilities. Another big challenge for Asia's pharmaceutical industry is a lack of effective IP protection, which partly contributes to the weak R&D capability and early stage development of Asia's pharmaceutical industry.

At present, most Asian pharmaceutical companies spend very small part of their sales revenue on R&D. For example, Ranbaxy, India's biggest and most ambitious pharmaceutical company, spent mere 4% of its revenue on new drug development in 2004 (EIU, 2005d). In contrast, Pfizer, the world's biggest drug manufacturer spent around 15% of its annual revenue, a big number of US$ 7.4 billion that was more than India's whole pharmaceutical market value, on R&D in 2005 (Pfizer, 2007). Sparked by India's introduction of international patent standard in 2005, which prevented local firms from producing copies of western blockbusters, Indian local pharmaceutical companies have sharply hiked their research and development budget in the past years, not only attempting to develop generic version of off-patented western drugs, but also aiming to develop their own blockbusters (EIU, 2005e). This R&D trend is not confined to India since China, South Korea, Singapore and Hong Kong have recently started to develop their own patented products. In the past, a lack of effective patent law in China greatly hampered both domestic and foreign companies' R&D

efforts, resulting in Chinese pharmaceutical industry's low level development and high dependence on copies of western drugs. After China entered WTO in 2001 and improved its patent environment thereafter, more and more Chinese companies built new facilities and research clusters to beef up R&D capabilities, in a bid to compete against multinational companies in China's market. Taking advantage of their vibrant business environments, tight connections with western countries, advanced information technology, and endless sources of capitals and talents, Singapore and Hong Kong play an important role in basic research and new drug development by building new labs and biotech companies. Asia-pacific Biotech News (2006) reported that Singapore has regarded Biomedical Science (BMS) as the fourth pillar of its manufacturing sector after electronics, chemicals and engineering. BMS has grown to account for 9.1% of total manufacturing output in Singapore since 1999 when the Singapore Economic Development Board (SEDB) began to attract leading global medical technology companies to establish operations in the country.

Although many Asian countries such as China and India have improved their patent systems by introducing international patent standards, Asian pharmaceutical industry still faces severe challenge of IP protection. To protect local pharmaceutical industries and drive down healthcare spending, Asian governments, especially Southeast governments, often take actions in order to take control of firm-owned drug patents. Malaysia, for example, became one of the first countries in Asia to issue a compulsory license over a drug patent in September 2004 (Euromoney, 2007a). During the bird flu crisis in 2005, Taiwan government also issued a compulsory license to produce Tamiflu, one of the promising drugs used to fight

the bird flu virus. Tamiflu was developed and produced by Swiss pharmaceutical company, Roche (Euromoney, 2007b).

2.5 Regulatory Requirements and Pricing Policy

Unlike western governments, the Asian governments have more influences on pharmaceutical markets through regulatory requirements such as patent systems, new drug registrations, manufacturing certificates and pricing policies. China, for example, demands local firms to meet mandatory requirements of Good Manufacturing Practice (GMP), and attempts to curb drug prices by means of Government Directed Price and Maximum Retail Price (SFDA, 2006b). In Korea, several multinational pharmaceutical companies seeking to penetrate Korean market have complained a lack of transparency of investment procedure and drug registration. China and India's numerous and puzzling government regulatory requirements not only confuse domestic firms, but also deter the investments from foreign pharmaceutical giants (Datamonitor, 2006h).

Multinational pharmaceutical companies also meet challenges of price controls in Asian countries. In March 2007, Abbott was forced to lower the price of a kind of anti-AIDS drug in Thailand, on the exchange that Thai government would not violate its patent. Thai government earlier said that it intended to make the drug's generic vision legal in the interest of public health if Abbott refused to cut the price as demanded (Hui, 2007). That is not the only case in Asia. Malaysia and Indonesia ever forced multinational pharmaceutical companies to reduce prices of patented drugs several times in order to control public healthcare spending (Euromoney, 2007c). On September 28, 2006, Chinese government

began to implement the 19th drug price reduction since 1998, cutting nearly 400 drugs' prices by an average percentage of 40 (HC360.com, 2007a).

2.6 China

2.6.1 Overview

China is the most exciting pharmaceutical market in the world because of its vast population of more than 1.3 billion and amazing economy with compound annual growth rate (CAGR) of over 9.0% since 2000 (See Appendix 5 and Appendix 6). China is also world's fastest developing drug market growing at CAGR of 20% during the ten year period from 1996 to 2005, with a total domestic sales revenue of US$12.6 billion in 2005 (State Food and Drug Administration, 2006c). By comparison, Japanese and Koran markets grew at CAGR of 1.9% and 8.6% respectively over the period of 2002-2006, with respective value of US$65.2 billion and US$ 7.1 billion in 2006 (Datamonitor, 2006i). The perspective of China's pharmaceutical industry is really alluring since China accounted for 20% of world's population, while mere 2% of global pharmaceutical market value in 2005 (SFDA, 2006d). At present, China's pharmaceutical market is world's seventh biggest market before Spain and Canada, and expected to become the fifth by 2010 and the largest by 2050 (PricewaterhouseCoopers, 2006).

With respect to public healthcare spending, China spent 4.7% of its total GDP on healthcare, representing US$70.1 per head in 2004 (WHO, 2007b). Table 3 demonstrates the profile of Chinese healthcare in 2004, which could help us to evaluate and understand Chinese pharmaceutical market.

Table 3 Profile of Chinese Healthcare in 2004

Indicator	Value
Total expenditure on health as percentage of gross domestic product	4.7
General government expenditure on health as percentage of total expenditure on health	38.0
Private expenditure on health as percentage of total expenditure on health	62.0
General government expenditure on health as percentage of total government expenditure	10.1
Out-of-pocket expenditure as percentage of private expenditure on health	86.50
Per capita total expenditure on health at average exchange rate (US$)	70.1
Per capita total expenditure on health at international dollar rate (PPP)	276.7
Per capita government expenditure on health at average exchange rate (US$)	26.6
Per capita government expenditure on health at international dollar rate (PPP)	105.1

Source: Health Financing, WHO, 2007

2.6.2 Industry Structure

China's pharmaceutical market is highly fragmented. The biggest ten companies from home and abroad accounted for only 15% of the Chinese pharmaceutical market value in 2005(SFDA 2006e). In contrast, the top ten pharmaceutical manufacturers accounted for 50% of the global market in 2005 (EIU, 2007g). SFDA (2006f) also reported that there were about 3,500 pharmaceutical manufacturers and 12,000 medicine distributors in 2005 to compete the US$12 billion worth market. However, the number of players was expected to fall in the future due to serious manufacture requirements, strict marketing regulations, tough competitions from foreign competitors, and the industry integration in a bid to reach economy of scale. Up to 2005, China's thousands of local pharmaceutical companies accounted for 60% of the drug market value but 40% of the industry profits, while hundreds of multinational pharmaceutical firms in China accounted for 40% of market but 60% of the total profits (SFDA, 2006g).

Based on geography and market size, China' pharmaceutical market is divided into four tiers: Tier 1 markets include Shanghai, Beijing and Guangzhou, accounting for 20% of total market but almost 50% of brand-name drug market; Tier 2 markets include Nanjing, Hangzhou, Chengdu, Chongqing, Shengyang, Shenzhen and some other big cities, accounting for about 30% of brand-name market; Tier 3 markets include Tianjin, Jinan, Zhengzhou, Xi'an, Qingdao, Dalian and some other medium cities; Tier 4 markets include countless small cities, towns and countryside market. Tier 2, Tier 3, and Tier 4 together account for 80% of the market value and are expanding faster than Tier 1 markets. It is estimated that 86% market will lie out of Tier 1 cities in 2008, so the second line cities will become primary growth driver in the near future in China.

2.6.3 Generic Drug

China is certainly the biggest generic market in Asia, not only in production but also in consumption (Datamonitor, 2006k). Generic drugs dominate the market from hospitals to drug stores. China's numerous local pharmaceutical manufacturers mainly produce generics and compete on the low value products. Statistics revealed that 97% of the drugs produced by China's local companies were generics or copies of off-patented drugs, accounting for 40% of total sales revenue but mere 15% of industry profits in 2005 (SFDA, 2006h). In 2005 alone, SFDA unbelievably approved at least 10,000 generic drugs filed by local firms. The popularity of generic drug partly stems from China's unestablished remuneration system. In China, Medical Insurances only cover about 30% of its population (Ministry of Healthcare, PRC, 2007a). Most of the insured people are government officials or employees from state-owned enterprises and public sectors. Patients from rural areas and private sectors

without insurances try to choose cheap generic products to cut drug costs since they have to pay their own healthcare spending.

Compared with generic markets in western countries, China's generic industry has distinctive feature since most generic drugs in China have their own brands. Like brand name drugs in western countries, China's generic drugs are prescribed by doctors or pharmacists according to brand names instead of general names or chemical names. In China's pharmaceutical market, it is very common that one same compound could have dozens of different brand names and various prices, leading to the chaos of generic market with a lot of patients and doctors complaining the misleading drug names and confusing prices.

2.6.4 Low R&D and Patent

Pharmaceutical R&D, a process of estimated 15 years and US$ 800 million to launch a new drug in western countries, is definitely a time consuming, unpredictable and expensive process. Most China's local pharmaceuticals are not large enough to afford the huge initial investment on new drug development. What is more, a lack of effective patent protection and limitation to local market partly contribute to the extremely low R&D in China, because companies can not cover their huge spending on R&D by thereafter profits from new drug sales, which are guaranteed by international market and long-time market protection. In an effort to capture more profits at shorter period with fewer investments, local drug manufacturers rationally choose to copy off-patented drugs, instead of developing new drugs. According to SFDA (2006i), Chinese local drug companies spent mere 1.2% of their annual

sales revenue on R&D in 2005. By comparison, big pharma, such as GSK, invested more than £2.8 billion, 15.9% of its annual turnover on R&D in 2004 (GSK, 2007).

In fact, China offers several key advantages in pharmaceutical R&D, such as low labour and raw material cost, low clinical trial expense, and a large number of untreated patients with genetic variations. These variations are important indicators when determining both safety and efficacy of new drugs. After China's entry of WTO in 2001 and the introduction of international patent standards, many leading foreign pharmaceutical companies began to conduct their research and development in China. For example, GSK was reported in 2007 to build a drug discovery center in Shanghai, China. The facility would focus on developing new treatments for neurological disorders (Chemical and Engineering News, 2007, p.19-19). Novartis was also reported in 2006 to set up a research and development center in Shanghai. The center was designed to develop new cancer drugs by two paths in parallel: Traditional Chinese Medicine (TCM) and western drug discovery (Capell, 2006, p.23-23). In an attempt to build a world-class pharmaceutical industry, especially in TCM field, Chinese government is now encouraging local pharmaceutical companies to reinforce investments in R&D through direct government grants, third-party financial support and other incentives such as tax credit.

2.6.5 Pricing and Drug Bid

In China, drug manufacturers partly lose their controls of retail prices. The National Development and Reform Commission (NDRC) and the local Provincial Price Bureaus are responsible for the registration and regulation of drug retail prices, given these drugs are on

National Medical Insurance Drug List or Provincial Medical Insurance Drug List. The pricing mechanism is based upon three considerations when setting the so-called Maximum Retail Prices: purchasing prices from drug suppliers, wholesalers' or retailers' margins with 15% at most, and prices of comparable products in the market. Hospitals and drug stores have to implement the Maximum Retail Prices, and any prices above this level will be prohibited by government. In order to make drugs more affordable to the Chinese public, especially to these patients without medical insurances, the government has introduced 19 times drug price cuts since 1998. The most recent drug price reduction in Sep 2006 involved anti-cancer, antibiotic, and western generic drugs, cutting nearly 400 drugs' prices by an average percentage of 40 (HC360.com, 2007b).

