Healthcare 2020
Japan’s pathfinder role in the global healthcare industry

Chris Beaumont
Regional Director,
North Asia,
Results International
Contents

Healthcare provision is experiencing a revolution ................................................................. 1

Large Pharma in fundamental Flux .............................................. 5

The case for change has been well-known for a while .......................................................... 6

Refocusing Pharma R&D: from large to small patient populations and rare diseases ............. 7

Patent cliff and the rise of generics .............................................. 7

A future model for drug research will be an increase in public-private partnerships ............... 7

A bigger role for generics ........................................................... 8

Rise of emerging markets and their role in driving growth .................................................... 8

Possible future structures .......................................................... 8

Global perspectives: The role of Japan ........................................ 9

Healthcare 3.0 has to be on all our agendas – connecting professionals, patients and people .................................................................................. 13

The Role of M&A in the Healthcare Revolution ................................................................. 13

About the author .......................................................................... 14
Healthcare provision is experiencing a revolution

The health systems of nations around the world will rapidly become unsustainable if they fail to adapt to the needs of their consumers, innovation and the necessity of providing cost effective solutions. Over the next decade, these demands, if ignored, will overwhelm the health systems, creating massive financial burdens for individual countries and leading to devastating health problems for the individuals who live in them. In a world in which economies are globally interdependent and the productivity of nations relies on the health of its citizens, the sustainability of the world’s health systems is a national competitive issue and a global economic imperative. With the need for new business solutions, transactions including M&A and licensing are likely to have an increasing role in effecting the transformations in healthcare necessary to respond positively to these changing demands. Indeed, Ernst & Young’s recent ‘Firepower Index’ anticipates M&A activity will increase at a time when Large Pharma are facing more competition and complex deal structures as they try to address a projected $100 billion growth gap.

Globally, healthcare is threatened by a confluence of powerful trends and in many respects Japan (which is the second largest national healthcare market after the US, with a gross annual spend in 2011 of approximately $559bn, representing about 8.5% of GDP) is at the forefront of many of these changes.

Japan is seeing the impact of:

- increasing demands (most rapidly ageing demographics; personalised medicine; prevention medical intervention; environmental impacts);
- rising costs and healthcare inflation;

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1 Statistical Handbook of Japan, Ministry of Internal Affairs and Communication, Statistics Bureau

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Figure 1
The cost of a long life
paying for new healthcare approaches (innovative treatments, personalised medicine; preventive medical intervention);

- new cross-border challenges and solutions (pandemics; medical tourism).

While other nations are also grappling with:

- mis-aligned incentives (individual national payer priorities; philanthropy; insurance payers);
- inconsistent quality (emerging economies).

One consistent global lesson that has emerged is consumerism with medical providers reorganising themselves in a patient-centric continuum through care management approaches. Payers are developing consumer-oriented benefits plans. Pharma and life sciences companies are using new pharmacogenomic discoveries to pursue personalised medicine. This coupled with the increased deregulation and new choices will provide new opportunities for marcoms specialists to create meaningful, new brand franchises.

IBM Healthcare has begun to define and assess value, changing perspectives across healthcare systems, particularly those with entrenched stakeholders. To address this new dilemma, they offer a well-known construct for healthcare systems to explain, balance, and resolve different levels of healthcare needs. Their construct, the “Hierarchy of Healthcare Needs Model,” was adapted from Maslow’s well-known “hierarchy of needs” model in psychology, which explains why people are driven by a particular need at a given time.

The macro-level implications of an ageing population also have fundamental implications for the sustainability of national healthcare systems in developed and developing countries alike, and are increasingly likely to strain existing infrastructures, as well as rely on transformational technological advances. In particular, in developed countries over the last twenty years there have been a need for new healthcare service provision solutions in light of the ageing of hospital infrastructure, and a need to invest to reap the benefits of capital investment in medical equipment and data/telecom. The need to deliver innovation and service, is a key driver for investment and disinvestment decisions across the industry.

