Canada’s Pharmaceutical Industry and Prospects
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1.0 Executive Summary

The pharmaceutical industry, at both the global and Canadian levels, has experienced an unprecedented amount of challenges and changes over the past several years. Global market growth is trending down and the current pace is below the historical 5-year average. The slowing trend is noteworthy along with the stark contrast that makes up this overall growth: developed markets of Europe and North America are expanding at rates below 3% while emerging markets are posting double-digit growth. This contrast in growth has forced many global MNEs to focus their investment and efforts in the higher growth emerging countries, which in turn is making it more competitive for MNEs to increase or even maintain their investment in Canada.

Similar to this contrast in geographical performance are the large differences in the drivers of growth in therapeutic areas. Biologics continue to become increasingly dominant in market share and as an exceptional driver of market growth. The contrast to this innovation in biologics is patent expiry precipitating record levels of revenue losses for brand products and triggering the expansion of the generic sector, globally and in Canada.

As the era of the large primary care blockbuster drug draws to a close from the patent cliff, pharmaceutical companies are re-organizing and adopting strategies to reduce risk, and overcome external factors and their poor pipeline productivity. These strategies include adopting new business models built upon external networks and third party partnerships focused on medical research and development. This trend towards a business model that relies on outsourcing of many business functions, including manufacturing, is providing contract service providers (CSPs) in Canada with growth opportunities.

One of the biggest issue going forward is the ability of Canadian companies to successfully compete with other countries on many keys factors including cost, talent and market attractiveness; market attractiveness as defined by regulatory requirements, market access, IP legislation and pricing controls. The evolution and growing dominance of biologics along with MNEs’ desire to improve their pipeline productivity has meant that biopharma SMEs in Canada have an opportunity to flourish. However, adequate access to capital is expected to have a profound impact on how well biopharma SMEs thrive and compete in the years ahead.

While recent pharmaceutical industry trends in Canada have been challenged with poor market growth and pressures from global competition, there still remains a very viable industry which if aided by stronger industrial sector support can flourish and successfully compete in this new and much more globally competitive business environment. Canada also has an opportunity to be a global leader in certain new growth areas.
2.0 Introduction

The pharmaceutical industry, both in Canada and globally, is transforming itself to respond to new realities. These pressures include but are not limited to an unprecedented expiration of patents for many blockbuster drugs, often referred to as the patent cliff, and on-going cost containment measures from both public and private payers. These external market forces, when combined with an increasingly competitive global corporate dynamic for investment and improved R&D return, have and will continue to reshape their operations. Changes occurring at the global level are having a profound impact for the Canadian pharmaceutical industry and are triggering new threats and opportunities.

This discussion paper assesses Canada’s current pharmaceutical industry and the dynamics within the industry in the context of Canadian and global market performance. The paper highlights the medium term outlook for the industry, identifying key factors that shape the industry in coming years. Drawing on the current and prospective outlook assessment of the industry, the discussion paper undertakes a SWOT analysis discussing future prospects, threats and opportunities facing the industry. This discussion paper does not examine the Canadian distribution channels.

The discussion paper is organized into three main sections. Following the introduction (2.0), section 3.0 discusses the current situation in the Canadian industry including the recent performance of the overall market and discusses the four segments of companies (brand, generic, contract service providers and biopharma SMEs) including R&D trends. Section 4.0 comments on the outlook and future prospects of the industry. The final section offers a SWOT analysis of the Canadian pharmaceutical industry.

2.1 Data Resources

IMS Brogan and Industry Canada worked collaboratively in producing this discussion paper. The analysis leveraged data and information from Industry Canada’s existing research, combined with the insight and intelligence of IMS Brogan’s experts and offerings. IMS Brogan complemented analyses conducted by Industry Canada by offering commentary and observations of the dynamism of the Canadian pharmaceutical industry. IMS Brogan used existing IMS studies and analyses where relevant.

IMS data resources:

- **Canadian and Global Thought Leaders** - IMS Brogan utilized our team of thought leaders to assist in providing valuable insights into the Canadian pharmaceutical industry prospects
- **PharmaFocus** – provided comprehensive, independent review of the Canadian pharmaceutical industry within the larger health care environment. The report covers a broad range of topics, from politics and health care, to government reform initiatives to regulatory, business and pharmaceutical marketing issues
- **Knowledge Link** – provided Pharmaceutical manufactures’ global strategy, Canadian and global sales trends, therapeutic areas, product pipeline and company news
- **LifeCycle** – provided information about product pipeline for insight on future product lines
- **IMS Company Profiles** – offered company structure, strategy, financial results, research and development program, product portfolio, and major events. Information is sourced from interviews with key executives of the company, stock analyst forecasts and commentary, and published information
- IMS World Review and IMS Country Review – offered comprehensive insight on performance trends of major pharmaceutical companies and countries, markets, therapeutic areas and classes
- Market Prognosis Canada – key environmental issues affecting MNEs, SMEs and generics segments in the medium term (to 2016)
- Canadian Drug Store & Hospital – MNEs and SMEs sales trends in Canada, and by therapeutic class
- Provincial Reimbursement Advisor (PRA) – offered insights into key reimbursement issues facing the Canadian pharmaceutical industry with respect to the changing provincial government policies and activities that influence market access and reimbursement of new drug products
3.0 Current Situation of the Canadian Pharmaceutical Industry

3.1 Review of Recent Overall Global and Canadian Market Performance

The Canadian pharmaceutical industry is undergoing tremendous challenges. In 2011\(^1\), the Canadian market was the 8th largest in the world and accounted for 2.6% of total global purchases, down slightly from a share of 2.7% in 2010 and 2007. Annual market growth has steadily declined since peaking above 16% in 2001. The industry contracted for the first time in 2011 (-0.9% growth). Through the first half of 2012, the Canadian pharmaceutical market is showing tepid recovery, up 0.9% after the decline in 2011. Figure 1 illustrates the trend in Canada and global dollar sales growth and shows Canadian annual growth rate.

The pace of growth in the global market has also slowed but remains stronger than Canada’s, largely due to the strong growth in emerging markets. Slowing growth in developed markets like Canada, the US (North American market grew 3.1% in 2011) and Europe (growth of 1.6% in 2011) has been offset by exceptional and sustained growth from emerging markets. Brazil and China posted growth of 18.9% and 17.1% respectively in 2011. Slowing global growth continues in 2012, at a pace of 3.5% through June 2012 and slower than the 5% experienced in 2011 and 2010. The contrast in market growth between developed and emerging markets is triggering critical investment choices for most MNEs.

Figure 1

Global growth: Canadian market has recently lagged, with stark contrast between developed and emerging markets

For the most part, the factors contributing to the slowdown in Canadian market growth since the second half of the past decade have also been responsible for dampening growth in other developed markets and the overall global rate. These factors include: record levels of loss of exclusivity for major brand products, a lack of new blockbuster products, sluggish uptake of new products, a slowdown in new product approvals and longer processing time to access public formularies. More recently, these market factors

\(^1\) Latest full year annual data available at time of writing
have been compounded in Canada and other global markets by declining R&D productivity, the global financial crisis and economic downturn, downward pressure on prices and cost containment policies from payers, and the shift in business operations towards emerging countries.

Market segments driving the Canadian pharmaceutical market also reflect considerable changes and contrasts in growth. In the past ten years, the Canadian market has seen dramatic growth in generics as the result of patent expiries and policies by payers targeting generic utilization, as well as the growing adoption of more expensive oncology, biotechnology and specialty drugs. Figure 2 compares the growth of key market segments in 2007 and 2012 (as of end of Q2). During the second half of the last decade, generics drove growth in the Canadian market. By 2012, biotechnology and specialty drugs lead growth while the generic segment struggled with negative growth. The annual value of dollar sales in specialty products reached $4.7 billion in 2011 (latest full year data available) while biotechnology drug recorded $3.4 billion in sales, namely in biological Response Modifiers and Analogs of Human Insulin. Generic sales continue to represent a big share of the Canadian market, however growth since 2010 has been negative as pricing reforms by payers are implemented: -5.3% in 2011 from level in 2010 and negative growth of -2.6% as of June 2012 (in Figure 2).

Figure 2

Annual growth in Canadian sales by market segment

<table>
<thead>
<tr>
<th></th>
<th>2007</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blue</td>
<td>6.3%</td>
<td>-2.6%</td>
</tr>
<tr>
<td>Grey</td>
<td>20.9%</td>
<td>12.4%</td>
</tr>
<tr>
<td>Green</td>
<td>3.0%</td>
<td>2.1%</td>
</tr>
<tr>
<td>Bright Blue</td>
<td>16.3%</td>
<td></td>
</tr>
<tr>
<td>Beige</td>
<td>11.8%</td>
<td>3.3%</td>
</tr>
<tr>
<td>Red</td>
<td></td>
<td>7.7%</td>
</tr>
</tbody>
</table>

Legend:
- Blue = Total Market
- Grey = Generic
- Green = All Branded
- Bright Blue = Biotech
- Beige = Oncology
- Red = Specialty

MAT to December 2007, MAT June 2012 except specialty segment (as of Dec 2011)
Source: PharmaFocus 2012, 2016 (March and November Update)

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2 Specialty pharmaceuticals are medicines that treat specific, complex chronic diseases with four or more of the following attributes: initiated only by a specialist, generally not oral, require special handling, unique distribution, high expense, warrant intensive patient counselling, and require reimbursement assistance.