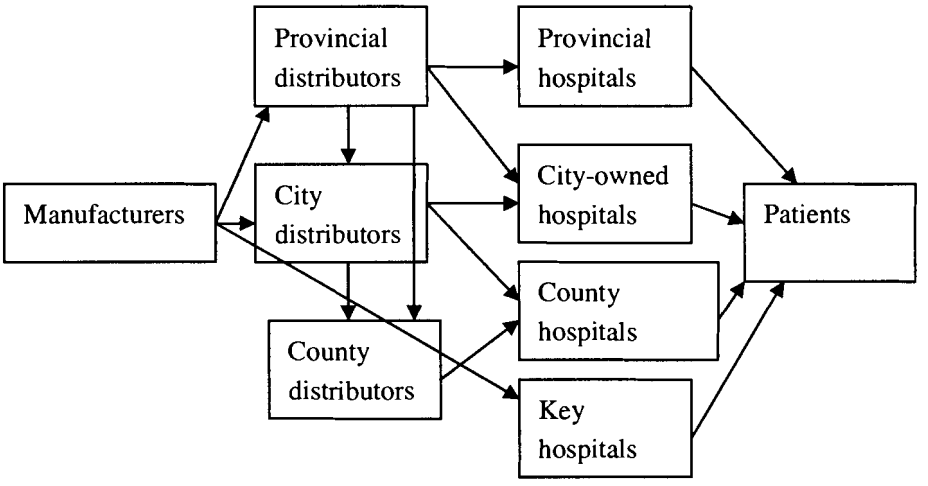
Even so, drug prices are inflated through distribution systems. It is often seen that drug prices maybe as much as ten times the production costs when the drugs reach the patients from factories because distributors and hospitals play tricks on invoices. To deal with the illegal tricks, Drug Bid was introduced since 2000. Drug Bid Committee, consisting of hospital administrations, local Healthcare Bureaus and local Medical Insurance Centers, takes charge of Drug Bid. Under the new regulation, only comparable drugs biding the lowest prices are allowed to be sold in hospitals. Drug Bid is composed of four processes: Hospitals choose target drugs in line with clinical demands; drug suppliers bid prices by internet; Drug Bid Committee evaluate the prices and make the final decisions; and hospitals purchase the in-bid drugs. Because hospitals are the main distribution channels in China, Drug Bid has huge impact on pharmaceutical companies and has also caused some new problems.

2.6.6 Complex Distribution

China's vast geography has made it very difficult to build and maintain a nationwide distribution network because of regional segmentations and local interest protection. Although a broad and efficient transportation infrastructure including railway system, highway network and third-party logistics has been built all over China, a lack of efficient distribution service and effective supply-chain management is still challenging China's pharmaceutical industry. The traditional state-owned regional distribution systems, which stem from State Planned Economy and emphasize local services, have few business connections with other regional networks, so it is challenging for pharmaceutical manufacturers to set up a nationwide supply-chain to distribute their products.

In general, China has three tiers of distribution systems: Province, City and County networks, which respectively serve provincial hospitals, city-owned hospitals and county-owned hospitals. Besides sales through distribution networks, direct marketing of drugs is allowed in China. In China, hospitals are still the main distribution channels to sell drugs to patients since more than 80% of the drugs are sold through hospitals (SFDA, 2006j), so it is urgent for pharmaceutical manufacturers to build an effective distribution network that could cover all target hospitals. Figure 4 demonstrates the supply chain: how drugs reach patients in China through complex distribution systems.

Figure 4 Supply Chain of Drugs in China



Based on author's research

2.6.7 Mixed Remuneration and Healthcare System

Up to 2003, 55% of urban residents and mere 21% of rural residents were covered by mixed Medical Insurances. The coverage represented that only 30% of population in China registered in mixed Medical Insurances (MOH, 2007b). The mixed Medical Insurance (See Table 4), only covers certain segments of Chinese population such as government officials, employees from state-owned enterprises and public sectors, and some voluntary participators. If patients are covered by National Basic Medical Insurance Scheme, local governments, by means of Medical Insurance Centers, will pay 60-80% of the total expense on drugs, given these drugs are on the National or Provincial Medical Insurance Drug List. Ministry of Healthcare, PRC (2007c) estimated that about 49% patients chose to self-medicate or not to take any medicines instead of going to hospitals for medical cares because most Chinese patients without insurances could not afford the high costs of drugs by their own out of pocket payments.

Table 4 Medical Insurances System in China, %

	Total		Urban		Rural	
	2003	1998	2003	1998	2003	1998
Basic Insurance	8.9	-	30.4	-	1.5	-
Government	1.2	4.9	4.0	16.0	0.2	1.2
Labor Insurance	1.3	6.2	4.6	22.9	0.1	0.5
Cooperative Insurance	8.8	5.6	6.6	2.7	9.5	6.6
Others	1.4	5.0	2.2	10.9	1.2	3.0
Commercial Insurance	7.6	1.9	5.6	3.3	8.3	1.4
Self payment	70.3	76.4	44.8	44.1	79.0	87.3

Source: Ministry of Healthcare, PRC, 2007

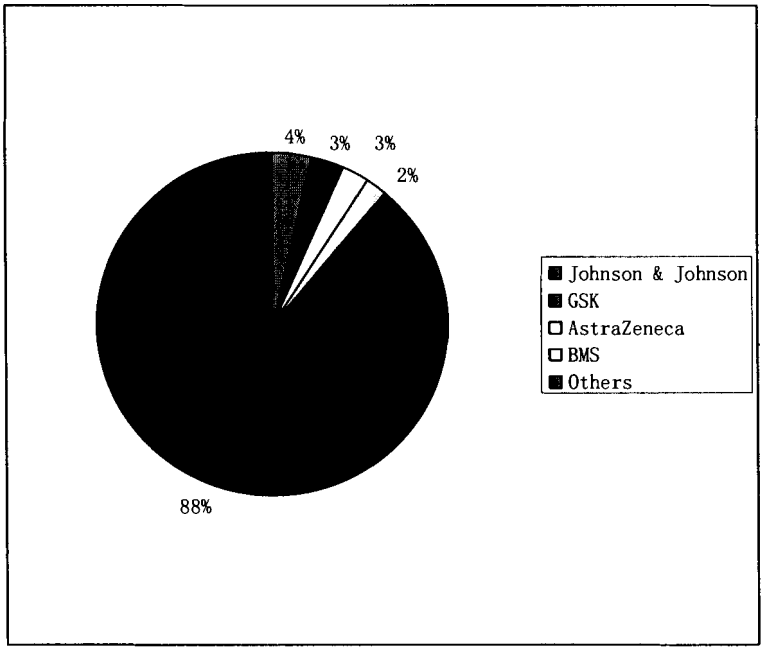
Hospital system in China can be divided into three tiers: Third Level hospitals are the largest and most sophisticated provincial or city–owned hospitals that provide advanced medical cares; Second Level hospitals are medium city-owned hospitals that provide residents general healthcare; and First Level hospitals are enterprise or school clinics that provide basic medical cares to workers or students. Ministry of Healthcare, PRC (2007d) revealed that there were 659 Third Level hospitals, 3555 Second Level hospitals and 2349 First Level hospitals in 2006. Although most hospitals in China are state-run and non-profit, many private and profit hospitals emerged in China after China's entry of WTO in 2001, and most of them were specialized hospitals with small or medium sizes.

2.6.8 MNC in China

So far, there are hundreds of foreign-invested pharmaceutical enterprises in China, and all the top 20 pharmaceutical companies in the world have set up joint ventures or wholly owned factories in China (SFDA, 2006k). GlaxoSmithKline (GSK) and Johnson & Johnson

are the first movers and the biggest winners in China's pharmaceutical industry, setting up joint ventures with Chinese partners in Tianjin and Xi'an in 1984, respectively. Other leading foreign pharmaceutical companies in China include Pfizer, Novartis, AstraZeneca, Sanofi-Aventis, Bayer, Roche and Merck. Providing brand-name products rather than generic drugs, foreign pharmaceutical companies accounted for 40% of the total market share but almost 60% industry profits in 2005 (SFDA, 2006l). The largest foreign pharmaceutical factory in China generated about US$ 400 million revenue in 2005 with EBIT of US$ 100 million (SFDA, 2006m). According to Datamonitor (2006j), the four biggest foreign pharmaceutical companies in China are Johnson & Johnson, GSK, AstraZeneca and BMS. They together accounted for nearly 10% of total Chinese market share in 2006 (See Figure 5).

Figure 5 China's Pharmaceutical Market Share in 2006



Source: Datemonitor, 2006

Multinational pharmaceutical companies not only played a critical role in manufacturing and marketing field by supplying brand name drugs and introducing Sales Representatives business model into Chinese pharmaceutical market since 1984, but also began to conduct R&D in China after 2001, taking advantage of low cost of raw materials and labours. Some news reported that leading foreign companies in China such as GSK and Novartis have already built their R&D centers in Shanghai. AstraZeneca and Roche were also reported to have plans to set up R&D facilities in Shanghai in 2006 (Chemical and Engineering News, 2007). China's low R&D cost, diverse genetic variations, and huge market potential are driving more and more foreign companies to commit R&D in China.

2.7 Summary

In summary, Asia's pharmaceutical industry is a complex, which consists of Japan's international pharmaceutical companies, India's leading generic manufacturers, China's numerous generic suppliers, and a number of multinational pharmaceutical giants. Asia's pharmaceutical market is fast growing due to its vast population, rapidly developing economy, and promoted public healthcare awareness. However, the fast growing market is highly fragmented and vulnerable, with thousands of local companies mainly competing on generics. The market is also challenging because of Asia's low per capita healthcare spending, a lack of effective IP protection, complex regulatory requirements, government interventions on prices and patents, and severe competition from local and international companies.

3 BACKGROUND OF CANCER IN ASIA

3.1 Cancer Epidemiology in Asia

Cancer is a serious medical and social problem hitting the world. According to World Health Organization (2007c), 7.6 million people died of cancer in 2005 out of total 58 million deaths worldwide. Based on projections, cancer deaths would continue to rise with an estimated 9 million in 2015 and 11.4 million in 2030 (WHO, 2007d). WHO (2007e) also said that more than 70% of all cancer deaths occur in low and middle income countries such as Asian and African countries, where resources available for prevention, diagnosis and treatments of cancers are limited or nonexistent.

Associated with heavy pollutions in Asia, the incidence of cancer has increased dramatically since Asian industrial revolution that thrived in 1980s. Asia's high cancer incidence also is in accordance with prevalent smoking, higher fat diets, and growing aging population. (Age is one of the main risk factors that lead to cancer). Asian Medical Forum (2007b) stated that number of new cases of cancer in Asia was projected to increase from 3.5 million in 2002 to 8.1 million by 2020. Cancer death rate in Asia was forecasted to rise from 112 per 100,000 people in 2005 to 163 per 100,000 in 2030 if current prevention and management strategies remain unchanged (Asian Medical Forum, 2007c). By comparison, International Agency for Research on Cancer (2007a) estimated in 2002 that cancer death rate worldwide was 137.7 per 100,000 men and 92.1 per 100,000 women. Paddock (2007) also

reported from Asian Medical Forum that of the 7 million cancer deaths worldwide in 2002, half of them were in Asia and nearly a quarter of them were in China. Cancer has been a heavy burden in China due to China's vast population, accounting for nearly 25% of world's total population, and China's relatively high cancer death rate, 144.57 per 100,000 people in 2006 (Ministry of Healthcare, PRC, 2007e).