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**Figure 2**
Hierarchy of Healthcare Needs Model

**Figure 3**
Overall number of active compounds in the pipeline; Citeline 2012

**Figure 4**
Five competitive forces interact to shape strategy
It has been some 33 years since Porter’s seminal Harvard Business Review paper on ‘how competitive forces shape strategy’, and his five forces (Figure 4) are a straightforward way to define the evolving healthcare industry structure and shape the nature of competitive interactions and resulting ROIs. The extent of the on-going healthcare transformation is reflected by accelerating activities across all forces, magnified by heightened globalism.

Large Pharma in fundamental Flux

The major Pharma companies (“Large Pharma”) have traditionally relied on the sales of patent protected blockbuster drugs – drugs that sold more than $1 billion annually and targeted large patient populations. For many companies, it was the sales of a crucial few blockbuster drugs that drove profitability. However, since the 1990s there has been a rapid decline in Pharma R&D productivity that happened in parallel with a steep rise in the cost of R&D for new drugs aimed at large patient populations. This is coupled with a resistance by payers to pay for incremental changes and reward real innovation. As a result, Pharma companies needed to develop new ways to reduce the costs and risks associated with developing new medicines as well as decrease their exposure to the inherent uncertainty in the discovery and development of blockbusters.

One approach to reduce risks was to refocus discovery initiatives. This has generally refocused R&D from large populations with some medical solutions to smaller patient populations with higher unmet medical needs. A notable example of this is oncology. The nature of therapeutics has evolved from chemistry and small molecules to the discovery and development of large amino acid based molecules (e.g. proteins including antibodies and peptides). There has been a broader adoption of ‘open innovation’ either through explicit collaborations in non-competitive areas, in order to share costs and mitigate R&D risks. There have also been more explicit attempts to collaborate in the discovery and development of new drugs, beyond the licensing of biotech-discovered development compounds and subsequent co-development and commercialization, to more fundamental research collaborations such as that announced in December 2012 when Eisai Co. and University College London have agreed to jointly develop drugs to treat neurological diseases including Alzheimer’s and Parkinson’s. This is an example of a Japanese company doing fundamental drug discovery research with a London university.

This exemplifies an evolution from an internal and closed platform to embracing external research collaborations and/or acquisitions of research capabilities and drug pipelines. A second strategy is to embrace the loss of patient cover for major drugs including blockbuster and diversify into generics and over the counter (OTC) products (many of the leading international Pharma companies have generic and OTC divisions; e.g. Novartis, Sanofi, GSK, Bayer and Pfizer). With the ongoing pressures on pipelines and healthcare budgets it is likely that the implementation of strategies and tactics which address these pressures will be a feature of Large Pharma businesses in the foreseeable future.

Table 1
Top-10 companies by Pipeline size 2012; Citeline

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<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>1 (2)</td>
<td>GlaxoSmithKline</td>
<td>257 (269)</td>
<td>147</td>
</tr>
<tr>
<td>2 (1)</td>
<td>Pfizer</td>
<td>225 (284)</td>
<td>152</td>
</tr>
<tr>
<td>3 (3)</td>
<td>Merck &amp; Co</td>
<td>223 (236)</td>
<td>150</td>
</tr>
<tr>
<td>4 (4)</td>
<td>Novartis</td>
<td>218 (200)</td>
<td>151</td>
</tr>
<tr>
<td>5 (5)</td>
<td>Hoffmann-La Roche</td>
<td>198 (183)</td>
<td>147</td>
</tr>
<tr>
<td>6 (6)</td>
<td>Sanofi</td>
<td>178 (182)</td>
<td>91</td>
</tr>
<tr>
<td>7 (12)</td>
<td>Takeda</td>
<td>149 (13)</td>
<td>80</td>
</tr>
<tr>
<td>8 (9)</td>
<td>Bristol-Myers Squibb</td>
<td>146 (149)</td>
<td>113</td>
</tr>
<tr>
<td>9 (8)</td>
<td>AstraZeneca</td>
<td>114 (167)</td>
<td>85</td>
</tr>
<tr>
<td>10 (7)</td>
<td>Johnson &amp; Johnson</td>
<td>142 (171)</td>
<td>85</td>
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</table>
The case for change has been well-known for a while

A now famous report published in 2002 (2012: Preparing Today for the Challenges in the Decade Ahead: SDG Life Science Practice: envisioning “the good, the bad and the awful”, for the Pharma industry a decade later), described the dire R&D situation facing Pharma companies. Despite having suggested the need for fundamental changes, the industry today most closely reflects “the awful” case scenario.