3 Biotechnology drugs as defined in IMS PharmaFocus reports include products (pharmaceutical or vaccine) that have been produced in living organisms and manufactured via recombinant DNA technology. Plasma-extracted proteins that are not synthesized through recombinant techniques are excluded. The Biotech market segment includes some oncology products.

4 Biological Response Modifiers are anti-TNF monoclonal antibody biologics for the treatment of diseases associated with autoimmune disorders such as rheumatoid arthritis, ankylosing spondylitis, Crohn’s disease, psoriasis, hidradenitis suppurativa and refractory asthma. Examples of anti-TNF products are Remicade, Simponi, Enbrel and Humira.
Considerable changes are also observed in the sales and composition of the leading therapeutic classes in the Canadian market. Several classes that now rank within the top 10 were not top sellers in 2007, for example Antiretrovirals, Seizure Disorders and Monoclonal Antibodies\(^5\). Figure 3 compares the top 10 therapeutic classes in 2007 and 2012 (as of end of Q2) and provides the compound annual growth rate in the previous 5-year period. The leading 10 therapeutic classes account for 36% of the total market in 2012, a steady modest decline from a share of 39% in 2007\(^6\). The top selling class, HMG-CoA Reductase Inhibitors (also known as statins) account for 6% of the market relative to 9% in 2007, with growth in recent years much slower than in the early part of the 2000s due to genericization of Lipitor and recently, Crestor. The second top selling class, Biological Response Modifiers, represents 6% of the market, doubled the share in 2007 and leads the Top 10 classes in growth (24% compound annual growth in 2007-2011). Leading products in the Biological Response Modifiers class include Remicade, Simponi, Enbrel, and Humira. Due to the genericization of key brands, several of the leading therapeutic classes are experiencing weak or negative growth in 2011 and so far in 2012: HMG-CoA Reductase Inhibitors; Proton Pump Inhibitors i.e. Nexium; Major Tranquilizers i.e. atypical antipsychotics products Seroquel XR and Risperdal; and Serotonin Reuptake Inhibitors i.e. Cipralex and Cymbalta. Moreover, the generization of key brands has impacted the position of several former top-selling classes in 2007 which are no longer in the top 10 group in 2012: Calcium Blocking Agents i.e. Norvasc, ACE Inhibitors i.e. Altace and Vasotec; and oral Diabetes Therapy i.e. Actos and Avandia.

**Figure 3**

Top 10 therapeutic subclasses, by sales in Canada: 2007 vs. 2012 and their growth in the previous 5 year-period

<table>
<thead>
<tr>
<th>Rank</th>
<th>2007</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% Market Share</td>
<td>CAGR 2002-2006</td>
</tr>
<tr>
<td>1</td>
<td>HMG-CoA Reductase Inhibitors</td>
<td>8.8</td>
</tr>
<tr>
<td>2</td>
<td>Proton Pump Inhibitors</td>
<td>5.8</td>
</tr>
<tr>
<td>3</td>
<td>Serotonin Reuptake Inhibitors</td>
<td>4.0</td>
</tr>
<tr>
<td>4</td>
<td>Calcium Blocking Agents</td>
<td>3.9</td>
</tr>
<tr>
<td>5</td>
<td>Major Tranquilizers</td>
<td>3.3</td>
</tr>
<tr>
<td>6</td>
<td>ACE Inhibitors</td>
<td>3.2</td>
</tr>
<tr>
<td>7</td>
<td>Asthma Therapy</td>
<td>3.0</td>
</tr>
<tr>
<td>8</td>
<td>Biological Response Modifiers</td>
<td>2.6</td>
</tr>
<tr>
<td>9</td>
<td>Diabetes Therapy, Oral</td>
<td>2.2</td>
</tr>
<tr>
<td>10</td>
<td>Diagnostic Aids, Others</td>
<td>2.1</td>
</tr>
<tr>
<td>Total Top 10 Subclasses</td>
<td>39.0</td>
<td>9.2</td>
</tr>
</tbody>
</table>

Source: Therapeutic Subclasses (USC-4) in IMS Brogan Canadian Drug Stores and Hospital Purchases. Based on Sales as of MAT December 2007 and sales as MAT June 2012. CAGR for previous 5-year period

Restrictive market access and pricing policies for both brand and generic have significantly impacted the performance of the Canadian industry. Payers seeking lower

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\(^5\) PharmaFocus 2016, November 2012 update. Three leading Monoclonal Antibodies products are Herceptin, Rituxan and Avastin, all from Roche. Seizure Disorder products include Lyrica and generic gabapentin; and Antiretrovirals include Atripla and Truvada.

\(^6\) Therapeutic class by USC-4 level
cost medicine shifted the market share towards the generic segment and more recently the latest round of provincial drug plan reforms have drastically cut generic prices in most provinces. Market access levels in public drug plans have also been persistently low. Only 20% of the drugs launched in the 2009-2011 period were granted provincial full formulary listing status and an increasingly higher proportion are being listed with restricted benefits. Figure 4 illustrates this general trend of fewer full benefit listings of new products in the four largest public formularies in Canada.

Figure 4

Percentage of new products with full listing status in large public formularies

Average % in a two-year period* of new products with Full Listing Status (for two-year periods ending Aug. 2009 to Aug. 2012)

The performance of companies operating in the Canadian market has been challenged by slower growth in sales and waning profitability. The profit margin of pharmaceutical manufacturers with operations in Canada declined from above 11% in 2006 to 7% in 2010. Return on equity had a similar decline from 11% to below 6% by 2010. The downward pressure on profit is reflected in the weakening sales growth. The top corporations in Canada in 2007 had posted a four-year compound annual growth of 8.1% (2002-2006). Sales growth slowed significantly by 2011. The compound annual growth of the top 10 corporation, based on their 2011 sales, was 3.9% in the four year 2006-2010 period (see Figure 5). Increasingly, MNEs are changing their business model by focusing on growing specialty therapeutic areas and diversifying to different geographic markets through acquisitions and alliances. The proceeding sections discuss in greater details the market environment of the four key segments of companies in the Canadian pharmaceutical industry.

3.2 Brand and Generic MNEs Anchor the Canadian Industry

Canada’s pharmaceutical industry consists of an ecosystem of multinational and local companies. Branded pharmaceutical MNEs traditionally develop and market new patented products; they represent the largest portion of drug sales and R&D investment

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7 Latest data year available from Statistics Canada
8 Statistics Canada, CANSIM Table 180-0003
in Canada. Most major branded pharmaceutical companies are foreign multinationals with subsidiaries in Canada. Valeant is the only Canadian-headquartered branded MNE. The generic segment is a mix of Canadian-based and foreign MNEs and smaller companies. Generic companies manufacture and market lower-priced generics once patents of branded products expire. Canada’s larger pharmaceutical companies include Apotex and Pharmascience. Biopharma SMEs in Canada are small and generally focused on early stage research and development with few marketed products. The fourth major player in the industry is contract service providers (CSPs), a mix of local smaller Canadian-headquartered companies and larger foreign companies. CSPs provide a wide array of contract services in the product lifecycle, from R&D and manufacturing to sales and administration.

While many companies sell into the Canadian market, the majority of these companies are headquartered outside Canada. Of the top 20 selling corporations in Canada, Apotex, Pharmascience and Valeant are the largest of the MNEs that are Canadian-based. Generally, Canadian-based companies in the industry are relatively smaller and serve niche specialty segments of the industry. These smaller companies are more numerous than MNEs but MNEs are dominant in terms of their size and sales in the Canadian market.

MNEs that dominate the brand and generic sectors in terms of sales in the Canadian market do not necessarily have a manufacturing or R&D footprint in Canada. Amongst the leading brand MNEs by their sales in the Canadian market, the following company have a manufacturing footprint in Canada: Johnson & Johnson, Pfizer, the vaccines division of Sanofi-Aventis (Sanofi Pasteur), Merck (Schering-Plough Canada Inc.), GlaxoSmithKline Inc and Valeant. Johnson & Johnson’s Canadian footprint consists of 400 administrative and sales staff along with more than 1,000 manufacturing and research and development employees at its Guelph and Montreal manufacturing sites. Pfizer operates a manufacturing facility and distribution center employing over 1,000 in Montreal. The company’s manufacturing plant in Brandon manufactures the raw material intermediate for its Premarin brand which is the largest pharmaceutical product export in Canada9.