Now, cancer is the number one cause of deaths in Asia. In China, cancer is the first major cause of deaths with a death rate of 144.57 per 100,000 urban people in 2006, accounting for 27.25% of total deaths (See Appendix 7). In Japan, 253.9 people out of 100,000 were died of cancer in 2004, accounting for 31.15% of total deaths, according to Japan Statistics (2007). In South Korea, Taiwan, Singapore, Hong Kong, Cancer is also the top killer, causing about 25-50% of total deaths. In South Korea, cancer was the cause of 27% of total deaths in 2005, with a death rate of 136 per 100,000 people (Korean Statistical Information System, 2007). In Taiwan, cancer has been one of the leading causes of death since it was responsible for 27.10% of total deaths in 2003, causing 156.01 deaths per 100,000 people (Department of Health, Taiwan, 2007). In Singapore, cancer caused 26.4% of total deaths in 2005 (Ministry of Health, Singapore, 2007a), while cancer deaths accounted for as high as 48.01% of total deaths in Hong Kong in 2006 (Census and Statistics Department, Hong Kong, 2007). Based on WHO (2007f), cancer caused 109 and 132 deaths per 100,000 people in India and Indonesia in 2002, respectively. In Thailand and Malaysia, the cancer mortality rates were respectively 129 and 139 per 100,000 people in 2002 (WHO, 2007g). Table 5 illustrates the cancer death rates of Asian main countries and areas according to above statistics.

Table 5 Cancer Death Rates of Asian Main Countries and Areas

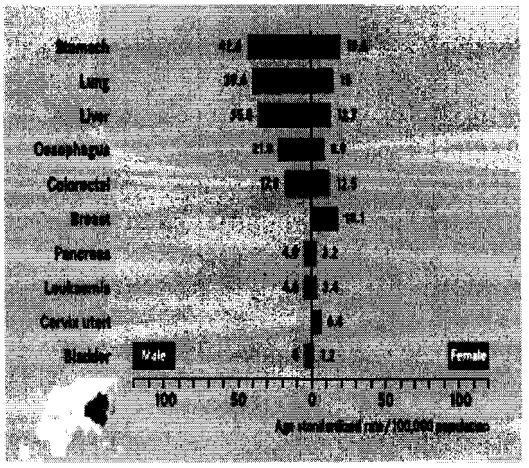
Countries and areas	Year	Death Rate 1/100,000	% of Total Deaths	Population Million, 2006
World	2002	115	n/a	6602.22
China	2006	144.57	27.25	1,321.85
Japan	2004	253.90	31.15	127.43
S Korea	2005	136	27	49.05
Taiwan	2003	156.01	27.10	22.86
Hong Kong	2006	177.30	48.01	6.98
Singapore	2005	120	26.4	4.35
Thailand	2002	129	n/a	65.07
Malaysia	2002	139	n/a	24.82
India	2002	109	n/a	1,129.87
Indonesia	2002	132	n/a	234.69

Source: Ministries of Health, Departments of Statistics, IARC, WHO, CIA Fact Book

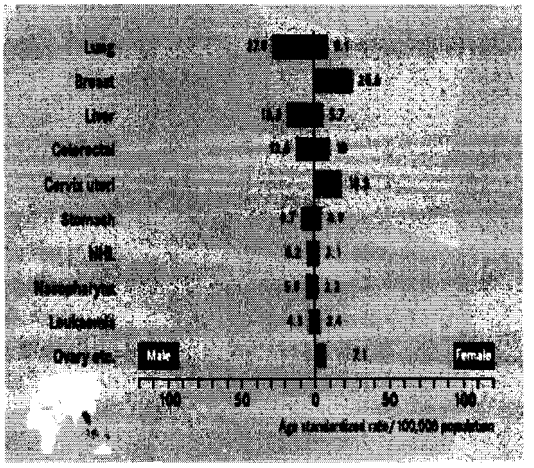
Mainly because smoking is popular in Asia among youths and males, and air quality is dramatically worsening along with industrialization, lung cancer is one of the most prevalent cancers in this region. Stomach, liver, colorectal, cesophagus, breast, cervix/uterus, and nasopharyngeal cancers are also very common in Asia. Parkin et al. (2002a) observed that China had the highest incidence rate of liver cancer and esophagus cancer in the world. They also argued that Japan had the highest rate of liver cancer in any industrialized countries, and Japan and China also had the highest rate of stomach cancer in the world (Parkin et al., 2002b, p.78-108). According to Globocan 2002 (See Appendix 8) and Yang et al. (2005a, p.243-250), lung, stomach, liver, esophagus and colorectal cancers were in sequence the most common cancers in China. Globocan 2002 database also showed that the five most common cancers in Japan were stomach, colorectal, lung, breast, and liver cancers; in India were cervix,

oropharynx, breast, escophagus and lung cancers; in Singapore were colorectal, lung, breast, stomach, and liver cancers, and in Indonesia were lung, breast, colorectal, cervix and liver cancers. Figure 6 demonstrates the incidences of cancers in Asian regions, based on IARC's World Cancer Report edited by Steward et al. (2003a). It is obvious that stomach, lung, liver and esophagus cancers dominate Eastern Asia, while lung, breast, liver and colorectal cancers are the main cancers in South-Eastern Asia. By comparison, the most common cancers worldwide are lung (12.3% of all cancers), breast (10.4%) and colorectum (9.4%), followed by stomach, liver and prostate cancers (Steward et al., 2003b). In terms of mortality rate, lung, stomach, liver and colorectum cancers are the most common cancers worldwide, respectively causing 17.2%, 11.9%, 8.7% and 8.6% of total cancer deaths (Shibuya et al., 2002, p.37).

Figure 6 Incidences of Cancers in Eastern Asia and South-Eastern Asia



Incidence of cancer in Eastern Asia.



Incidence of cancer in South-Eastern Asia.

Source: IARC, 2003

3.2 Current Treatments in Asia

Traditionally, cancer patients in this region are primarily treated with surgery, chemotherapy, radiotherapy, or more often, a combination of these treatments. Surgery is probably the most available and affordable treatment in Asia due to its economy and effect. Surgery is conducted to cut as much as cancer tissues or cancer tumors without destroy normal cells or tissues.

Chemotherapy is also a kind of popular method of cancer treatment through killing cancer cells by anti-cancer drugs. Anti-cancer drugs destroy cancer cells by stopping them from growing or multiplying. Anti-cancer drugs used in cancer chemotherapy specifically attack cancer cells that are rapidly dividing. These anti-cancer drugs are targeted at cancer cells because cancer cells spend more of their time dividing and reproducing than normal cells (National Cancer Institute, 2007a). However, normal cells can also be harmed by anti-cancer drugs, especially those that divide quickly, resulting in so-called side effects (National Cancer Institute, 2007b). Most of the cancer centres in Asia use chemotherapy for both long-term and outpatient treatments because of its economy and convenience.

Radiation therapy is another well established and mature treatment method that kills targeted cancer cells by x-rays or gamma-rays. According to National Cancer Institute (2007c), radiation therapy injures or destroys cancer cells in targeted tissues through damaging their genetic material by rays. After the genetic materials are destroyed by rays, it is impossible for these cells to continue to grow or divide. To prevent normal cells from damaging, accurate site and rational radiation dose are critical for this treatment method. Used

to treat almost every type of solid tumors, including brain, breast, lung, prostate, and stomach cancers, radiation therapy is becoming common in Asia. In 2004, China had 683 sets of x-ray Linear Accelerator and 174 sets of Head Gamma Knife, covering 5% of 13,900 hospitals (Ministry of Healthcare, PRC, 2007f). It is estimated that almost all provincial or Third Level hospitals in China have Linear Accelerator equipments and one third of Third Level hospitals in China possess Gamma Knifes.

Besides the traditional therapies for cancer, new treatments are emerging in Asia, representing an improvement of technology and therapy for cancer. These novel treatments include biological therapy or immunotherapy, which destroys abnormal cells through activating patients' immune systems by protein drugs such as vaccines; gene therapy, which prevents cancer cells from dividing through introducing genetic materials into cancer cells; hyperthermia therapy, which kills cancer cells through exposing cancer tissues to extremely high temperatures; photodynamic therapy, which destroys target cells by a combination of photosensitizer and a particular type of light; and cryosurgery, which ruins abnormal tissues through producing extreme cold by liquid nitrogen (National Cancer Institute, 2007d).

With respect to diagnostic technology, laboratory diagnosis or detection of cancer is commonly seen in Asian cancer centers. The diagnosis is based on mature technologies of histopathology, immuno-histochemistry, cytometry, angiography and polymerase chain reaction (PCR). As for scanning or imaging diagnostic technology, sophisticated and advanced equipments such as spiral computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomograph scanning (PET) are becoming available in Asian

countries. For example, China had 4,752 CT, 98 PET, and 1,110 MRI in 2004, respectively representing possession rate of 29.2%, 0.6% and 7.2% (Ministry of Healthcare, PRC, 2007g).

3.3 Remuneration in Asia

Due to high incidence of cancer and huge spending on cancer treatments, cancer has been a heavy burden on Asia. Many countries in Asia have developed various health remuneration systems to increase their healthcare capacities via both social health insurance schemes and business insurances. However, there are still significant differences among Asian countries' healthcare reimbursement systems due to different income levels and social development stages. According to World Health Report 2000 (WHO, 2003a), more than 50% industrialized or high income countries have selected universal social health insurances as their healthcare financing mechanisms, but not a single developing country had a well established social health insurance scheme so far. Asian countries can be divided into three general categories in terms of different reimbursement systems: those with well-developed social health insurance systems, those with mixed reimbursement systems, and those without effective reimbursement systems.

In China, mixed Medical Insurance covers about 30% of total people, including civil servants, employees from big enterprises and public sectors, and voluntary participators (MOH, 2007h). Like China, most countries in South-East Asia region employ mixed reimbursement systems. Mixed insurance system consists of social health insurance scheme that only covers certain segments of population, business insurance plan, and private out of pocket payments. India, Indonesia and Thailand have set up mixed health reimbursement

systems with certain percentage of coverage under social health insurance schemes (WHO, 2003b). In India, the Central Government Healthcare mainly covers 4.5 million civil servants, and the scheme of General Insurance Corporation covers about 7.2 million employees from formal companies. The two health insurance schemes in India cover less than 10% of the population and account for 17% of total medical expenditure (WHO, 2003c). In Thailand, 24% of total people are covered by national health insurance schemes called Social Security for Employee and Civil Servant Medical Benefit Scheme. The remaining 76% of population are covered by so-called the Universal Coverage (WHO, 2003d).

Besides China South-Eastern Asia, many emerging countries and areas in Asia such as Singapore, Hong Kong and Taiwan also introduced mixed health insurances. For example, healthcare in Singapore is financed by a combination of employee medical benefits, compulsory savings in the form of Medisave, healthcare insurance such as Medishield, government-aid programs such as Eldershield and Medifund, and out-of-pocket payments for private hospitals and clinics (Ministry of Health, Singapore, 2007b).

Japan and South Korea have built well-established and universal social health insurance schemes. Japan has set up universal medical care insurance system since 1961. Under the national insurance scheme, patients are free to select medical institutions and all citizens are granted to receive free medical cares (Ministry of Health, Japan, 2007). Since 1989, almost 96% of both urban and rural Korean people have been covered under the mandatory social health insurance system. The remaining 4% Korean people are covered by Medical Aid Program for the poor (WHO, 2003e).