R&D costs to launch a new drug have more than doubled in this millennium. This was in part due to a higher bar for regulatory approval based on safety concerns, and the fact that the low-hanging fruits – the easily discoverable drugs – have already been developed. One consequence is that the number of new drug applications submitted to the FDA has declined significantly. Moreover, innovators often concentrate their efforts on products with potentially high market returns. However, if the costs and difficulties of medical product development continue to escalate, innovation will stagnate or decline. The situation is compounded by the reluctance of payers to, in the opinion of the Pharma companies, adequately reward true innovations, particularly when the increasing likelihood of failure to get a new product to market is considered. A particular challenge for Pharma companies is the unpredictability of innovation and the need to take a risk adjusted view of discovery and have a number of discovery and developmental projects ongoing in parallel. However, in 2012 the FDA approved 39 new molecular entities for marking in the US, up from 35 in 2011. Also, drug development pipelines are generally believed to be richer with an estimated potential value of $64bn, more than enough to offset recent loses from patent expirations.

Figure 6
Pharmaceuticals 2012

<table>
<thead>
<tr>
<th>Innovation</th>
<th>“Good”</th>
<th>“Bad”</th>
<th>“Awful”</th>
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</thead>
<tbody>
<tr>
<td>Genomics targeted therapies drive growth</td>
<td>Genomics revolution does not translate into therapies</td>
<td>R&amp;D cut back</td>
<td></td>
</tr>
<tr>
<td>New diagnostic tools</td>
<td>R&amp;D productivity stagnant</td>
<td>Focus on diagnostic and preventive therapy</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medical Decisions</th>
<th>“Good”</th>
<th>“Bad”</th>
<th>“Awful”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personalised medicine based on individual profiles</td>
<td>Increasing empowerment of patients, more DTC marketing</td>
<td>Tight reimbursement constraints of therapeutic choices</td>
<td></td>
</tr>
<tr>
<td>Target groups of similar physicians for highly specialised therapies</td>
<td>Optional lifestyle drugs</td>
<td>Preemptive care at the expense of other treatments</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Regulatory Environment</th>
<th>“Good”</th>
<th>“Bad”</th>
<th>“Awful”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smaller or unconventional trials</td>
<td>Rising regulatory hurdles</td>
<td>Shift in focus from efficacy to safety data</td>
<td></td>
</tr>
<tr>
<td>Clinical trials simulation</td>
<td>Global harmonisation</td>
<td></td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Drug Pricing</th>
<th>“Good”</th>
<th>“Bad”</th>
<th>“Awful”</th>
</tr>
</thead>
<tbody>
<tr>
<td>New treatments command high prices</td>
<td>Genomics continue to put pressure on patents and prices</td>
<td>Massive price erosion in US</td>
<td></td>
</tr>
<tr>
<td>Breakthrough cures change negative public atmosphere</td>
<td>Consolidation slows price erosion but cannot stop it</td>
<td>Global acceleration of generics</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Business Model</th>
<th>“Good”</th>
<th>“Bad”</th>
<th>“Awful”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reversal of consolidation trend</td>
<td>Focus on a few therapy areas</td>
<td>Genics dominate most areas</td>
<td></td>
</tr>
<tr>
<td>Proliferation of specialists</td>
<td>Rapid consolidation of industry</td>
<td>Aggressive cost controls</td>
<td></td>
</tr>
<tr>
<td>Availability of venture capital</td>
<td>Tight capital market</td>
<td>Financial distress prevalent</td>
<td></td>
</tr>
</tbody>
</table>

Figure 7
The R&D Process: Long, Complex, and Costly
(Source: Impact of Healthcare policy on the economy; Healthy Healthcare Lecture VI, October 2009, Ira Wolf, Japan Representative, Pharmaceutical Research and Manufacturers of America)
Another way to mitigate these soaring costs and enhance pipelines is to achieve economies of scale through M&A, as organic growth options are limited. For Pharma companies, successful acquisitions can allow the acquiring company to extend beyond their geographical and product base, broadening their franchises by accessing new and emerging markets. This strategy has been successfully embraced over recent years by pharmaceutical companies, with emerging markets now worth as much as the EU in revenues but critically growing more strongly. Over the last 20 years there has been ongoing and considerable consolidation in the industry. By 2007 this had increased the market share of the top 10 Pharma companies to almost 50 percent of the world’s drug market.