Amongst the top 10 selling generic corporations, four of the corporations have manufacturing facilities in Canada: Teva, Apotex, Pharmascience and its division Pendopharm, and Sandoz. These four top generic corporations operate more than 10 of the 21 generic manufacturing facilities in Canada.10 Apotex, the largest Canada-based pharmaceutical company is a leading generic manufacturer with a focus on gastrointestinal, cardiovascular and central nervous system drugs. Teva’s Canadian penicillin plant produces for North America, Europe and Israel. Sandoz, the second largest global generic drug company operates an 800-employee facility in Boucherville QC, specializing in injectables for its global family. Sandoz produces more than 90% of injectable medications used in Canada, among them anaesthetics, painkillers, cancer drugs and antibiotics.11 Cobalt operated a manufacturing facility in Mississauga but announced the shutdown of this facility by 2013 after it was acquired by US-based Watson Pharmaceutical Inc.12 According to the Canadian Generic Pharmaceutical Association, the generic sector has a workforce of 11,000 employees based mainly in the Montreal-area, greater Toronto and Winnipeg13.

The composition of companies within the industry has changed reflecting global market conditions and shifting dynamics within the industry. Figure 5 illustrates the changing

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10 Number and location of manufacturing sites in generic sector provided by Industry Canada
11 PharmaFocus 2016
12 Information on manufacturing facilities provided by Industry Canada
13 Based on 2010 data, as reported in the October 2011 report “EU Pharmaceutical IP Proposals in the CETA Negotiations: Potential Impact on the Generic Pharmaceutical Industry in Canada”.

composition of the leading companies in Canada\textsuperscript{14}. Pfizer exemplifies the impact of the patent cliff on its growth, market share and position atop the Canadian market relative to 2007. Roche is now in the top 10, largely due to its strength in the fast growing speciality segment. Coinciding with the heightening of the patent cliff, 2007 was the first time in the Canadian pharmaceutical industry that two generic companies were amongst the top 10 corporations: Apotex and Novopharm. By 2011, the top 10 still consisted of two generic companies but with Novopharm wholly owned by foreign-owned Teva. Schering-Plough was an independent company amongst the top 10 companies in 2007 that now exist within Merck. More recently, the fast growing companies, in terms of Canadian sales, are companies outside the list of the top 10 in Figure 5. These fast growing companies include Shire, Lundbeck, BMS-Gilead and Nycomed (now part of Takeda) are predominantly smaller companies focused on niche and specialty products. Smaller generic companies Sandoz and AA Pharma are also fast growing.

\textbf{3.3 \hspace{1cm} Performance of Brand and Generic Sectors}

The performance of the Canadian brand and generic sectors in recent years has largely been a story of the patent cliff (the loss of revenues to branded products due to genericization). The value of patent losses in 2006 was $341 million in Canada, spiked dramatically to $1.2 billion in 2007 and has remained above $1 billion each year since. Patent losses are expected to reach an estimated $2.4 billion in 2012, an all-time high, reflecting patent expiries of major top selling brands such as Crestor and Plavix (Figure 6 below).

\textsuperscript{14} Source: PharmaFocus 2012 and PharmaFocus 2016. Four-year CAGR (2006-2010) was 3.9% for the 2011 group of Top 10 Corporations. The four-year CAGR (2002-2006) of the 2007 group of Top 10 corporations was 8.1%.
The patent cliff is a significant and near-immediate revenue loss for the brand sector. As a result of patent expiries, the market share of the brand segment in the Canadian market has contracted. In 2011, sales of brand products reached $16.7 billion and accounted for 75.6% of the Canadian market. In 2007, this share was 79.5% and totalled $15.1 billion\textsuperscript{15}. The revenue-generating abilities of top selling brand products and their importance to the overall market also reflect this diminished share. The top 10 brand products in 2007, in terms of volume accounted for 17.7% of the total market, with $3.36 billion in total purchases in 2007. All these brands have now been genericized. In 2011, the top 10 brands accounted for 14.9% of the total market (down from 15.6% in 2010 and 17.4% in 2009), with $3.29 billion in total purchases. The patent cliff is one of the drivers shifting the business model from blockbuster drugs to targeted niche drugs that are higher priced. These niche areas typically have small number of patients.

The financial impact from this loss of exclusivity to major brand products is a central challenge to the performance of brand companies. The historical growth rate of the 10 leading brand corporations during the second half of the last decade is markedly slower than during the first half. In 2011, the group of the 10 leading brand corporations posted negative growth of 1% and market share was just under 60%. In 2007, the group of top 10 corporations accounted for 65% of the Canadian market.\textsuperscript{16} Amongst the top 10 corporations based on their Canadian sales, Pfizer and GlaxoSmithKline were the two corporations that experienced negative growth in 2011. Purchases of Pfizer products in Canada dropped 25.5% from 2010, coinciding with the end of Lipitor’s period of exclusivity. It was a very different scenario for Pfizer in 2007 when the company led the Canadian brand segment in sales and growth (over 9%) largely due to Lipitor and Norvasc. The fastest growing and top selling brand company in Canada in 2011 was Johnson & Johnson (up 6.6% from 2010), boosted by the company’s biologics products Remicade and Simponi along with cancer drug Velcade (from its subsidiary Janssen). As

\textsuperscript{15} Based on IMS PharmaFocus reports
\textsuperscript{16} IMS World Review 2012, Canada
mentioned previously, Roche is now amongst the top 10 corporations in Canadian sales and captures greater share of the market relative to 2007 due to its strength in the fast growing speciality segment.

Brand MNEs are experiencing an imbalance between the genericization of their key branded products and the revenue performance of new product launches that are not offsetting revenue losses from patent expiries. Further evidence of this weak product pipeline: in 2011, three of the 10 fastest-growing brands were reformulations. There have been fewer innovative product launches and the uptake of new products has not sufficiently offset revenue loss from patent expiries. The market share attained by new branded drugs including new active substances and line extensions in the Canadian market has declined significantly in the past ten years. For example, new products launched in the Canadian market in 2003 accounted for 0.63% of the Canadian market. New products launched in 2008 accounted for 0.21% of the Canadian market in 2008 and products launched in 2011 accounted for 0.08% of the market in 2011 (see table in Figure 7)\footnote{Sales are based on calendar year; as such the month or quarter of when new drugs are launched in a particular year will impact the annual market share. Year 2 through Year 6 are based on 12-month calendar year sales of each group of new products. For example, Year 2 for 2006 group of new products is Jan-Dec 2007. Year 2 for 2009 group of new products is Jan-Dec 2011.}. The regulatory process for market approval and subsequent formulary review of new products has been noted as a contributing factor to the low performance of new product launches. For example, approval of new drugs by Health Canada and subsequent formulary review processes at the provincial level can span over two and-a-half years, combined.\footnote{Fraser Institute. Access Delayed, Access Denied 2012: Waiting for New Medicines in Canada. April 4, 2012.}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure7.png}
\caption{Canadian market share of new products launches, 2006-2011 (New active substances and line extensions)}
\end{figure}

The Canadian generic sector posted strong growth throughout much of the last decade however, by 2009 the sector began to face strong headwinds, namely from lower generic pricing policies introduced in public and private drug plans. Some generic companies also encountered manufacturing issues because they were unable to access active ingredients, leading to difficulties supplying to their customers. The supply issue
amongst generic manufacturers occurred in Canada, US and other parts of the world. Sales in the Canadian generic market fell to negative territory for the first time in 2011 (down 5.3% from 2010 level) and through the second quarter of 2012, dollar sales growth is also negative. The negative growth is a stark contrast to the 18% growth experienced in 2004, 2007 and 2008. Canadian market performance of the generic segment is anticipated to remain weak during the short term despite another wave of patent expiries in 2012, as further reforms by public and private drug plans are phased in\textsuperscript{19}. The recent slowdown in the Canadian generic market is reflected in the performance of leading generic companies. In 2011, the top 10 selling generic corporations in the Canadian market recorded $5.0 billion in total sales, a contraction from $5.3 billion in 2010. This is down sharply from growth above 20% in 2008. The industry is highly concentrated with the top 10 generic corporations accounting for over 90% of generics sales in Canada.

### 3.4 Changing Business Models of MNEs Make Way for CSPs

The patent cliff and challenging market conditions combined with low pipeline productivity of MNEs acted as catalysts for the transformation of the business model of MNEs. Global brand companies have rationalized their marketing and sales teams along with underutilized R&D and manufacturing capacity in mature markets. Several examples of such rationalizing include: Pfizer reduced its global workforce by 10,000 between 2006 and 2008. AstraZeneca (7,600 employees), Merck (7,200 employees) and Bayer (6,000 employees) also significantly reduced their workforce\textsuperscript{20}. Those brand MNEs that are maintaining their manufacturing facilities are reinventing their production models to focus on high-end manufacturing and foraying into other areas such as medical devices, OTC and consumer healthcare products.