3.4 Summary

In Asia, cancer has become the main cause of deaths and almost half of world's cancer deaths happened in Asia. Asia's high cancer incidence is in accordance with heavy pollutions, changing age structure, and westernized diets and lifestyles. The most common cancers in Asia are stomach, lung, liver, colorectal, cesophagus, and breast cancers. Cancer has been a heavy social and economic burden in Asia because of cancer's high death rate and huge spending on its treatments. Although treatments such as surgery, radiotherapy, and chemotherapy can prolong patients' lives and improve their qualities of life, most cancers ultimately cause deaths when extending to other organs. Under current remuneration systems, many cancer patients in Asia choose not to go to hospitals for medical cares because they can not afford the expensive treatments, relying on their own out of pocket payments.

4 ASIA'S CANCER MARKET STUDY

4.1 Asia's Brain Cancer Drug Market

4.1.1 Knowledge of Brain Cancer

The brain is the centre of memory, thoughts and emotion, as well as a control site of many body processes such as behaviour and speech. Neurons are the most important cells within brain, generating electrical signals which determine all the functions of brain including thought, memory, emotion, speech and movement. Unlike other types of cells that can grow and divide, neurons do not divide after birth so that they rarely develop into cancers (American Cancer Society, 2007a). Supporting and nourishing neurons, Glial cells are the main brain cells that can develop into tumors, called gliomas, which accounts for 42% of all brain tumors and 77% of total malignant tumors. The main type of glioma is astrocytoma, accounting for 35% of all brain tumors. Astrocytoma mainly consists of glioblastoma multiforme and anaplastic astrocytoma, which make up about two-thirds of all astrocytomas and are the most common malignant brain tumors of adults (ACS, 2007b).

Most brain cancers are secondary tumors, which extend from cancers that started somewhere else in the body such as lung or breast, and then spread to the brain. Primary brain cancer is malignant brain tumors that start in the brain. Primary brain tumors can start in any of the different types of tissues or cells within the brain or spinal cord, of which Glial cells are most common. Unlike other cancers, primary brain tumors rarely metastasize to distant organs.

They cause damages because they spread locally and destroy normal brain tissues in the place where they arise. With a few exceptions, primary brain tumors are never benign because they grow in such a vital area of body that they can cause severe damages even if they do not extend elsewhere. Unless it is possible to completely remove brain or spinal cord tumors, they will continue to grow and eventually lead to cancer deaths (ACS, 2007c).

Brain tumors may be treated by surgical removal, radiation therapy, chemotherapy, or more often a combination of treatments (ACS, 2007d). In most cases, the first step is surgical removal of tumor as much as possible while keeping safe without destroying normal tissues. However, main brain tumors such as anaplastic astrocytomas or glioblastomas are not cured by surgery because cells from the tumors get too far into the normal surrounding brain tissues (ACS, 2007e). Those brain tumors that are not cured by surgery are treated with radiation to kill remaining cancer cells. Radiation treatment may be useful for brain tumors that are in locations where surgical resection would damage essential tissues or when the patient's condition does not permit surgery (ACS, 2007f). Systemic chemotherapy uses anti-cancer drugs that are given by IV or taken by mouth. However, for some types of brain cancers, chemotherapy is limited due to the blood-brain barrier. Although malignant tumors such as astrocytomas can disrupt the blood-brain barrier, the disruption may not be complete (ACS, 2007g). Advanced treatments may prolong survival, but most malignant brain tumors are not curable, so a significant unmet medical demand exists for a curable solution. In an attempt to fight primary brain cancers, PRX321, developed by Protox, is expected to have potential of treating recurrent malignant gliomas such as glioblastoma multiforme and anaplastic astrocytoma.

4.1.2 Market Study

In Asia, brain cancer is relatively a kind of low incidence rate cancer, compared with other cancers. For example, the Age Standardized Rate (ASR) of brain cancer in China was 4.2 per 100,000 people for male and 3.1 per 100,000 for female in 2000, and was forecasted to grow to 4.4 for male and 3.3 for female in 2005 (Yang et al., 2005b, p.243-250). Compared with stomach (41.9 per 100,000 for male and 19.5 for female in 2000), liver (38.9 for male and 14.5 for female in 2000), lung (43.0 for male 19.1 for female in 2000), esophagus (27.6 for male and 12.1 for female in 2000) and breast cancers (19.9 per 100,000 in 2000), brain cancer is relatively rare in China (Yang et al., 2005c, p.243-250).

The ASR of brain cancer worldwide was 3.7 per 100,000 for male and 2.6 per 100,000 for female in 2002 (Parkin et al., 2002c, p.78-108). According to IARC's Cancer Incidence in Five Continents, Vol. VIII, edited by Parkin (2003a), the ASR of brain cancer in 2002 was 3.8 per 100,000 people for male and 2.9 for female in Hong Kong, and 3.8 for male and 2.8 for female in Taiwan. Based on Globocan 2002 database released by IARC (2007b), the ASR of brain cancer in China was 3.9 per 100,000 people for male and 2.8 for female; in Japan, 2.4 and 1.8; in Korea, 3.3 and 2.6; in Indonesia, 1.4 and 0.8; in Malaysia, 2.4 and 1.8; in Singapore, 2.6 and 2.2; in Thailand, 2.2 and 2.0; in Malaysia, 1.8 and 2.4; and in India, 2.6 and 1.6.

Table 6 shows the incidence of brain cancer in Asia based on Parkin (2003b) and Globocan 2002, representing the possible market capacity for PRX321 for the treatment of brain cancer.

Table 6 Incidence of Brain Cancer, ASR per 100,000, 2002

Countries and areas	Male	Female	Population Million, 2006
Hong Kong	3.8	2.9	6.98
Taiwan	3.8	2.8	22.86
China	3.9	2.8	1,321.85
Japan	2.4	1.8	127.43
Korea	3.3	2.6	49.05
Singapore	2.6	2.2	4.35
Thailand	2.2	2.0	65.07
Malaysia	1.8	2.4	24.8
Indonesia	1.4	0.8	234.69
India	2.6	1.6	1,129.87
World	3.7	2.6	6602.22

Source: IARC, Globocan of IARC and World Fact Book, 2007.

In general, brain cancer is a kind of comparatively low incidence rate cancer worldwide, but Cumulative risk of brain cancer in Eastern Asia is relatively high, especially in Greater China where brain cancer has higher incidence than the rest of Asia (See Table 6). Considering Eastern Asia's huge population, well-established remuneration systems in Japan and Korea, and some highly developed economies such as Japan, Korea, Hong Kong, and Taiwan, the market potential for brain cancer drugs such as PRX321 should be encouraging in Asia, at least in Eastern Asia.

4.1.3 Competition

Since PRX321 is a kind of anti-cancer drug, it is understandable that the biggest competition for PRX321 comes from surgery therapy and radiation therapy that are main

treatments for brain malignant gliomas. Chemotherapy is limited for the treatment of brain cancer due to the distinct blood-brain barrier. Blood-brain barrier prevents the anti-cancer drug entering the brain, and therefore killing brain cancer cells. Although PRX321 targets malignant gliomas such as glioblastoma multiforme and anaplastic astrocytoma that can disrupt the blood-brain barrier, the disruption may not be complete enough to result in brain cells' well response to anti-cancer drugs.

With respect to anti-cancer drug, Temodar (Temozolomide), supplied by U.S. based Schering-Plough, is one of the main competing products for PRX321. Schering-Plough is one of the Big Pharmas in the world, recorded sales revenue of US$10.6 billion in 2006 with net income of US$1.5 billion (See Appendix 9). It currently employs 33,500 worldwide and sells its products to more than 120 countries (Schering-Plough, 2007a). In Asia, Schering-plough has extended business network, operating in China, Japan, Hong Kong, India, Indonesia, Malaysia, Singapore, Thailand, and Taiwan (Schering-Plough, 2007b). Temodar is a kind of anti-cancer drug that prevents cancer cells from dividing by inhibiting DNA replication. In 2005, Temodar was approved as a landmark anti-cancer drug by FDA for the treatment of newly diagnosed glioblastoma multiforme, the most prevalent form of malignant brain gliomas. In fiscal year of 2006, Temodar capsule recorded global net sales of US$703 million, representing an increase of 20% over previous year (Schering-Plough, 2007c). So far, most of Temodar's revenue was generated in U.S. and Europe. In July 2006, Temodar was approved in Japan for treating malignant brain gliomas, with a new brand name as Temodal. It is not legally sold in Asian market except Japan, but Temodal is in processes for approvals in some

Asian countries such as China. The current situation of Temodal in Asian market gives PRX321 a possible business opportunity.

Another important competing product is CeeNU (Lomustine), a kind of generic anti-cancer drug that is widely used for the treatment of brain cancer. Known as alkylating agent, lomustine stops the growth of cancer cells by alkylateing and crosslinking DNA, thereby inhibiting DNA and RNA synthesis. Lomustine is lipophilic and therefore can cross the blood-brain barrier. Lomustine is also the most available brain cancer drug in Asian market due to its long-history use and economy. Unlike Temodar and Lomustine, which are chemical compounds, PRX321 is a kind of naturally occurring protein toxin. If PRX321 could be proved with fewer side-effects in clinical trials, the market potential for PRX321 is promising in Asia, given the huge population and relatively high incidence of bran cancer.

According to PHRMA (2007a), there were 27 new brain cancer drugs in clinical trials in U.S. in 2006, including Gliatak, Cereport, Advexin, Azixa and Cervene. Table 7 extracts some brain drugs in clinical trials, based on PHRMA. It is thinkable that some of them will enter Asian market in the future after gaining approvals from FDA, and therefore create competition in Asian market.

Table 7 Part Brain Cancer Drugs in Clinical Trials in 2006

BRAIN CANCER

Product Name	Sponsor	Indication	Development Stati
Cerepro™	Ark Therapeutics *London, England*	glioma	Phase I completed
cilengitide	Merck KGaA *Darmstadt, Germany* Scripps Research Institute *La Jolla, CA*	glioblastoma	Phase II www.merck.de
Corlux™	Corcept Therapeutics *Menlo Park, CA*	(see also prostate, other)	in clinical trials (650) 327-3270
Cotara™	Peregrine Pharmaceuticals *Tustin, CA*	glioblastoma (see also colorectal)	Phase III (714) 508-6000
		glioma	Phase II (714) 508-6000
DCVax®-Brain®	Northwest Biotherapeutics *Bothell, WA*	glioblastoma	Phase II (425) 608-3000
DTI 015	Direct Therapeutics *Redwood City, CA*	glioblastoma (see also liver)	Phase II (914) 696-7700
efaproxiral	Allos Therapeutics *Westminster, CO*	gliobastoma (see also lung, other)	Phase II (303) 426-4731

Source: 2006 Report: Medicine in Development for Cancer, PHRMA.

4.2 Asia's Prostate Cancer Drug Market

4.2.1 Knowledge of Prostate Cancer

The prostate mainly consists of gland cells that secrete fluid, which is added to semen to protect and nourish sperm cells in semen. 99% of prostate cancers are developed from gland cells with pre-cancerous conditions called prostatic intraepithelial neoplasia (PIN) and atypical small acinar proliferation (ASAP) (American Cancer Society, 2007h). Unlike other cancers that can grow and extend quickly, most prostate cancers grow very slowly. In fact, 70% to 90% of the men in North America had prostate cancer by age 80, but in many cases, neither they nor their doctors even knew they had prostate cancer (ACS, 2007i).