Refocusing Pharma R&D: from large to small patient populations and rare diseases

This R&D productivity crisis has forced Pharma companies to re-evaluate aspects of their business model. They have long focused their innovation efforts on blockbuster drugs that would address the needs of large patient populations, in many cases based on the incremental improvement of established therapeutically proven drugs. However, the development of blockbuster drugs is expensive because quantitatively establishing a new drug’s superiority over existing drugs is usually very difficult, especially in an area already well addressed with effective therapies and thus required larger clinical trials to demonstrate clinical benefit in a statistically robust manner.

At the same time, there was greater attention given to bioPharma drugs, as the number of approved bioPharma drugs increased rapidly. It was evident that in comparison to more traditional R&D, bioPharma research offers ways of addressing certain disease mechanisms which are not accessible with small molecule based therapeutics. These large molecule based drugs had the added advantage of being more difficult to copy because of the added intrinsic manufacturing complexities associated with these molecules. Thus, Pharma companies have been investing in bioPharmas. They have either established internal bioPharma capabilities themselves, and/or pursued acquisitions of bioPharma companies (e.g AstraZeneca’s acquisitions of CAT and MedImmune).

At the same time many blockbuster patents are close to expiration – the so-called patent cliff. This has naturally created a rapid rise in generics and the industry structure was further changed by a growing realisation of the increasing importance of emerging markets.

Patent cliff and the rise of generics

When a patent expires, generic versions of a drug generally rapidly erode a blockbuster’s sales. The competition posed by generics is considered to be especially severe in America where the use of generics is widely accepted. Even in Japan, where the current level is low at around 20%, it is the government’s stated intent that the proportion of generics should increase materially.

The “patent cliff” peaked in 2011-2012, and it was expected that Pharma companies would face the loss of $140 billion in annual sales due to patent expiries by 2016 – as much as 20% of the world drug market. All major Pharma companies would be severely affected. For example, Merck faced generic competition for three of its top selling products, which represented 44% of the company’s revenue.

A future model for drug research will be an increase in public-private partnerships

As a consequence of the shift to Open Innovation, there have been more new types of partnership. Pharma companies have been very interested in partnering with leading research universities around the world. For example, Pfizer in 2008 announced a $25 million initiative with Washington University, to collaborate more closely in the area of biomedical research. A greater R&D role is now played by academic institutions. Open Innovation is much more mature in the US, because of the early passing of the Bayh-Dole Act in 1980. The equivalent in Japan was only enacted in 2001.

For example, since the 1980s MIT’s Langer Lab has spun off a number of companies with products that treat heart disease, cancer, schizophrenia, and diabetes, among other diseases. The Langer Lab is on the front lines of translational research turning discoveries made in the lab into a range of drugs and drug delivery systems. Dr. Langer has helped start 25 companies and has 811 patents, issued or pending, to his name. This is not too far behind Thomas Edison, who had 1,093. More than 250 companies have licensed or sublicensed Langer Lab patents. Polaris Venture Partners, based in Boston, have to date invested $220 million in 18 Langer Lab-derived businesses.

While Pharma companies employ large R&D teams, they may not be as freewheeling and flexible. The basis for many long-range discoveries has “come out of academia, including gene therapy, gene sequencing and tissue engineering”, according to Langer, who recognised that the large size of Pharma groups
can be an “impediment”, as innovation often needs to go against prevailing wisdom. What Pharma companies do particularly well are the running of research and clinical development programmes, gaining regulatory approval for their products, as well as marketing and supplying the drugs to patients. Access to non-Pharma innovations is now through a combination of first the licensing of IP and subsequently the acquisition of the licensor. This pattern is replicated in the Pharma and medical devices sectors.