With increasing competition and lower generic pricing policies from payers, companies in the generic sector will likely follow the trajectory of brand companies towards cost reduction and rationalizing assets. Canada’s leading generic company Teva consolidated its operations after acquiring Ratiopharm in 2010 and sold the Montreal manufacturing facility formerly operated by Ratiopharm. This facility previously employed over 300 people will now be operated by Halo Pharmaceuticals, a contract manufacturing organization (CMO) with a smaller workforce. MNEs in the generic segment will be challenged in their ability to sustain activity and investment in Canada since the value proposition for attracting investment in the generic sector is a combination of a fast growing domestic market and a low-cost operating environment, as in the case of India. The Canadian market is relatively small and operational costs are higher than competing operations in emerging markets. On the other hand, highly productive facilities with flexible production capacity combined with investment and tax incentives can position a jurisdiction with a small domestic market to attract generic investment, mainly to produce for export markets\textsuperscript{21}.

MNEs with operations in Canada have and are responding to market conditions and competitive global corporate dynamics by rationalizing and reducing their level of direct investment. The shift towards outsourcing and indirect investment in Canada by MNEs\textsuperscript{22} has created opportunities for contract service providers (CSPs) in Canada.

In Canada, employment in pharmaceutical manufacturing contracted by 8% during 2007-2011 to approximately 27,000 workers however the number of manufacturing facilities increased modestly during the second half of the last decade (according to

\textsuperscript{19} PharmaFocus 2016  
\textsuperscript{20} PwC Pharma2020: Marketing the Future  
\textsuperscript{21} Source: Industry discussion  
\textsuperscript{22} Direct investment is investment performed within company, directly at a company operation/facility.
Statistics Canada data). Contract service providers (CSPs) are filling some of the operations and services vacated by MNEs. For example, former manufacturing facilities of several MNEs (AstraZeneca, BMS, GSK, Pfizer, Novartis, Roche, Shire and Teva) are now operated by contract manufacturers. Teva’s Montreal facility (formerly owned by Ratiopharm) was sold to Halo Pharmaceutical in 2012. Halo will manufacturer several Teva products for international markets. Similarly, in 2008, BMS sold its facility to Uman Pharma and Pfizer sold its Arnprior facility to Korean-based Keata Pharma; the Arnprior facility now operates as Pillar5 Pharma. Although MNEs are reducing their level of direct investment, their spending in terms of outsourcing the manufacturing function has benefited the CSP segment.

CSPs engaged in manufacturing (contract manufacturing organizations) in the Canadian industry are a mix of Canadian-based companies such as CPL, Confab Laboratories, Pillar5 Pharma and Trillium Health Care Products which have formed manufacturing alliances with MNEs and global CSPs. Global CSPs such as Jubilant HollisterStier (parent company is India’s Jubilant Life Science), Piramal Healthcare (India) and Patheon have an established presence in Canada, reflecting that MNEs in the industry are not just the brand and generic companies. Patheon originated in Canada during the 1970s and relocated its headquarters to the US after the Canadian company was purchased by JLL Partners/ JLL Patheon Holdings LLC in 2007.

In addition to manufacturing, two other business functions that MNEs are predominantly outsourcing to contract service providers are in research activities and sales and administration. Contract research organizations (CROs) provide support in the R&D process and areas such as in-licensing from biopharma SMEs and academic institutions, developing the potential research and out-licensing findings to pharmaceutical companies. There are over 80 pharmaceutical CROs operating in Canada mostly providing services in pre-clinical research and conducting clinical trials. Mississauga-based PharmaMedica Research, for example specializes in Phase I research.

The impetus for MNEs to outsource their functions is based on several considerations. For brand companies, genericization erodes the margins of branded products. Outsourcing low margin products enables companies to control and optimize costs. CSPs offer cost advantage to MNEs through their focused and lean production, waste reduction and resource conservation. These cost efficiencies are particularly important in environment of low margin manufacturing. CSPs have specialized capacity thus typically have lower costs than larger and integrated pharmaceutical MNEs. Moreover, in challenging markets where demand is increasingly volatile, outsourcing business functions enable MNEs to respond swiftly to changing conditions without cumbersome efforts in adjusting their operational capacity, so that they can focus on innovation and their core functions.

3.5 R&D and Biopharma SMEs

Canada ranks low on the global corporate priority for R&D investment, despite having the 8th largest global market. Most pharmaceutical MNEs spend less than 1% of their global direct R&D investment in Canada. Boehringer Ingelheim and Canadian-based Valeant are the only two companies that have allocated more than 2% of their global R&D investment in Canada. Indeed, the wave of closures to R&D facilities announced in

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23 Statistics Canada, Cansim Table 281-0024 Employment (SEPH) and Table 301-0006
24 Industry Canada research
26 Industry Canada research
27 PwC Pharma2020: Challenging business models
28 Industry Canada research
29 Industry Canada research
2012 suggests uncertainty in the ability of Canadian business units of global MNEs to sustain and attract higher levels of R&D activity. Several recent examples of global MNEs rationalizing their R&D activities in Canada include: Boehringer Ingelheim will shut down its Laval R&D facility by early 2013 (170 employees); in 2012 AstraZeneca closed its neuroscience research facility in Montreal affecting approximately 17% of the company’s Canadian workforce; Johnson & Johnson closed its Montreal R&D division in 2012 (132 jobs); and Sanofi announced layoffs of 100 people at its Laval R&D facility. Closures of Canadian R&D facilities by MNEs are occurring because these facilities were engaged in therapeutic areas that are no longer areas of global corporate focus or as the result of outsourcing and in-licensing to minimize costs and risks associated with in-house product development. Moreover MNEs are consolidating research centres to clusters located closer to company headquarters, or are located in attractive geographic markets. Conditions of attractive markets include investment infrastructure and government incentives such as taxation.

Clinical research is recognized as an area of strength for the Canadian pharmaceutical industry. Indeed, Canadian R&D facilities of global pharmaceutical companies are primarily devoted to clinical research management instead of pure research. Within clinical research, Phase III typically receives the largest proportion of clinical research spending. Clinical research generally represents 45% of pharmaceutical R&D spending in Canada, the largest portion of pharmaceutical R&D spending in Canada30. Canada is second to US in number of active clinical trial sites (4,449 and 27,610 respectively)31. The reputation and importance of clinical research in Canada can be attributed to Canada’s healthcare infrastructure and health research networks. However, the number of clinical trials received in Canada has declined since 2010 from 1,241 to 1,069 trials received in 2012.32 The emergence of low cost clinical research competitors from emerging markets and their improving quality, combined with increasing hospital and academic overhead charges in Canada and the strong Canadian dollar will continue to challenge Canada’s advantage in clinical research.33 Despite these challenges, Canada’s clinical research and R&D capacity has advantages in patient enrolment and networks connecting MNEs, biopharma SMEs, academia and research centres. Canada’s existing expertise and pipeline along with initiatives by academic research institutions that have areas of alignment with strategic directions of global MNEs, can position the Canadian industry to weather low cost competition in clinical research34. Roche’s decision to invest $190 million in a global clinical research centre in Mississauga is indicative of this capability35.

Canadian biopharma SMEs have one of the strongest R&D pipelines in the global industry with over 800 products, 50% of which are in the early R&D phase36. However, access to capital is the biggest hurdle to commercialization for biopharma companies and Canadian companies lack the financial and marketing capacity to endure the lengthy process from early research to commercialization37. The Canadian biopharma industry is comprised of a few large companies such as Valeant and Paladin and many small and early stage companies. In 2011, Valeant and Paladin Labs accounted for 75% of market capitalization of publically-traded biopharma companies38.

30 Industry Canada research
31 Provided by Industry Canada
32 ClinicalTrials.gov
33 Industry Canada research
34 Industry Canada research
35 http://www.roche.com/portal/ca/media_releases?siteUuid=re7234008&paf_gear_id=45200037&pageId=re7540115&synergyaction=show&paf_dm=full&nodeId=1415-6cd4b409c82c11e087c0f1249af7fc9
36 Industry Canada research
37 PharmaFocus 2012
38 Biopharma companies as defined in IMS PharmaFocus reports; definitions differ from Industry Canada’s in-house research
The Federal government’s investment in genomics research in the early part of the 2000s is often credited as a catalyst for the growth of the biotechnology industry and Canadian-based biopharma companies. During 2000 to 2007, Genome Canada invested more than $700 million across Canada and combined with other partners, Genome Canada motivated a total of $1.5 billion investing in 115 research projects.\textsuperscript{39} During these years, the infrastructure for Canada’s biotech industry was enhanced and well regarded. However over the past several years due to challenges within the global economy and the biopharma industry, the Canadian industry has struggled to transition SMEs and their early-stage research into viable commercial positions.

Biopharma SMEs are challenged in raising capital and cite the regulatory process as an added hindrance. The financial crisis and economic downturn compounded the headwinds for biopharma companies. By the end of 2008, 92 publically-traded biopharma companies in Canada had lost 80%-90% of their market capitalization. By 2011, the market capitalization of the top 30 publically-traded Canadian biotechnology companies increased by 18% over 2010, mainly from the rise in share prices of Valeant and Paladin Labs. Public-financing remains the dominant source of financing for biopharma companies in terms of dollar value. For example in 2011 companies raised $1.8 billion through public issuances compared to $130 million from venture capital.\textsuperscript{40} Biopharma SMEs in Canada have difficulty attracting venture capital because of weak returns from initial public offerings (IPOs) and cumbersome regulatory processes. Viability of the biopharma segment is estimated to require an investment of about $2-3 billion annually however the segment receives a fraction of this amount annually\textsuperscript{41}.