Unlike other kinds of cancers that are mainly diagnosed by advanced scanning or imaging technology, prostate cancer could be diagnosed by traditional laboratory technology, called prostate biopsy (ACS, 2007j). If certain symptoms or the results of early detection tests

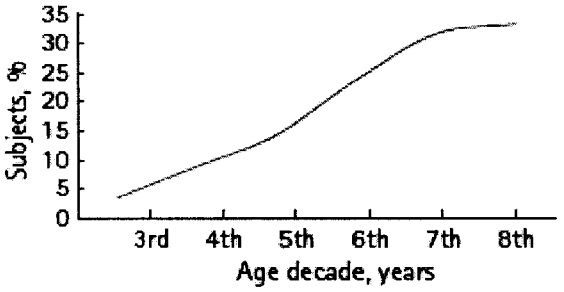
such as prostate-specific antigen (PSA) blood test or digital rectal exam (DRE) suggest prostate cancer, prostate biopsy will be conducted to diagnose prostate cancer (ACS, 2007j). Prostate cancer can be graded from 1 to 5, based on the degree of severity. Because prostate cancer often grows very slowly, some patients, especially those who are older or have other serious health problems, may never need treatment for their prostate cancer. Instead, an approach known as expectant management or watchful waiting, which involves closely monitoring the cancer without active treatment, maybe recommended if prostate cancer is expected to grow very slowly without causing any symptoms, or small enough to contain within one area of the prostate (ACS, 2007k).

Besides radical prostatectomy surgery, radiation therapy and chemotherapy, other treatments such as hormone therapy and cryosurgery are also used to treat prostate cancer. Hormone therapy is also called androgen deprivation therapy (ADT). The goal of ADT is to reduce the levels of the male hormones, called androgens. Androgen can stimulate prostate cancer cells to grow, so lowering androgen levels could make prostate tumors shrink or grow more slowly (ACS, 2007l). However, hormone therapy is a kind of conservative treatment and does not cure prostate cancer. Cryosurgery is sometimes used to treat localized prostate cancer through freezing then destroying tumors. In this approach, very cold nitrogen gases are passed through the needles that are placed through the skin between the anus and scrotum by transrectal ultrasound technology. Nitrogen gases create ice balls that destroy the localized cancerous prostate glands (ACS, 2007m).

4.2.2 Market Study

Age is one of the strongest risk factors for prostate cancer. Prostate cancer is very rare among men before the age of 40, but the incidence rises rapidly after the age of 50. About two thirds prostate cancers are found in men over the age of 65 (ACS, 2007n). Figure 7 demonstrates the relationship between age and incidence of prostate cancer.

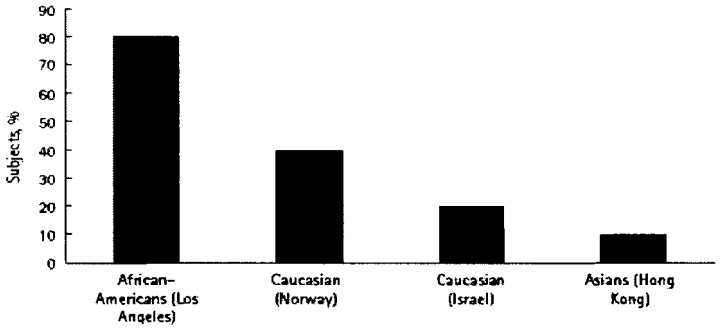
Figure 7 Worldwide Incidence of Prostate Cancer According to Age, %



Source: British Journal of Urology, 2004

The incidence rate of prostate cancer also has tight relationship with race and nationality, besides age. According to ACS (2007o), prostate cancer occurs more often in African-American men than in men of other races. Prostate cancer is the most common cancer, along with skin cancer, in American men. Behind lung cancer, Prostate cancer is also the second leading cause of cancer deaths among American men, accounting for about 9% of cancer-related deaths in men (ACS, 2007p). With respect to nationality, prostate cancer is more common in North America, Northwestern Europe, Australia, and on Caribbean islands. It is less common in the rest of the world, especially in Asia. Figure 8 illustrates the racial difference of prostate cancer prevalence, according to British Journal of Urology (2004).

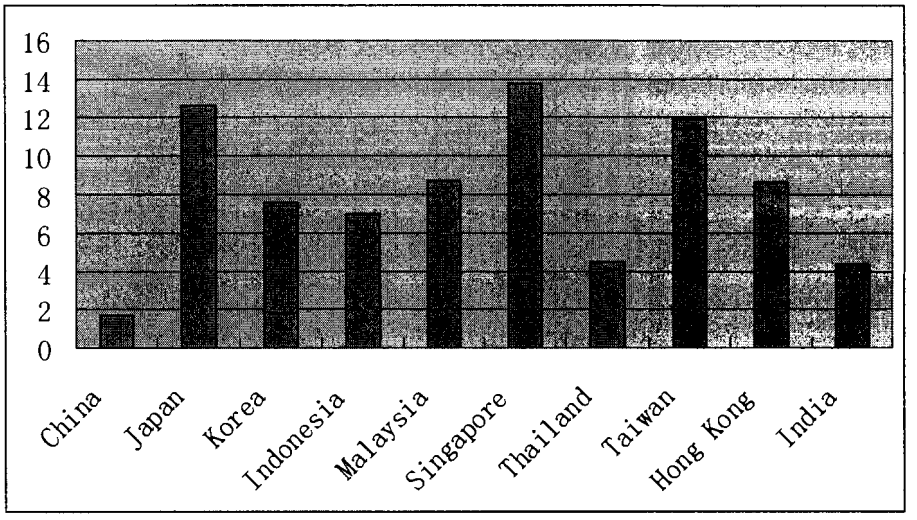
Figure 8 Racial Difference in Incidence of Prostate Cancer, Age>70



Source: British Journal of Urology, 2004

According to Globocan 2002, in 2002, the age standardized incidence rate (ASR) of prostate cancer was 1.7 per 100,000 men in China, 12.6 in Japan, 7.6 in Korea, 7.0 in Indonesia, 8.7 in Malaysia, 13.8 in Singapore, 4.4 in India and 4.5 in Thailand. Based on IARC's Cancer Incidence in Five Continents, Vol. VIII, edited by Parkin (2003c), the ASR of prostate cancer in 2002 was 11.9 per 100,000 men in Taiwan and 8.6 in Hong Kong. By comparison, the ASR of prostate cancer was 124.8 per 100,000 men in U.S., and 25.3 per 100,000 men worldwide in 2002 (IARC, 2007), representing a huge difference from Asia. Figure 9 shows the incidence rates of prostate cancer in Asian countries and areas. The incidence rates, in combination with male population, represent Asian market potential for PRX302. From the figure 9, Japan, Singapore, Taiwan and Hong Kong are high risk areas for prostate cancer with relatively high incidence rates, and China has the lowest prostate cancer incidence rate in Asia.

Figure 9 Incidence of Prostate Cancer in Asia, ASR per 100,000, 2002

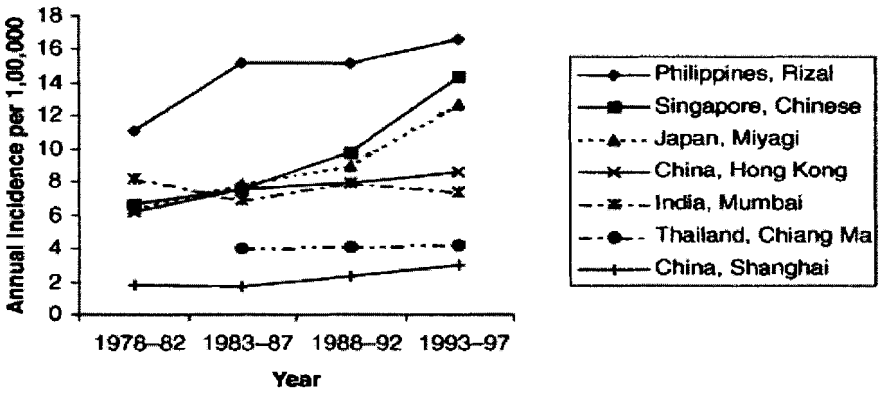


Source: Globocan 2002, IARC, 2003

Asian prostate cancer market seems unattractive due to extremely low incidence of prostate cancer compared with world level. However, there has been a recent trend in Asia towards increasing incidence of prostate cancer, with some low risk regions reporting more rapid rises than high risk western countries (Sim et al., 2005a, p.834-845). Sim et al. (2005b) observed that the ASR of prostate cancer increased by 40-118% in most of the indexed sites except India and Thailand over a 20 years period from 1978 to 1997 (See Figure 10). Although the absolute value of the ASR in Asia was still not comparable to that in North America and North Europe, the percentage changes of ASR in many Asian countries were reported quite similar to high-risk countries. Sim et al. (2005c) also reported that the incidence rate of prostate cancer increased dramatically with age. The rapid increase of ASR in Asia is attributed to aging societies, promoted public health awareness, improved scanning technologies, and westernized diets and lifestyles. Considering Asia's huge ageing population

and rapidly increasing ASR of prostate cancer, Asian prostate cancer drug market is still considerable for PRX302.

Figure 10 ASR Change over Time in Seven Selected Asian Regions



Source: European Journal of Cancer

4.2.3 Competition

Prostate cancer in Asia is mainly treated with surgery and hormone therapy instead of anti-cancer drug chemotherapy. In Asia's prostate cancer drug market, the biggest and strongest competitors for Protox are Takada and AstraZeneca.

Takeda Pharmaceutical Company Limited, the largest pharmaceutical company in Japan and one of the leading pharmaceutical companies in the world, generated total value of US$11 billion during the fiscal year of 2006, an increase of 7.7% on previous year (See Appendix 10). As a multinational pharmaceutical company, Takeda attains 49.3% of total revenues in overseas markets and has subsidiaries and affiliates in U.S., Europe and Asia (Takada, 2007a). In Asia, Takeda has operations in China, Singapore, Taiwan, Indonesia, Thailand, and Philippines (Takada, 2007b). Takeda produces and markets a kind of luteinizing hormone-releasing hormone analogue, called Lupron Depot, which is used for

hormone treatment of prostate cancer. Lupron Depot is the best selling luteinizing hormone-releasing hormone analogue in the world and widely used in Asian market.

AstraZeneca International is one of the top ten pharmaceutical giants in the world, with sales revenue of US$ 26.5 billion and an operation profit of US$ 8.2 billion in 2006 (AstraZeneca, 2007a). AstraZeneca currently employs over 66,000 people and operates at more than 100 countries worldwide (AstraZeneca, 2007b). Asia is one of its key markets after Europe and U.S. In Asian market, AstraZeneca operates in 28 countries including all main countries and areas, and markets two prostate cancer drugs: Casodex and Zoladex (AstraZeneca, 2007b). Casodex, which is only available in China and Japan, is an anti-androgen drug for hormone treatment of prostate cancer. Zoladex, sold around Asia, is the second largest selling luteinizing hormone-releasing hormone analogue in the world, after Lupron Depot (Astrazeneca, 2007c).

According to PHRMA (2007b), 79 new prostate cancer drugs were in clinical trials in U.S. in 2006. It is possible that some of them will become competing products in Asian market in the future. Table 8 extracts some new prostate cancer drugs in U.S., based on PHRMA.