A bigger role for generics

Health insurance payers and governments around the world saw the use of low-cost generics as central to healthcare cost containment, and thus have been actively promoting the use of generics. Compounding the drought in new drugs, the erosion by generics is the most profound in the US, where almost 70 percent of Pharma drugs prescribed in 2008 were generics. According to a recent Pharmexecil report, the 2012 share of generic products in the Japanese market stood at 9 percent by value and less than 21 percent by volume (compared to 17 percent in 2010). The government had been targeting a level of 30 percent, but it is acknowledged that the failure to achieve this level reflects a reluctance of both patients and doctors alike, as well as slow changes in the regulatory environment. A recent relaxation in laws relating to clinical trials and bioequivalence studies by the Japanese government, allowing for the approval for a drug even if these studies are conducted on Asian populations in place of the existing Japanese-only condition, may make it easier for generic drug makers to export their products in the near future. In a recent Barclay’s global Pharma report, it was shown that both Lupin and Cadila have a significant presence in the Japanese generics market. Lupin’s acquisition of a Japanese company and Ranbaxy’s cross border deal involving its takeover Daichi Sankyo had helped their market entry. Moreover, Dr Reddy’s Laboratories Ltd had formed a joint venture with Fujifilm to jointly produce and market generic drug products in Japan.

Historically, research-orientated Pharma firms avoided low-profit drugs like generics. It is difficult to mesh the high margin patent protected business model with the lean production and sales model generally associated with the generics industry. Where companies address both models they generally employ distinct business units (e.g. Novartis with Sandoz, its generics subsidiary). However, with the onset of low R&D productivity, many of them have begun to invest in the generics business to diversify and create a new revenue stream. Moreover, global Pharma companies see generics as a way to rapidly establish a strong presence in the fast-growing emerging markets where low costs are a prerequisite.

Rise of emerging markets and their role in driving growth

The global Pharma market is based predominantly in developed countries. In 2008, the U.S., the E.U., and Japan accounted for almost 70 percent of the global market. However, the growth of these mature markets is expected to be slow. This creates pressure on Pharma companies, urging them to look for new growth markets, such as those in fast-growing emerging countries (BRICs, Mexico, Turkey, and South Korea), where generics and OTC are already well established. Pharma sales and sales growth in these countries have been expanding materially faster than the average, jumping from 16 percent of the global market in 2006 to 21 percent in 2007 and almost a third by 2008. A presence in these markets thus becomes a strategic necessity for all the global Pharma players in order to achieve sustainable growth.

In November 2012, there were further indications that Big Pharma were determined to further expand its footprint in emerging markets. GlaxoSmithKline made two new deals worth more than $1bn in India and Nigeria. The transactions were significant in that they are different from traditional investments. To date, most of the industry’s past M&A initiatives in emerging markets have been focused on securing new drugs and generics, these GSK investments are aimed at strengthening its presence in consumer healthcare.

Against this backdrop of fundamental structural change and ever increasing consolidation we are witnessing an unparalleled increase in firms looking at their global deployment which is creating a flux in site investment / divestment.

Possible future structures

The history of the Pharma industry over the last 20 years has been the story of constant evolution with companies growing through the development of innovative products and acquisitions.

There is no reason to believe that this evolution will not continue as traditional companies merge or are acquired, to achieve synergies from operational cost savings and combined pipelines. We will also see acquisitions to gain access to new markets and technologies. Other companies grow by providing new and novel solutions to healthcare problems. One clear lesson from history is that novel treatments which effectively address unmet medical needs will be valued by patients and the market. Those companies that focus on innovation and are successful will be the future champions. As with all true innovations it is difficult to predict what the future success story will be but it is clear already that stem cell research and gene therapies represent possible disruptive technologies. The increasing use of robotic surgeons, mechanical prosthetics and robotic carers, also has the potential to change the provision of healthcare. Companies that successfully commercialise highly valued novel technologies will shape the industry in the future. The most likely source of these future champions will be current champions, they have the

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1. Pharmaceuticals Export Promotion Council of India Workshop on “Regulatory Compliances in Japan” for Pharmaceuticals, Q3 2012
expertise and funds to identify and acquire the “next big thing”. There will be new champions, Vertex Inc. and Gilead Sciences are examples of potential future champions. The key message is that innovation is the key and true innovation is valued in the first, emerging and third world.