Many biopharma SMEs ceased to exist during the recent economic downturn. Those biopharma SMEs that weathered through the downturn reduced staff, sold research assets/products, ended programs and developed alliances/partners. Paladin Labs (which acquired VIRexx Medical) sold off some of its technology to weather against difficult financial market conditions. While rationalization in the biopharma segment means that surviving companies generally have stronger financial positions and commercialization prospects than previously, some experts in the industry believe the sector is weak and has a declining Canadian-based footprint, in part due to acquisitions. Ironically, for many Canadian biopharma SMEs the typical success path is to be acquired.\textsuperscript{42}

Alliances with MNEs provide biopharma SMEs with a cash infusion to maintain product development and an income stream to sustain operations and growth. For MNEs, alliances with, or acquisitions of biopharma SMEs with promising product pipelines are avenues to address their low pipeline productivity. Xenon Pharmaceuticals of Vancouver, BC is a leading example of this alliance model. The company, with its core business of drug discovery and development, has developed significant income-generating partnerships with global MNEs such as Roche, Novartis, Merck, Takeda and Teva. In 2012 alone, the company signed deals with Teva and Roche totalling $1 billion. This model recently led to the first novel gene therapy treatment approved in a developed market (orphan disease lipoprotein lipase deficiency)\textsuperscript{43}. Another example is the 2010 deal between Merck and Canada’s Alectos Therapeutics – a partnership providing Alectos with a cash infusion and in return, Merck acquired the worldwide, exclusive licensing arrangement to research, develop and commercialize Alectos’ Alzheimers product. Also recently, Angiochem based in Montreal entered into an exclusive licensing agreement with Geron, providing Angiochem with licensing fee revenues and Geron with exclusive licensing rights to Angiochem’s anti-cancer compound.

\textsuperscript{39} PharmaFocus 2012
\textsuperscript{40} PharmaFocus 2016
\textsuperscript{41} Based on discussions with industry advisors
\textsuperscript{42} BIOTEC Canada and PricewaterhouseCoopers Survey, 2011 as noted in PharmaFocus 2015 p407
\textsuperscript{43} Based on discussions with industry advisors and http://www.xenon-pharma.com/2013/02/xenon-receives-a-milestone-payment-for-marketing-approval-of-glybera-in-europe/
3.6 Coming Together to Survive: M&A’s and Alliances

Since the heightened period of the patent cliff in 2007, the global pharmaceutical industry has faced substantial revenue and cost pressures. Not surprisingly, the dramatic rise in the value of patent losses in 2007 coincided with a jump in the value of global pharmaceutical mergers and acquisition to $73 billion, up 28% from 2006.\(^4\) Amongst the 57 large value acquisitions in 2007 (global), 60% were acquisitions by MNEs and 42% of the companies bought were biopharma companies. The response to conditions in the global industry since 2007 has been an onslaught of mergers and acquisitions as companies sought to consolidate their cost base, expand research pipelines and broaden their geographic market reach. In 2008, in the midst of the patent cliff and the economic downturn, pharmaceutical MNEs accounted for more than 70% of high-value transactions in healthcare M&A (transactions exceeding $100 million)\(^45\). In 2008, there was a record of 36 major alliances involving pharmaceutical companies compared to more normal levels of 29-30 major alliances per year involving pharmaceutical companies, globally. Examples include:

- Genpharm, which was amongst the top 10 generic corporations in Canada as part of Merck Generics, was acquired by Mylan in 2007\(^46\).
- In 2007, Canada-based Apotex purchased Belgium’s Topgen E.S.V. to increase access in the European generic market.
- Ranbaxy, an India-based company is a top generic selling company in Canada came under the control of Japanese pharmaceutical company, Daiichi Sankyo in 2008.
- One of the top selling generic companies in Canada, Cobalt Pharmaceuticals (the Canadian operation of generic MNE, the Arrow Group) was acquired by US-based Watson Pharmaceutical Inc in 2009.
- In 2009, Merck acquired Schering-Plough and Pfizer acquired Wyeth. Both these acquisitions were motivated by the acquirers’ quest to enhance their underperforming product pipelines. The Merck and Pfizer acquisitions of Schering-Plough and Wyeth respectively lead to the reduction and consolidation of their Canadian facilities.

Mergers and acquisitions can provide scale advantages in targeted areas, access to large or growing markets and additions to product pipeline. For example, in 2010, one of Canada’s leading companies, Biovail acquired US-based Valeant. The acquisition was intended to improve their financial position and cost structure, and significantly expand their presence in key North America product markets. Upon completion, the combined company retained the Valeant name. The new Valeant is building its product pipeline through acquisitions, in part to counter declining sales and genericization of its key products. Another example of a global MNE acquiring the pipeline of a Canadian biopharma SME was the acquisition of Enobia Pharma by US-biopharma company, Alexion Pharmaceuticals in 2011. Montreal-based Enobia specialized in developing novel therapeutics for bone disorders and its enzyme replacement therapy (ENB-0040) received orphan designation in the US and the EU in 2008.

Starting in 2008 and throughout the financial market crisis, non-pharmaceutical players began to enter the pharmaceutical landscape. For example in 2008, 15% of high-value global M&A transactions in healthcare were acquisitions by non-pharmaceutical and non-biotech entities, a relatively high proportion. Prominent private equity firms include KKR

\(^4\) PharmaFocus 2012 p373
\(^45\) PharmaFocus 2013 p356
\(^46\) Genpharm’s name changed to Mylan in 2009
& Co, Carlyle Group and TPG Capital. KKR for example, acquired one of Germany's leading wholesale drug distributors Andreae-Noris Zahn ($522 million) in 2010\textsuperscript{47} and in 2011, purchased Capsugel, a dosage delivery product company from Pfizer ($2.4 billion)\textsuperscript{48}. Private equity firms or diversified conglomerates entered the pharmaceutical space when market valuations of pharmaceutical companies were relatively cheap, in part brought about by the patent cliff that reduced corporate earnings. To access capital during the economic downturn, some pharmaceutical companies sold the future revenue stream of their products to equity firms, further contributing to the rise of equity firms in the pharmaceutical industry.\textsuperscript{49}

4.0 **Canada’s Pharmaceutical Future Prospects 2013-2016**

4.1 **Medium Term Outlook of the Canadian Pharmaceutical Market**

The overall Canadian market is expected to experience on-going challenges and uncertainties until 2014 which will weigh on corporate performances. Conditions in the industry are expected to be brighter in the 2014-2016 period with annual forecasted growth ranging from 3% to 5%, doubling the sluggish growth forecast for 2012 and 2013. The compound average annual growth forecast for the 2012-2016 period is 2.8% with the brand and generic segments anticipated to grow at a similar pace.\textsuperscript{50} While this projected growth rate is encouraging compared to the last several years, Canada's growth will continue to lag those of emerging markets.

Market growth in Canada and in developed markets will continue to be outpaced by fast growing emerging markets (see Figure 8). China and Brazil, the largest emerging markets are anticipated to grow 13% and 17% annually in the medium term. Emerging markets will drive overall global expansion and they will continue to gain sales volume and market share. The value of the global market is forecasted to reach the $1 trillion in 2014.

\textsuperscript{47} PharmaFocus 2015  
\textsuperscript{48} PharmaFocus 2016  
\textsuperscript{49} PharmaFocus 2013  
\textsuperscript{50} PharmaFocus 2016 November 2012 Update
The two main positive drivers of growth in the medium term will be launches of expensive innovative and specialty drugs, and the expansion of access to primary healthcare services that will increase sales volume. The impact of the patent cliff will be less of a drag on Canadian market growth as the value of patent losses is expected to taper-off after 2012, stabilizing to below $500 million by 2017. In addition to the patent cliff, other key events anticipated to affect the medium term performance of the Canadian market include the end of Quebec's Bap-15 rule which provided formulary access of 15 years for brand products, and the breadth of generic pricing reforms by public and private payers. While generic pricing reforms announced by provinces have largely been implemented, more provinces may move towards broadly implementing 20%-25% generic pricing policies. In January of 2013, the provinces (except Quebec) collectively agreed to set generic pricing for six generic drugs to 18% of brand, as of April 1, 2013. Figure 9 shows the broader path of generic pricing, as currently planned by provincial policies.

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Source: IMS Market Prognosis, September 2012.