Table 8 Part Prostate Cancer Drugs in Clinical Trials in 2006

PROSTATE CANCER

Product Name	Sponsor	Indication	Development Status
Abegrin™	MedImmune *Gaithersburg, MD*	(see also skin)	Phase II (301) 398-0000
adecatumumab	Serono *Rockland, MA*	(see also breast)	Phase II (800) 283-8088
AGS-PSCA	Agensys *Santa Monica, CA* Merck *Whitehouse Station, NJ*		Phase I (310) 820-8029 (800) 672-6372
Amplimexon®	AmpliMed *Tucson, AZ*	(see also breast, lung, multiple myeloma, pancreatic, skin)	Phase I (520) 529-1000
androgen receptor antagonist	Bristol-Myers Squibb *Princeton, NJ*		Phase I (212) 546-4000
AP 23573	ARIAD Pharmaceuticals *Cambridge, MA*	(see also breast, leukemia, ovarian, sarcoma, solid tumors, other)	Phase II (617) 494-0400
AT 101	Ascenta Therapeutics *San Diego, CA*	(see also leukemia, lymphoma, solid tumors)	Phase II (858) 436-1200
ATRA-IV®	Antigenics	(see also kidney, leukemia,	Phase II

Source: PHRMA, 2007

4.3 Asia's BPH drug Market

4.3.1 Knowledge of BPH

The prostate stays about the same size in adults as long as male hormones keep constant, but excessive male hormones may cause prostate to enlarge. In older men, the inner part of the prostate around the urethra may continue to grow and become enlarged, generating a condition called benign prostatic hyperplasia (BPH). BPH can cause problems with urinating because it adds extra pressure on the urethra (ACS, 2007q). BPH's symptoms include the need to frequently empty the bladder and the sensation that the bladder is not empty. BPH can also cause a weak urinary stream, dribbling of urine or difficulty to urinate (American Urological Association, 2007a). BPH sometimes leads to bladder damage, urological system infection, blood in the urine, and even kidney damage (AUA, 2007b). BPH can be diagnosed by laboratory technologies such as prostate biopsy. In order to help assess

the severity of such symptoms, the American Urological Association (AUA) developed BPH Symptom Score Index to evaluate BPH disease, ranging from mild to severe (AUA, 2007c).

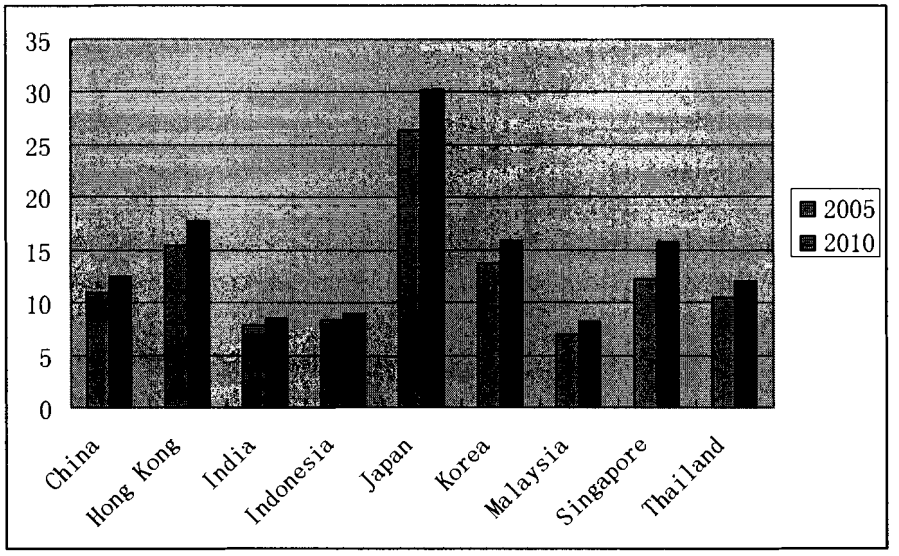
BPH is treated according to severity of symptoms. Currently, the main treatments include watchful waiting, medication treatment, minimally invasive treatment and surgery (AUA, 2007d). Watchful waiting is recommended as the first option for men who have mild symptoms and do not feel particularly troublesome. Drug treatment is the most common option for controlling moderate symptom. There are a number of different prescription drugs for the treatment of BPH. The available drugs include alpha-blocker used to relax smooth muscle of prostate and bladder neck, and 5-alpha reductase inhibitor used to shrink the enlarged prostate by lowering the level of male hormone (AUA, 2007e). Medication treatment can reduce symptoms in some but not for all men with BPH, and works slowly. Minimally invasive treatment refers to catheterization to drain urine; holmium laser enucleation of prostate to vaporize additional prostate tissues; interstitial laser coagulation; prostatic stent to open urethra; and TUMT or TUNA to heat and vaporize enlarged prostate tissues (AUA, 2007f). Surgery often does the best job for relieving symptoms, but has more risks than other treatment methods. Surgery treatment includes TURP, the most common surgical procedure to remove prostate's innermost core; and TUIP, which is committed to cutting extra prostate tissues and opening prostatectomy (AUA, 2007g). Sometimes, herbal therapy and combination therapy are used to relieve BPH symptoms.

4.3.2 Market Study

Age is the main risk factor for BPH. AUA (2007h) estimated that approximately 50% of men between the ages of 51 and 60, and up to 90% of men over the age of 80 have BPH symptoms (AUA, 2007i), so BPH disease is very common among men above age 60. Unlike prostate cancer, BPH has no strong racial and regional difference, although African American still have higher incidence than other people. Epidemiology researches worldwide provide compelling evidences that the incidence of histologic BPH is similar throughout the world (Roehrborn et al., 2002a, p.1297-1360). Roehrborn (2005a) also argued that the incidence of BPH is approximately 10% for men in their 30s, 20% for men in their 40s, 50% to 60% for men in their 60s, and 80% to 90% for men in their 70s and 80s. No doubt, most men will suffer some symptoms consistent with BPH if they live long enough.

With the population trend towards aging in Asia, BPH has been a very common disease among Asian men too. Gu (2000) observed that the age standardized incidence rate of BPH in Beijing, China was ranged from 16.1% to 18.7% in 1997. Normally, percentage of people aged above 60 is adopted as a measure factor for incidence of BPH. According to UN common database (2007), the percentage of population aged 60+ in China was 10.9 in 2005, and expected to grow to 12.5 in 2010; in Hong Kong, 15.4 in 2005 and 17.7 in 2010; in India, 7.9 and 8.5; in Indonesia, 8.4 and 8.9; in Japan, 26.3 and 30.2; in Korea, 13.7 and 15.9; in Malaysia, 7.0 and 8.1; in Singapore, 12.2 and 15.8; and in Thailand, 10.5 and 12.0. Figure 11 demonstrates percentage of group aged 60+ in Asian countries and areas. Based on the similar high prevalence of BPH worldwide and Asian population's age structure, the Asian market for BPH drugs such as PRX302 is really exciting.

Figure 11 Percentage of Population Age 60+ in Asian Countries and Areas



Source: United Nations, 2007

4.3.3 Competition

The promising Asian BPH market attracts a pile of BPH drug suppliers, including local and multinational pharmaceutical companies, so the competition for PRX302 will be very tough in Asian market in the future.

Astellas Pharma Inc., a local competitor for Protox, is regarded as one of the biggest pharmaceutical companies in Japan. Astellas recorded sales revenue of 7.8 billion during the fiscal year of 2006 along with net income of US$1.1 billion, an increase of 26.7% over 2005 (See Appendix 11). Astellas is also a multinational company with business operations in Asia, Europe and U.S. In Asia, Astellas operates in China, Hong Kong, Korea, Taiwan, Thailand and Philippines (Astellas, 2007a). Astellas mainly markets BPH drug called Prograf and a kind of immunosuppressant called Harnal in Asia (Astellas, 2007b). Prograf, also named Flomax in U.S., is a kind of tamsulosin hydrochloride, which belongs to alpha blockers. It is

widely used to relax smooth muscle so as to relieve BPH symptoms by blocking alpha receptors in certain areas of the body such as prostate grand.

Marketing Proscar, a kind of 5-alpha reductase inhibitor used to lower male hormone to solve BPH problems, Merck is another strong competitor for Protox in Asian BPH market. Merck & Co., Inc. is a global leading and research-driven pharmaceutical company, which discovers, develops, manufactures and markets medicines and vaccines to address unmet medical needs (Merck, 2007). In fiscal year of 2006, Merck recorded sales of US$ 22.64 billion and a net income of US$ 4.43 billion (See Appendix 12). Merck currently operates in 120 countries with 70,000 employees, 31 factories and 11 major research centers worldwide (Pharmaceutical Business Review, 2007). Merck has very long history of operations in Asia, in the name of Merck Sharp & Dohme (MSD). So far, MSD operates in 10 Asian countries and areas, including China, Japan, India, Korea, Singapore, Hong Kong, Taiwan, Malaysia, Thailand, and Indonesia (MSD, 2007). Recognized as a kind of golden standard for BPH treatment, Proscar is widely used and well known in Asia.

Table 9 lists some other competitors and their products in Asian BPH market, besides Aetellas and Merck.

Table 9 Competition in Asian BPH Market

Company	Product	Mechanism
Pfizer	Gardura	Alpha-blocker
Sanofi-Aventis	Uroxatral	Alpha-blocker
GSK	Avodart	5-alpha reductase inhibitor
Kangenbei	Qianlikang	Herbal therapy

4.4 Summary

The Asian cancer market is boosting recently in accordance with high incidence rate of cancer, reforming remuneration systems, and improving diagnostic technologies. With respect to specific cancer market, the brain cancer market in Asia is relatively cold due to brain cancer's comparatively low incidence rate worldwide, while the prostate cancer market in Asia is much less lucrative than in U.S. and North Europe because Asia has extremely low incidence rate of prostate cancer. As for Asia's BPH market, the market potential is huge because of Asia's vast aging population and the high incidence rate of BPH around the world. However, Asia's BPH market is also well established, with tough competition from dozens of current drugs and many non-drug treatments.

5 CONCLUSION AND RECOMMENDATIONS

5.1 Summary of market study

In summary, the Asian pharmaceutical market is fast growing and really lucrative for pharmaceutical companies because of Asia's vast population, rapidly increasing incomes and gradually aging societies. As a result of fast growth with a CAGR of 4.7% over the five years period from 2001 to 2005, the Asian drug market has become one of the main components of world market and is expected to be the biggest pharmaceutical market in two decades.

However, the rapidly developing market is highly fragmented and vulnerable, with thousands of local generic companies competing against hundreds of multinational companies. Asian pharmaceutical market is also challenging due to Asia's low per capita healthcare spending, a lack of effective IP protection, complex regulatory requirements, government interventions on prices and patents, and severe competition from local and multinational companies.

Associated with vast aging population and fast developing economies, the Asian cancer market is boosting recently in accordance with high incidence rate of cancer, reforming remuneration systems, and promoted public healthcare awareness. The market trend will continue because Asia's high cancer incidence has tight relationships with heavy pollutions along with industrialization, improved scanning tools, change of age structure, and westernized diets and lifestyles. In general, the Asian cancer market is attractive and lucrative

for pharmaceutical companies. However, the market is also risky with severe competition not only from both local and multinational companies, but also from both existing cancer drugs and non-drug treatments for cancer.

5.2 Internal Analysis

Protox was founded in 2002 based on Dr. Tom Buckley's research on protein toxins at the University of Victoria. Dr. Tom Burckley is an internationally recognized expert on channel-forming proteins. At present, the company is managed by an experienced team, which has proven experience in new drug development, conducting clinical trials, and building effective business partnerships. Besides, Protox takes credit for a convincing Scientific Advisory Board with members having outstanding academic records and prominent scientific accomplishments. In general, the company's organization is small, efficient, innovative, close to leading edge of biotech technology, and staffed by the best scientists and experienced management team.