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51 IMS Market Prognosis 2012-2016, September 2012
52 The 2012 Ontario Budget had announced intentions to implement a policy to reduce the price of the top 10 generic drugs to 20% of their equivalent brand prices.
53 Provincial collaboration as part of the Health Care Innovation Working Group, of the Council of Federation - an intergovernmental secretariat comprising of Canadian premiers.
http://www.councilofthefederation.ca/pdfs/NR-CoF-Generic%20drugs%20(Final)-Jan%2018.pdf
Therapeutic growth will occur in areas of unmet clinical need, expensive specialty drugs and in innovative/novel mechanisms. IMS anticipates the leading products in the global market place will be specialty products and biologics in the area of oncology, autoimmune, antivirals, immunostimulants, immunosuppressants and multiple sclerosis. Through the first half of 2012 for example, 11 new molecular entities were launched in the global market, all of which are specialty products. Biologics will account for at least 17% of global sales by 2016, slightly higher share than the 15-16% in 2011. The Canadian market reflects this global therapeutic outlook. Currently, there are 93 active products in Phase III of Canada’s pipeline. Of these products, 39% are high-cost cancer and anti-tumor necrosis factor (anti-TNF) biologics. Figure 10 shows an estimate of future launches of new active substances, line extensions and new indications by therapeutic areas that will have significant impact in the Canadian market.

55 PharmaFocus 2016 November 2012 Event

Biologics treat a wide breadth of therapeutic areas and products considered biologics are also classified in under other therapeutic classes. For example, certain products in oncology and insulin classes are considered biologics.
Several biologic drugs will lose patent protection during the 2012-2016 period. Given the complexities of biologics, their manufacturing process and the regulatory requirements, subsequent entry biologics (SEBs or biosimilars) will experience slower market entry than traditional generic products. Since 2009, one SEB has been approved and launched in Canada – Novartis’s Omnitrope (somatropin). Several SEBs are already available in Europe where the pricing of these SEBs are 20%-30% lower than branded versions instead of the 90% pricing discount on generic versions of conventional branded drugs\textsuperscript{57}. These price points for SEBs are likely sufficiently attractive from a profit margin perspective for companies to pursue development of SEBs. IMS estimates the impact of SEBS will continue to be limited in the short term and become more significant in Canada beyond 2016\textsuperscript{58}.

### 4.2 Evolving Business Model of Industry

Companies will continue seeking opportunities to strengthen their core areas and allocate their resources to these areas and to growing markets. Consequently, companies will continue to expand outsourcing strategies, relying on CSPs or partners. At the same time, companies will seek market diversification to reduce risk. For example:

- Johnson & Johnson, the leading company in terms of sales in Canada, has indicated vaccines as a new area of focus: in 2011 the company acquired Dutch company Crucell which specializes in influenza vaccines. It is also focusing its R&D efforts on five main therapy areas: neuroscience, infectious disease (HIV/HCV), cardiovascular/metabolism, oncology and immunology. The company has established R&D facilities in fast growing markets of China and India.

\textsuperscript{57} PharmaFocus 2016, p316
\textsuperscript{58} PharmaFocus 2016
• Pfizer is positioning itself as a leader in oncology. Oncology is the dominant area in Pfizer’s pipeline and the company established a specialized Oncology Business Unit, with a significant interest in emerging markets. In 2010, Pfizer, Lilly and Merck established the Asian Cancer Research Group to focus on patients with lung and gastric cancer, the most common types of cancer in Asia. Pfizer is also increasing its involvement in generics, especially in emerging markets like China.59

Just as some brand MNEs have moved into generics and OTCs - for example Sandoz is the generic subsidiary of Novartis - generic MNEs have moved and continue to migrate into the branded space.
• Apotex is moving towards specialty hyperimmune products, largely attributed to its ownership stake in Cangene.60
• Teva plans to double branded revenues by 2015, partly to offset flat revenues and increasing competition in the generics sector. The company acquired Cephalon in 2011. Cephalon’s portfolio includes branded products in the CNS, oncology and pain management.
• Valeant is focusing its effort on dermatology and central nervous system classes. Valeant’s North American operations focus on orphan drugs in the specialty branded space. Its anti-epilepsy drug Potiga received NOC in Canada in 2012. Valeant’s other global operations focus on generics and OTC.

Global pharmaceutical companies are shifting production to emerging markets for cost savings and to gain access to fast growing demand in these markets. However, CSPs in Canada are attractive alternatives due to complex manufacturing processes for certain products as well as safety and legal liability concerns that necessitate proximity to the end market in Canada and the US. Nonetheless with intensifying international competition, CSPs based in Canada will seek to differentiate themselves in providing quality and through advantages of scale in their services to appeal to and meet demands of global MNEs. Some CSPs will move up the value chain and broaden to life sciences, healthcare services and products. Consolidation amongst CSPs is expected with global CSPs absorbing local CSPs, particularly those in manufacturing.

Canadian operations of global MNEs need to address strategies that ensure their position within the global corporate family in order to garner a bigger share of the investment pie. MNEs, whether they are brand manufacturers or global CSPs, weigh their investment decision based on revenue and profit as a function of pricing, market access and size, local advantages, resources and proximity to end users. For example, the Montreal manufacturing facility of Jubilant Life Sciences Limited (Jubilant DraxImage) is strategic to the company’s radiopharmaceutical unit in its proximity to nuclear resources.

Private equity firms and diversified conglomerates will become bigger players in the pharmaceutical space, funding new business models and financing product development. MNEs seeking to off-load low growth products outside their core areas represent opportunities for private equity firms and other conglomerates to purchase these assets and increase their presence in the pharmaceutical industry.

4.3 R&D Model

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59 IMS Company Profile - Pfizer, June 2012
60 Cangene is a publically-traded company. In 1995 Cangene merged with Apotex subsidiary Rh Pharmaceuticals.
Waning market growth coupled with strong growth in emerging markets may undermine Canada’s ability to attract higher levels of R&D investment from global MNEs. Pharmaceutical companies fund the development of new drug products with the profits from current products and future revenue stream. The returns to R&D investment required in pursuing product development are predicated by a product’s revenue potential. The commercial attractiveness of a product is influenced by the extent of uptake and utilization, price regulation, the degree of access to public and private drug plans and intellectual property policy. A recent retrospective study on a sample of older top selling brand products that recently ended exclusivity, observed that despite a shorter patent protection policy, Canada is an attractive market relative to the US and several EU countries. In this study, these brands retained a higher share of their sales after loss of exclusivity. Current free trade negotiations between Canada and the EU (CETA) may have implications on the attractiveness of the Canadian market thus potentially impacting the level of future R&D investment in Canada. The end of Quebec’s BAP-15 and on-going pricing controls from the PMPRB will also have repercussions on Canada’s ability to attract R&D investment.

Some companies in the Canadian industry are tapping into innovative avenues, alliances and partners to fund and reduce the cost risk associated with developing products and expanding their pipeline. Valeant is partnering with GlaxoSmithKline (GSK) to develop an epilepsy drug. Public-private-academic partnership in the drug discovery phase is another R&D model companies are adopting. In Quebec, the Consortium for Drug Discovery is attracting investment from MNEs. Novartis is partnering with the Population Health Research Institute (in Hamilton). Roche is working with Vancouver’s Centre for Drug Research and Development (CDRD). The CDRD is one of 22 federally-recognized national Centres of Excellence in Commercialization and Research. These centres, along with the federal program, Network of Centres of Excellence (BL-NCEs) offer research expertise, objective support and serve as an avenue for companies to reduce their R&D risk. AstraZeneca and Pfizer, in partnership with the Quebec government are participating in the creation of the Néomed Institute to stimulate research and commercialization of new drugs. Earlier in 2012, Merck announced investments in three Montreal research centres. Research partnerships are also spanning geography. Lorus Therapeutics, based in Toronto is partnering with Cancer Research UK to undertake clinical testing of a new cancer treatment (IL-17E). These international partnerships are both an opportunity for smaller Canadian companies to tap into global expertise but are reminders of the mobility of R&D investment. A supportive infrastructure for partnerships and research networks within Canada comparable to the level of support provided in other countries may strengthen the competitiveness of Canada’s research clusters, and the pharmaceutical industry’s ability to attract partners and project investments.

Some MNEs in the industry are also creating venture capital funds to ease the finance crunch faced by biopharma SMEs. For example, GlaxoSmithKline Inc. has created a $50-million GSK Canada Life Sciences Innovation Fund to invest in Canadian biotech projects. Since 2010, 20% of venture capital deals involving biotechnology companies involved pharma corporate venture capital funds; these deals averaged US$4M per investment. Fostering the Canadian biopharma sector that currently possesses a solid pipeline, as well as bridging the financing gap for these companies will lend support to R&D activities in Canada.

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61 The study is a comparison of market exclusivity period in Canada, the US, UK, Germany and France; conducted by IMS Brogan for Industry Canada.
62 Industry Canada research
63 http://neomed.ca/news/creation-of-the-neomed-institute/
64 PharmaFocus 2016
4.4 Health Care Trends that Will Shape the Industry in the Medium Term

In addition to factors discussed in the previous sections, this section highlights several broader trends that are expected to shape the outlook for pharmaceutical industry and the level of investment in Canada over the next several years.

Canada's position in the global industry
The importance of the Canadian pharmaceutical market is being eclipsed by the strong growth of emerging markets. Based on current trends, the Canadian market is on a falling trajectory out of the top 10 leading markets as such Canada’s clout as a global player is declining. Fast growing markets of China, Brazil, India and Russia are seemingly more attractive investments from the perspectives of global MNEs.