Protox's strategy is to develop novel targeted therapeutics for cancers by engineering naturally occurring anti-cancer toxins. Protox has already established its competitive advantages by engineering toxins through its unique technology platforms, INxin™ and PORxin™. The engineered versions of naturally occurring toxins, PRX321 and PRX 302, are potent and targeted therapeutics for cancer with fewer side effects than current drugs. PRX321 and PRX302's distinctive modes of action ensure that they specifically bind and kill cancer cells so as to reduce the possible damages to normal cells and tissues.

However, it is uncertain that Protox's clinical trials will reach the expected endpoints since Protox so far has not finished all the clinical trials required by FDA.

As an early-stage biotech company, Protox is dedicated to developing novel cancer drugs, instead of expanding downstream to sales and marketing. So far, Protox does not have sales and marketing capabilities and therefore has no sales revenue. The company is financed by equity investments such as seed capital, VC capital and IPO. A lack of marketing capability and additional funding affects Protox's ability to develop and commercialize its novel products. To obtain extra funding and take advantage of big companies' sales and marketing capability, Protox is looking for potential partners.

Table 10 summarizes the SWOT analysis of Protox, combining the results of market study with internal analysis.

Table 10 SWOT Analysis of Protox

Strengths	**Weaknesses**
- Experienced management team - Convincing scientific advisors - Unique technology platforms - Fewer side-effects due to distinctive modes of action - Small, efficient and innovative organization	- No sales and marketing capability - No sales revenue to support the company - No effective partnerships - Efficacy and safety uncertainty - Cancer market is a well-established market with tons of existing drugs.
Opportunities	**Threats**
- Fast growing Asian pharmaceutical market - Vast aging population and westernized lifestyles - Increasing per capita income - High cancer prevalence - Promoted healthcare awareness - Improving scanning technologies	- Tough competition from local and multinational drug companies - Competition from non-drug treatments - Complex regulatory requirements - Extremely low per capita healthcare spending - Government interventions on prices and patents - IP protection challenge

5.3 Recommendations

In Asia, brain cancer is a kind of low incidence rate cancer compared with other kinds of cancers. According to Globocan 2002, the ASR of brain cancer in China was 3.9 per 100,000 men and 2.8 per 100,000 women in 2002 (IARC, 2007d). In contrast, the ASR of lung cancer in China was 42.4 per 100,000 men and 20.2 per 100,000 women in 2002, and the ASR of stomach cancer was 41.4 and 19.2, respectively (IARC, 2007e). In spite of the low incidence of brain cancer worldwide, many Eastern Asia countries such as China, Japan and South Korea have higher ASR than world level of 3.7 per 100,000 men and 2.6 per 100,000 women in 2002 (IARC, 2007f). Considering Eastern Asia's vast aging population, amazing economies, huge existing pharmaceutical market, and relatively well-established remuneration systems, the brain cancer market is considerable for anti-cancer drugs such as PRX 321. The competition for brain cancer drugs is mainly from surgery therapy and radiation therapy due to blood-brain barrier, which prevents anti-cancer drugs entering cancer cells. Some generic suppliers and Big Pharmas such as Schering-Plough also provide anti-cancer drugs, which are said to cross blood-brain barrier. If PRX321 can effectively break through the brain blood barrier and specifically kill cancer cells, it will be rewarding for Protox to explore Asian brain cancer market.

The prostate cancer market in Asia is much less attractive than in other regions, especially in U.S. and North Europe, because Asia has extremely low incidence rate of prostate cancer. Prostate cancer is one of the most common cancers in western countries, especially in U.S. and North Europe. According to Globocan 2002, in 2002, the ASR of

prostate cancer in U.S. was 124.8 per 100,000 men, and the world level was 25.3 per 100,000 men. By comparison, in 2002, the highest ASR in Asia was mere 12.6 per 100,000 men in Japan, and the ASR in China was as low as 1.7 per 100,000 men (IARC, 2007g). Although the absolute value of prostate cancer ASR in Asia is not comparable to that in western countries, the growth rate of ASR in Asia is higher than that in the rest of the world (Sim et al., 2005d, p.834-845). The competition for prostate cancer drug such as PRX302 is mainly from surgery therapy and hormone therapy, which are the mainstream treatments for prostate cancer. In the Asian prostate cancer market, several multinational companies such as Takeda and AstraZeneca offer hormone drugs. If Protox can testify in clinical trials that PRX302 has fewer side-effects than existing prostate cancer treatments, it would be encouraging for Protox to enter Asia's prostate cancer market.

With respect to Asia's BPH market, it possesses huge market potential due to Asia's vast aging population and the similar high incidence rate of BPH around the world. According to Roehrborn (2002b), the incidence of BPH is similar throughout the world. Roehrborn (2005b) also estimated that the incidence of BPH is approximately 10% for men at the age of 30s, 20% for men at the age of 40s, 50% to 60% for men at the age of 60s, and 80% to 90% for men at the age of 70s and 80s. With the population trend towards aging in Asia, especially in Japan (26.3% people were over age of 60 in 2005), South Korea (13.7%) and China (10.9%), BPH has been a very common disease among Asian men. However, Asia's BPH market is well established, with tough competition from a pile of existing drugs and non-drug treatments. Most of the dozens of existing drugs, offered by local and international firms, are alpha-blockers and 5-alpha reductase inhibitors, which work slowly for the treatment of BPH.

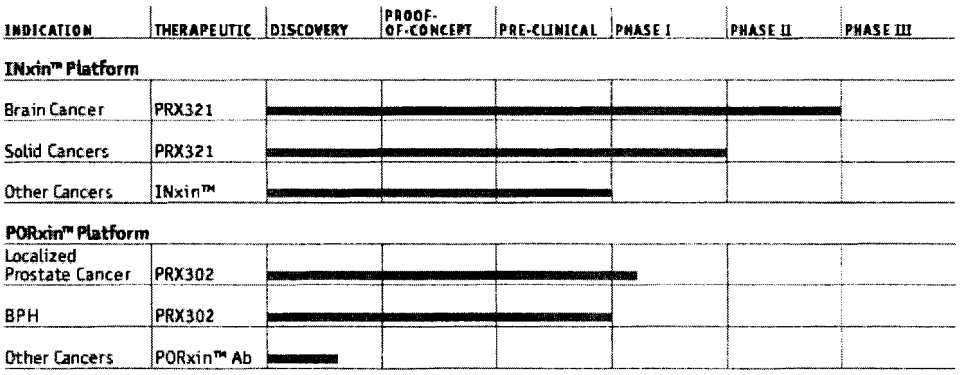
If PRX321 can be tested to have excellent clinical efficacy for the treatment of BPH, the Asian BPH market will be highly lucrative for Protox.

Based on the market study, lung, liver, stomach, colorectal and esophagus cancers are the most common cancers in Asia. On the basis of Globocan 2002, stomach cancer is the most common cancer in Eastern Asia, with an ASR of 46.1 per 100,000 men and 20.6 per 100,000 women in 2002 (IARC, 2007h). Similarly, the ASR of lung cancer in Eastern Asia was 42.7 per 100,000 men and 17.7 per 100,000 women in 2002; the ASR of liver cancer was 36.9 and 13.4, respectively; the ASR of colorectal cancer was 19.6 and 12.5, respectively; and the ASR of esophagus cancer was 24.1 and 9.7, respectively (IARC, 2007i). If Protox's drug candidates can be tested to have fewer side-effects than existing cancer drugs, it could be exciting for Protox to explore Asia's some other more lucrative segments such as stomach, lung, liver, esophagus, or colorectal markets. However, this suggestion is built on the fact that stomach, lung, liver, esophagus and colorectal cancers have much higher ASR than other cancers in Asia. A further market study to analyse current situations and competitions about relevant cancer markets is needed to evaluate these cancer markets.

APPENDICES

Appendix 1 Product Pipeline of Protox

Pipeline



Source: Protox Therapeutics Inc. 2007

Appendix 2 Population, Rate of Increase, Birth and Death Rates, Surface area and Density of the World, Major Areas and Regions: 2003

Major areas and regions Régions macro géographiques et composantes	Mid-year population estimates - Estimations de population au milieu de l'année (millions)							Annual rate of increase - Taux d'accroissement annuel (%)	Crude birth rate - Taux bruts de natalité	Crude death rate - Taux bruts de mortalité	Surface area (km2) - Superficie (km2) (000s)	Densit Densit
	1950	1960	1970	1980	1990	2000	2003	2000 - 2005			2003	
WORLD TOTAL - ENSEMBLE DU MONDE	2 520	3 024	3 697	4 442	5 280	6 086	6 314	1.2	21	9	136 056	46
AFRICA - AFRIQUE	224	282	364	479	636	812	868	2.2	38	15	30 250	29
Eastern Africa - Afrique orientale	65	82	109	146	198	256	275	2.4	41	17	6 300	44
Middle Africa - Afrique centrale	26	32	41	54	73	96	104	2.6	46	20	6 613	16
Northern Africa - Afrique septentrionale	53	67	86	112	144	175	184	1.7	26	7	8 525	22
Southern Africa - Afrique méridionale	16	20	26	33	42	52	54	0.7	24	17	2 675	20
Western Africa - Afrique occidentale	64	80	102	134	178	234	252	2.4	42	18	6 138	41
LATIN AMERICA AND CARIBBEAN - AMERIQUE LATINE ET CARAIBES	167	219	285	362	444	523	546	1.4	22	6	20 546	27
Caribbean - Caraïbes	17	20	25	29	34	38	38	0.9	20	8	234	165
Central America - Amérique centrale	37	50	68	91	113	136	143	1.6	24	5	2 480	58
South America - Amérique du Sud	113	148	192	242	297	349	365	1.4	21	6	17 832	20
NORTHERN AMERICA - AMERIQUE SEPTENTRIONALE[2]	172	204	232	256	283	315	324	1.0	14	8	21 776	15
ASIA - ASIE[3]	1 396	1 699	2 140	2 630	3 169	3 676	3 815	1.2	20	8	31 870	120
Eastern Asia - Asie orientale	671	792	987	1 178	1 350	1 479	1 507	0.6	13	7	11 763	128
South Central Asia - Asie centrale méridionale	496	617	780	978	1 226	1 485	1 560	1.6	26	9	10 791	145
South Eastern Asia - Asie méridionale orientale	178	223	286	358	440	519	541	1.4	21	7	4 495	120
Western Asia - Asie occidentale[3]	51	67	88	116	154	193	206	2.1	26	6	4 822	43
EUROPE[3]	547	604	656	692	721	728	729	0.0	10	12	22 050	33

Source: United Nations, Common Database, 2007

Appendix 3 Per Capita GDP at Current Prices in US Dollars

Region/Sub-region	2001	2002	2003	2004	2005
Australia & New Zealand	18705.83	20750.33	26378.54	31511.37	33868.22
Central America	5035.385	5173.868	5053.445	5328.778	5895.347
Eastern Africa	249.0256	247.0247	264.3685	278.2036	307.0881
Eastern Asia	4185	4155.84	4499.655	4941.248	5159.216
Eastern Europe	2414.176	2718.931	3319.444	4255.906	5290.819
Middle Africa	362.2976	399.7698	476.4719	592.6882	714.374
Northern Africa	1375.029	1312.998	1373.547	1568.535	1812.579
Northern America	33907.48	34701.15	36314.8	38665.94	41118.87
Northern Europe	23862.83	26168.1	30729.98	35845.92	37419.82
South America	3273.31	2538.102	2710.858	3222.373	3985.298
South Central Asia	518.7206	549.4035	615.27	708.6813	813.3232
South-Eastern Asia	1092.362	1205.634	1325.602	1450.634	1586.985
Southern Africa	2443.078	2276.505	3381.757	4321.857	4767.885
Southern Europe	13856.28	15274.02	19072.11	22018.73	22960.3
Western Africa	425.8976	442.1233	518.7403	571.4746	673.5505
Western Asia	3532.636	3708.323	4195.959	4934.669	5849.795
Western Europe	23305.97	25099.7	30521.44	34532.41	35320.62
Africa	694.3191	676.4466	791.8141	920.2016	1047.065
Americas	15107.83	15092.11	15716.39	16829.57	18148.32
Asia	2226.768	2245.767	2444.785	2706.996	2896.781
Europe	12799.1	14001.56	17036.71	19761.59	20833.32
Oceania	14354.05	15862.24	20094.43	23924.62	25645.35
World	5105.539	5244.463	5821.27	6460.21	6879.301