Market conditions: regulations and policy
Payers are exerting greater influence in pricing controls and in market access for expensive specialty drugs and therapies. The balance of power is shifting from pharmaceutical companies to healthcare providers and payers, as payers strive towards maximizing value to sustain their drug plans in the face of growing demand. The current pressure to reduce drug prices, particularly from deficit-challenged governments, will have major repercussions on the sale and development of new products. Several other policies by payers that will affect the industry include:

- In addition to further generic pricing reductions, confidential listing agreements with manufacturers and implementation of a national competitive bidding process in public drug plans for a handful of selected multi-source products.
- Real life outcomes for products listed will shape how far payers are willing to reimburse certain products (pay-for-performance model).

Regulatory pathways regarding subsequent entry biologics (SEBs) will impact the extent to which SEBs are developed and launched, and impact the number of players in this space. In Canada, SEBs cannot be declared as interchangeable with an original biologic. SEBs are subject to data protection legislation and require registration through the new drug submission route as well as new clinical trial data. In the US, the FDA issued guidelines in February 2012 providing new biotech drugs a 12-year period of exclusivity and requiring generic manufacturers to submit extensive chemical and biological testing data.

Federal and provincial policy and regulations can enhance or detract from the business climate for the Canadian pharmaceutical industry. Decisions and interpretations by Health Canada, the Patented Medicine Prices Review Board and provincial regulatory bodies affect the attractiveness of the Canadian market and consequently the investment decisions of global companies. Governments support the industry through mechanisms such as tax incentives, subsidies and market access arrangements. In recent years, program support for the industry has been geared towards specialty areas and biotech products. However the dollar values of these investment incentives are small relative to investments by governments in other countries. An increase in government policy supporting R&D may further strengthen Canada’s expertise in niche areas within biologics and oncology.

Changing nature of medicine research and delivery
Personalized medicine research is expanding rapidly around the globe. In Canada, federal and provincial governments are supporting this area through funding commitments. In February 2012, Canada announced a significant $67.5 million funding boost for its personalized medicine sector. Developing personalized medicines is
resource-intensive, requiring companies to leverage multiple partners. Because of the high development risks associated with personalized medicines, investment incentives will play an even bigger role in influencing investment decisions in Canada.

5.0 SWOT Analysis of the Canadian Industry

SWOT analyses are usually done across two dimensions – environmental factors that are internal to a firm and external factors to that same firm. This SWOT analysis is applied at an industry level so the internal factors classified as strengths or weaknesses will be at the industry level while external factors classified as opportunities or threats will be along the broader operating environment for the industry in Canada. This SWOT analysis considers these factors for the four segments of companies within the pharmaceutical industry in Canada.

Strengths

- Canada remains a significant market, with drug consumption and drug prices still quite high in global rankings.
- Canada’s primary strength is in the talent of its workforce, a key criterion for R&D or manufacturing investment decisions.
- Canada has globally recognized strengths in having research talent to carry out clinical trials. Canada has significant existing clinical research infrastructure and several provinces are taking steps to further enhance the clinical trial climate.
- Effective government incentive programs, such as Industrial Research Assistance Program (IRAP), SR&ED and others, have generated a diverse set of biopharma SMEs with robust early stage pipelines and productive discovery platforms.
- World renowned research expertise in oncology, CNS and stem cells.
- Long-standing, proven strength in the development and manufacturing of vaccines.
- Significant infrastructure and expertise in manufacturing complex products, such as sterile injectables, complex small molecules, and (on a small scale) biologics.
- Long history of established, high-quality generics manufacturing which generates significant export.
- Canada's relative economic stability versus the US, the EU, and especially the high growth emerging markets like China and India.

Weaknesses

- Forecast of market growth for Canada lags considerably behind other competing countries.
- Clinical trials costs in Canada are rising rapidly compared to other countries.
- Access to large longitudinal databases is limited by privacy and coordination issues.
- Declining R&D activities in Canada by global MNEs has weakened the research environment.
- Canada’s skilled talent pool is not uniformly distributed across all regions, segments, and specialties of the industry, resulting in shortages of available talent in areas such as large-scale biologics manufacturing.
- Canada's major innovation incentive (SR&ED) is often difficult to access by Canadian business divisions of global MNEs, and does not address the changing model of innovation in the industry.
• Canada lacks the critical mass of Canadian-based MNEs to drive the industry/commercialization.

• Canadian commercialization incentives, while effective in supporting early growth of biopharma SMEs, can be insufficient to carry those same SMEs to market readiness, resulting in an "innovation gap".

• The overall risk capital pools available to Canadian SMEs is risk averse and often insufficient to carry products to market, requiring Canadian SMEs to either partner or sell assets to global MNEs.

• MNE manufacturing currently has limited biologics capability in Canada.

• The Canadian drug market alone is insufficient to financially support or justify the full development costs of a pharmaceutical product.

Opportunities

• Focus on areas of growth such as biologics, biosimilars, specialty/orphan diseases, and companion diagnostics. Canadian capabilities are aligned with areas of focus of global MNEs: oncology, targeted therapeutics and vaccines. Canadian policy and a favourable business climate can seed the ability of these segments to benefit from this growth.

• Tap into licensing and co-development arrangements. Canadian biopharma SMEs have strong discovery/early stage pipelines that are attractive to MNEs. SMEs can benefit from MNEs’ new model of relying on other companies to discover and develop molecules and then in-licensing this innovation. The extensive network of public-private partnerships and public research networks in Canada are well positioned to leverage this new research model.

• Capture a greater share of global contract service business as MNEs continue to contract out major business functions.

• Canadian companies can look to markets such as China, India and Brazil to partner on co-development, gain greater market access and distribution, and to offer a wider range of contract services. In particular, Chinese companies are not well versed in the R&D process and are looking for foreign partners to assist. Companies such as Sinopharm have rapidly grown through aggressive M&A and are also turning their attention to developing innovative products, for which they will need foreign partners who are experienced in these capabilities. Similarly, companies in India are seeking to in-license products for their local Indian market.

• Canadian generic companies can service fast-growing countries where millions of newly middle-class people can now afford medications.

• Canadian generic companies can focus towards becoming a leader in the SEB space, in particular developing and producing high cost, low volume SEBs.

• Build on Canada’s strength and improve the cost advantage of clinical research. Seize this opportunity through well-linked electronic medical records and databases of patients to inform clinical trial design and speed up the patient enrolment process. Canadian policy can also assist by consolidating ethics and legal requirements to avoid duplication.

• From a policy perspective, Canada can lead the world in implementing regulatory changes in growth segments such as biosimilars and companion diagnostics.

Threats

• New business model for branded MNEs may present challenges to Canada’s healthcare system; challenges such as significantly higher prices per drug, unclear pathway for companion diagnostics, growth of SEBs and orphan drugs.
• Foreign CSPs have been consolidating and creating arrangements with brand and generic MNEs to expand their global reach. Regional Canadian players risk being excluded from partnering opportunities or being acquired if they are not able to compete globally.

• As new CSPs from emerging markets mature and become more competitive they will directly compete with Canadian companies.

• Low market growth along with unfavourable policy framework ranging from regulatory approval process to market access and IP protection make Canada less attractive for commercial investment.

• Competing countries are deploying aggressive tactics to attract industry investment. The availability of funding and programs to directly incent MNEs’ R&D and manufacturing investment in Canada is low compared to some competing locations.

• Financial implications from the patent cliff and M&A activities may not be over, with potential for further rationalization of operations.

• Provincial plans to tender multi-source drugs at lower prices could further weaken the generic sector.

• A new CETA between Canada and the EU might not extend the effective patent period in Canada compared to other developed countries thus lowering the investment appeal to MNEs but may retain the generic manufacturing base.
### Long-Term Outlook Positive in Canada, Led by Brands and Generics

Forecast of Total Market Purchases at Actual Prices (Brand and Generic), 2011, and 2012 to 2016 Forecast Update

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Brand Market</td>
<td>$16.78</td>
<td>$16.94</td>
<td>$17.03</td>
<td>$17.92</td>
<td>$18.55</td>
<td>$19.26</td>
</tr>
<tr>
<td>% Growth (+/- 1.5%)</td>
<td>+0.6%</td>
<td>0 – 1%</td>
<td>-0.5 – 1.5%</td>
<td>4 – 6%</td>
<td>3 – 4%</td>
<td>3.5 – 4.5%</td>
</tr>
<tr>
<td>Generic Market</td>
<td>$5.38</td>
<td>$5.38</td>
<td>$5.48</td>
<td>$5.58</td>
<td>$5.87</td>
<td>$6.16</td>
</tr>
<tr>
<td>% Growth (+/- 1.5%)</td>
<td>-5.3%</td>
<td>-1 – 0%</td>
<td>1.5 – 3.5%</td>
<td>1 – 3%</td>
<td>5 – 6%</td>
<td>5 – 6%</td>
</tr>
<tr>
<td>Total Market</td>
<td>$22.16</td>
<td>$22.31</td>
<td>$22.51</td>
<td>$23.50</td>
<td>$24.42</td>
<td>$25.42</td>
</tr>
<tr>
<td>% Growth (+/- 1.5%)</td>
<td>-0.9%</td>
<td>0 – 1%</td>
<td>0 – 2%</td>
<td>3 – 5%</td>
<td>4 – 5%</td>
<td>4 – 5%</td>
</tr>
</tbody>
</table>


### Payers seeking lower cost medicine continues to shift share to generics

Prescription Volume Market Share – Brand versus Generic, 2005 to 2011 and YTD August '12

<table>
<thead>
<tr>
<th>Year</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>YTD August 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRx Market Share – Brand Sector</td>
<td>56.1%</td>
<td>54.9%</td>
<td>51.7%</td>
<td>48.2%</td>
<td>45.3%</td>
<td>42.7%</td>
<td>40.0%</td>
<td>37.8%</td>
</tr>
<tr>
<td>TRx Market Share – Generic Sector</td>
<td>43.9%</td>
<td>45.1%</td>
<td>48.3%</td>
<td>51.8%</td>
<td>54.7%</td>
<td>57.3%</td>
<td>60.0%</td>
<td>62.2%</td>
</tr>
</tbody>
</table>


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Canada’s Pharmaceutical Industry and Prospects
Pharmerging market share will increase to 30%, their investment appeal will only grow

<table>
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<tr>
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<tbody>
<tr>
<td>United States</td>
<td>11%</td>
<td>11%</td>
</tr>
<tr>
<td>Canada</td>
<td>11%</td>
<td>11%</td>
</tr>
<tr>
<td>EU5</td>
<td>19%</td>
<td>8%</td>
</tr>
<tr>
<td>Rest of Europe*</td>
<td>35%</td>
<td>21%</td>
</tr>
<tr>
<td>Japan</td>
<td>1%</td>
<td>2%</td>
</tr>
<tr>
<td>S. Korea</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Pharmerging Tier 1 (China)</td>
<td>3%</td>
<td>7%</td>
</tr>
<tr>
<td>Pharmerging Tier 2</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Pharmerging Tier 3</td>
<td>4%</td>
<td>1%</td>
</tr>
<tr>
<td>Rest of World</td>
<td>8%</td>
<td>11%</td>
</tr>
</tbody>
</table>

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<tr>
<th>2016 Market Share, US$</th>
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</thead>
<tbody>
<tr>
<td>United States</td>
</tr>
<tr>
<td>Canada</td>
</tr>
<tr>
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<tr>
<td>S. Korea</td>
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<tr>
<td>Pharmerging Tier 1 (China)</td>
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<tr>
<td>Pharmerging Tier 2</td>
</tr>
<tr>
<td>Pharmerging Tier 3</td>
</tr>
<tr>
<td>Rest of World</td>
</tr>
</tbody>
</table>

*Rest of Europe excludes Russia, Turkey, Poland, Romania, Ukraine, which are included in Pharmerging Tier 3: Argentina, Egypt, Indonesia, Mexico, Pakistan, Poland, Romania, South Africa, Thailand, Turkey, Ukraine, Venezuela, Vietnam.

Appendix 2: Description of IMS Data Sources

The analysis in this study draws upon proprietary IMS Canadian and global sources and databases.

**IMS Knowledge Link®**
IMS Knowledge Link integrates global pharmaceutical business intelligence in a unique web-based system and is designed to facilitate market research activities at all levels.

IMS Knowledge Link offers a distinct advantage; enables users to gather a wealth of information from one place instantaneously:

- Evaluate the progress of over 9,400* drugs in active R&D pipelines from pre-clinical phase to Phase III and review registered and recently marketed products (* at January 2006).
- Analyze global and national sales data and trends for over 2000 pharmaceutical companies, over 320 therapeutic classes, 4,500 launched products and 38 country profiles.
- Gain a detailed insight into over 120 major pharmaceutical companies at a strategic and local level including interviews with key company executives, full strategic analysis, product and R&D reviews, company financial data, mergers and acquisitions and forecasts from leading pharmaceutical analysts.
- Review patent protection in 9 major countries for over 1,800 molecules and anticipate the impact of patent expiry.
- Over 45,000 patent records, covering over 3,000 molecules in 9 major countries.
- Launch information for the top 15 products in ALL therapy areas in up to 70 countries.
- Monitor industry news every day from Reuters Health and review R&D news on a weekly basis.
- Industry and R&D news from 35,000 stories from IMS archived since 1995, updated weekly and a rolling 12-month archive from Reuters Healthcare News, updated daily.

**IMS Pharmafocus®**
IMS Pharmafocus provides insights about Canadian politics and health care, government reform initiatives and regulatory changes in addition to current business and pharmaceutical marketing issues.

**IMS Company Profiles®**
IMS Company Profiles provides information to support understanding of company structure, strategy, financial results, research and development program, product portfolio, and major events. Information is sourced from interviews with key executives of the company, stock analyst forecasts and commentary, and published information.

**IMS World and Country Review®**
IMS World Review and the IMS Country Review provides comprehensive insight on performance trends of major pharmaceutical companies, markets, therapeutic areas and classes. IMS World Review provides information about market trends and offers breakdown of sales by country, by therapy classes and products.

**The Canadian Drug Store and Hospital Purchases Audit®**
The IMS Brogan Canadian Drug Store and Hospital Purchases audit is a syndicated source of drug purchasing patterns in Canada. The CDH contains national and provincial estimates of sales volumes of dollars and units of pharmaceutical products purchased by retail pharmacies and hospitals.
Pharmaceutical products including Rx and OTC products as well as some diagnostic products are tracked through the CDH. The CDH tracks purchases made by drug stores and hospitals from the manufacturer (direct sales) or from drug wholesalers (indirect sales). The CDH is available monthly and includes a rolling 71 months of history. Detailed information from product form/strength to molecules to manufacturer to markets. The CDH is also included in the IMS Health international MIDAS database used by pharmaceutical companies around the world.

CDH purchase dollars and units are presented by retail, hospital, and total purchases at the following levels:

- Therapeutic Class (USC) - market
- Manufacturer
- Product
- Product package (SKU) – form strength and pack
- Purchase dollars reflect the invoice price paid by drug stores and hospitals.
- CDH is dynamic and will therefore reflect transfers and history corrections.
- Returns are captured and entered in the current month.

Information is gathered and crossed referenced from several sources:

- Government records
- New releases
- Pharmaceutical manufactures
- Data suppliers (pharmaceutical wholesalers & distributors)
  - Validated by the IMS Brogan Statistical Department
  - Validated with other IMS Brogan datasets.

**IMS Lifecycle®**
IMS Lifecycle combines three of the world’s most powerful pharmaceutical databases into one platform, giving you insight into drug strategies at three critical and defining stages of the drug’s life cycle: R&D, launch activity, and patent expiry. IMS LifeCycle comprises the following three IMS databases under one common interface:

- R&D Focus
- New Product Focus
- Patent Focus

IMS LifeCycle contains:

**R&D Pipeline information**: Profiles of 29,000 drugs in R&D with 9,300 drugs in active development, updated weekly

**Launch information**: Over 300,000 profiles of local products launches with local trade names and local launch dates, recorded since 1982 and updated monthly

**Patent Information**: Over 4,600 drug patent families with over 85,000 patent records with expiry and extension dates, updated monthly.

**IMS PharmaQuery®**
PharmaQuery is IMS’s online research tool designed to unravel the complexities of pricing and reimbursement. It provides detailed information on the rules and regulations, theories and practices, trends and developments, in pricing and reimbursement worldwide.

PharmaQuery has four distinct services:

- **Pricing and Reimbursement Systems**: comprehensive database of healthcare systems in key world markets, including detailed pricing and reimbursement regulations, updated annually.
- Healthcare System (Facts & Figures, Provision & Funding)
- Pricing (Prescription Drugs, Generic Drugs, Hospital, Drugs, OTC Drugs)
Reimbursement (Admission to Reimbursement, Reimbursement Categories, Reimbursed Prices, Hospital Reimbursement, Changes in Reimbursement Status, Changes in Reimbursement Pricing)
Pharmaeconomics (Pharmaeconomic Requirements)
Price Build Up (Wholesalers, Retail Pharmacies, Dispensing Doctors, Sales Tax)
Cost Containment (Industry Paybacks, Promotional Costs, Patient Co-payments, Prescribing Controls, Generics, Rx-to-OTC Switches, Parallel Trade)
Future Developments (Outlook)
Additional Resources (Names & Addresses, Terminology, Links, Flowcharts, Tables, Background)

Pricing and Reimbursement News: weekly news service delivered direct to your desktop, hyperlinked throughout the site to related News stories and background information in PharmaQuery Systems. Archived back to over 6,000 fully searchable News stories dating from 1998.

Pricing and Reimbursement Benchmarks: Comparative facts and figures on key pricing & reimbursement indicators across 31 countries.

Monthly Pharma Pricing and Reimbursement Magazine: news, views and analysis of international developments in the world of pharmaceutical pricing and reimbursement.