Source: United Nations, Common Database, 2007

Appendix 4 Growth Rate of GDP at Constant 1990 Prices: Percentage

Region/Subregion	2001	2002	2003	2004	2005
Australia & New Zealand	3.79	3.41	3.93	2.49	2.62
Central America	0.18	0.96	1.68	4.18	2.97
Eastern Africa	4.75	1.66	1.84	5.72	4.37
Eastern Asia	2.09	2.88	3.83	4.69	4.63
Eastern Europe	4.57	4.14	6.33	7.09	5.57
Middle Africa	4.46	6.43	4.27	8.36	7.29
Northern Africa	3.46	3.4	7.61	5.13	4.77
Northern America	0.85	1.74	2.65	4.12	3.34
Northern Europe	2.11	2.04	2.3	3.27	2.31
South America	0.37	-1.13	2.22	6.41	4.99
South Central Asia	4.9	4.9	7.98	6.87	7.84
South-Eastern Asia	2.23	4.76	5.36	6.24	5.38
Southern Africa	2.95	3.69	3.14	4.57	4.21
Southern Europe	2.55	1.36	1.22	2.04	1.47
Western Africa	4.45	4.1	6.12	5.21	5.25
Western Asia	-1.02	3	3.8	7.72	5.98
Western Europe	1.42	0.51	0.36	1.98	1.17
Africa	3.75	3.62	5.36	5.34	4.89
Americas	0.78	1.42	2.58	4.32	3.52
Asia	2.16	3.28	4.46	5.36	5.23
Europe	2.05	1.3	1.42	2.67	1.84
Oceania	3.72	3.38	3.89	2.49	2.61
World	1.69	1.94	2.76	4.02	3.43

Source: United Nations, Common Database, 2007

Appendix 5 China's GDP, Per Capita GDP and Growth Rate

Period	GDP at current prices		GDP at constant 1990 prices		Per Capita GDP	Growth rate
	Million					
	Yuan Renminbi	US Dollars	Yuan Renminbi	US Dollars	US Dollars	Percent
2001	9859290	1191157	5348143	1118108	945	8.3
2002	10789760	1303590	5834824	1219856	1027	9.1
2003	12173030	1470699	6418306	1341841	1151	10
2004	14239420	1720401	7066555	1477367	1339	10.1
2005	16238250	1981648	7766144	1623627	1533	9.9

Source: United Nations, Aggregates Database, 2007

Appendix 6 Population of China (ex Hong Kong)

Country or Area	Population projections variants	2006
China	Medium variant projection	1,323,636,000[1]
China	High variant projection	1,325,055,000[1]
China	Low variant projection	1,322,217,000[1]
China	Constant fertility scenario	1,323,465,000[1]

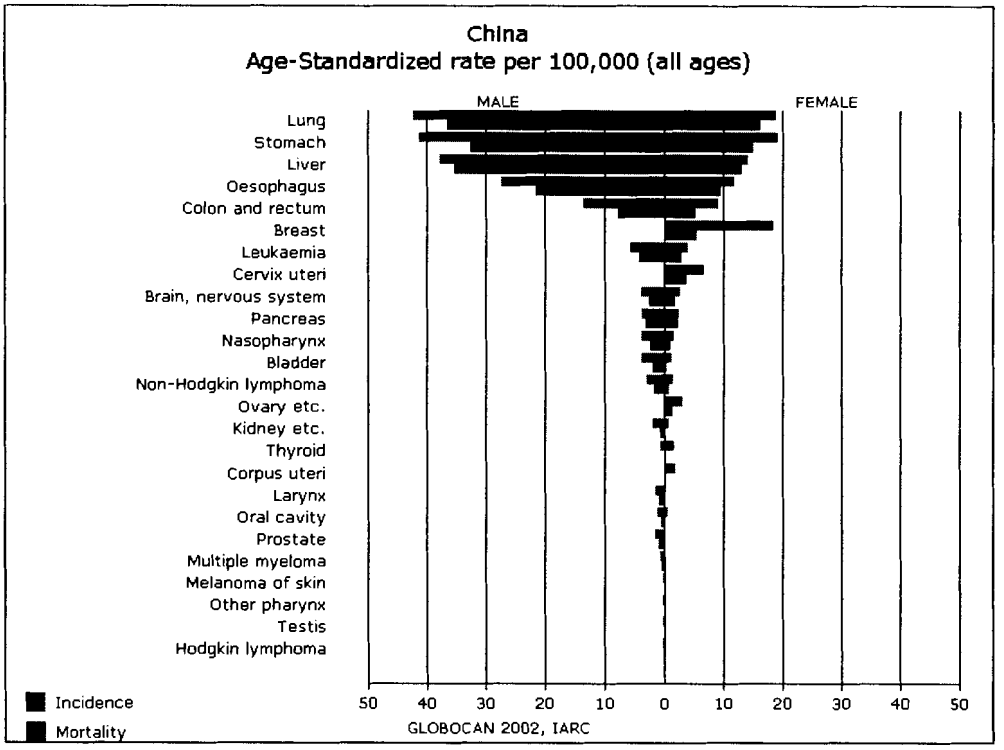
Source: United Nations, Aggregates Database, 2007

Appendix 7 Death Rate of Ten Main Diseases in China in 2006

Rank	City			County		
	Cause	**Death Rate 1/100000**	**%**	**Cause**	**Death Rate 1/100000**	**%**
1	Malignant Neoplasms	144.57	27.25	Malignant Neoplasms	130.23	25.14
2	Cerebrovascular Disease	93.69	17.66	Cerebrovascular Disease	105.48	20.36
3	Heart Disease	90.72	17.10	Diseases of the Respiratory System	84.94	16.40
4	Diseases of the Respiratory System	69.29	13.06	Heart Disease	71.84	13.87
5	Injury & Poisoning	32.36	6.10	Injury & Poisoning	46.12	8.90
6	Endocrine,Nutritional & Metabolic Diseases	17.59	3.32	Diseases of the Digestive System	17.00	3.28
7	Diseases of the Digestive System	15.61	2.94	Endocrine,Nutritional & Metabolic Diseases	8.16	1.57
8	Disease of the Genitourinary System	7.28	1.37	Disease of the Genitourinary System	6.65	1.28
9	Disease of the Nervous System	4.95	0.93	Disease of the Nervous System	4.16	0.80
10	Mental Disorder	3.44	0.65	Mental Disorders	3.77	0.73
	Total		90.41	Total		92.32

Source: Ministry of Healthcare, PRC, 2007

Appendix 8 Cancer prevalence in China



Source: Globocan 2002, IARC

Appendix 9 Financial highlights of Schering-Plough, Year of 2006

2006 Financial Highlights

Dollars in Millions, Except Per Share Figures	2006	2005	% Chan
Operating Results			
Net sales (1)	$10,594	$ 9,508	11
Income before income taxes (2)	1,483	497	
Net income (2)	1,143	269	
Net income available to common shareholders (2)	1,057	183	
Diluted earnings per common share (2)	0.71	0.12	
Investments			
Research and development	$ 2,188	$ 1,865	17
Capital expenditures	458	478	(4)
Financial Condition			
Total assets	$16,071	$15,469	
Shareholders' equity	7,908	7,387	
Other Data			
Cash dividends per common share	$ 0.22	$ 0.22	
Cash dividends per preferred share	3.00	3.00	
Average shares outstanding for diluted EPS (in millions)	1,491	1,484	

(1) Net sales and percent change are on a GAAP basis and do not include the positive impact of sales made by the cholester joint venture.

(2) 2006 and 2005 include Special charges of $102 million and $294 million, respectively.

For further details, see Notes to Consolidated Financial Statements.

Source: Schering-Plough corporate website.

Appendix 10 2006 Financial Highlights of Takeda

Financial Highlights

	FY 2006 (April 2006 - March 2007)	FY 2005 (April 2005 - March 2006)
Net Sales	¥1,305 billion (US$11,061 million)	¥1,212 billion (US$10,361 million)
Net Income	¥335.8 billion (US$2,846 million)	¥313.2 billion (US$2,677 million)
Earnings Per Share	¥386.00 (US3.27)	¥353.47 (US3.02)
Dividends Per Share	¥128.00 (US$1.08)	¥106.00 (US$0.91)

Note: The U.S. dollar amounts represent translations of Japanese yen, for convenience only, at the rate of ¥118=US$1 for FY 2006 and ¥117=US$1 for FY 2005 .

Source: Takeda Corporate Website

Appendix 11 Financial Results of Astellas for Fiscal Year 2006

Financial Results of Astellas for Fiscal Year 2006

Japan, May 15, 2007 – Astellas Pharma Inc. (hereinafter referred as "the Company") today announced the financial results for the fiscal year 2006 (FY2006), ended March 31, 2007.

1) Consolidated financial results for FY2006 (April 1, 2006 – March 31, 2007)

(all amounts are in million of yen – fractions dropped)

	FY2005	FY2006	Changes (%)
Net sales	879,361	920,624	+4.7%
Operating income	193,020	190,514	-1.3%
Ordinary income	202,588	197,813	-2.4%
Net income	103,658	131,285	+26.7%
Per share profit (Yen)	183.88	244.07	+32.7%
R&D expenses (% of net sales)	142,076 (16.2%)	167,945 (18.2%)	+18.2%

Source: Astellas Corporate Website

Appendix 12 2006 Financial Highlights of Merck

FINANCIAL HIGHLIGHTS

Merck & Co., Inc. and Subsidiaries Years Ended December 31 ($ in millions except per share amounts)	2006[1]	2005[2]	2004[3]	Percentage Change from Preceding Year 2006	 2005
Sales	**$ 22,636.0**	$ 22,011.9	$ 22,972.8	**+3%**	-4%
Net income	**4,433.8**	4,631.2	5,830.1	**-4%**	-21%
Earnings per common share assuming dilution	**$ 2.03**	$ 2.10	$ 2.62	**-3%**	-20%
Cash dividends paid per common share	**$ 1.52**	$ 1.52	$ 1.48	-	+2%
Average common shares outstanding assuming dilution (millions)	**2,187.7**	2,200.4	2,226.4		
Total assets	**44,569.8**	44,845.8	42,572.8		
Net cash flows provided by operating activities	**6,765.2**	7,808.5	8,799.1		
Capital expenditures	**980.2**	1,402.7	1,726.1		
Net income as a % of average total assets	**9.9%**	10.6%	14.0%		
Number of stockholders of record	**184,200**	198,200	216,100		
Number of employees	**60,000**	61,500	62,600		

[1] Amounts for 2006 include the impact of restructuring actions, acquired research expenses associated with acquisitions made during the

Source: Merck Corporate Website

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