New champions may well come from established leaders moving more explicitly into the areas of healthcare/health and well-being, and there is already evidence from the food nutrition and food science arenas, from which we can hypothesize will empower consumers by creating a platform of informed choice. A case in point is Nestlé, the world’s largest food company, which has made its strategic intent clear with the creation of Nestlé Health Science (NHS) and the Nestlé Institute of Health Sciences in 2010, with the commitment to create a new market between food and Pharma. Nestlé Health Science’s ambition is: “Pioneering science-based nutritional solutions to deliver improved personalised health care for people with medical conditions.”

For Nestlé, R&D is a key driver of innovation in the area of Nutrition, Health and Wellness within the multinational food company. They have 28 Product Technology and R&D centres worldwide, which facilitate early stage innovation into future Nestlé products. In late November, NHS formed a new 50-50 joint venture, called Nutrition Science Partners Limited, with Chi-Med, gaining access to one of the leading traditional Chinese Medicine libraries. Going forward it will be interesting to observe how traditional Pharma companies respond to this new global health competitor.

Big Pharma have sought to accelerate partnerships and licensing deals as they attempt to bolster falling innovation and compete globally. One notable example is the case of Takeda, under the enlightened leadership of President and CEO Yasuchika Hasegawa, has recently demonstrated its global strategic intent through heightened M&A activities (with acquisitions in the following sectors: oncology – Millennium; bioPharma – Nycomed; biotech – Intellikine; primary care – URL Pharma; vaccine – LyoCyte), broader R&D partnership arrangements (cf BC Cancer Agency; Advinus), and a desire to transform a Japan-centric firm to one which could effectively compete globally in a rapidly changing market.

Takeda in December took a relatively unusual decision to pass an Alzheimer’s disease drug candidate to the University of Tokyo for clinical testing and only receive royalties (typically up to 10 percent) if it goes to market. Pharma companies typically enjoy the fruits of university research, but not the other way round. Takeda’s deal with the University of Tokyo takes a new approach that could increase the success rate of drug development. Takeda, out of all Japanese Pharma companies, spends the most on R&D – 310 billion yen a year. The company’s focus includes cancer and lifestyle diseases like diabetes, and it had halted development of the drug candidate in question. The university is also active in Alzheimer’s research and plans to begin clinical trials of the candidate drugs at affiliated hospitals in March 2013.

Doing things differently will only enhance Japan’s reputation for innovation and put them at the forefront of healthcare dynamics.

Healthcare marcoms opportunities will grow exponentially in the next decade, as people become more engaged and demand more control of their healthcare provision!
Global perspectives: The role of Japan

Healthcare organisations and governments around the world are urgently seeking solutions to temper costs while still providing access to safe, quality care. Yet, conventional approaches are failing, even in the most advanced nations of the world – Europe, Asia, the Middle East, Australia, Canada and the United States. As they are often viewed as a local industry, healthcare organisations have not exchanged ideas globally as much as other industries such as manufacturing and services. While each country faces unique hurdles – regulatory, economic, and cultural – the challenges they face are remarkably similar. In response, common themes are emerging to tackle the complex challenges of sustainability.

Japan’s response to its rapidly ageing and declining population will be observed by policy makers around the world as the same trends are beginning to affect economies from Italy to South Korea. That said, it can be argued that Japan’s innovations in healthcare will play a central role in enhancing its leadership role in Asia, due to its demographic opportunity, relative wealth and love of technology empowered solutions.

Japan is the “ageing experiment” the rest of the world will be learning from decades from now. The demographic issues are so pressing and profound, new solutions need to be and are being developed today. Japan’s ageing population is magnified by the fact that it is a country where the population has already started to decline and the current policy does not allow for an immigration-based solution with foreigners being employed as health professionals. China with 106.1 million people over the age of 65 has the highest number of elderly citizens, but in proportion to the total population it is not included in the world’s top 25; however the numbers in Germany (16.5 million), Italy (11.7 million) and Japan (27.5 million) exceed 20 percent of their population. Significantly, those Japanese over 65 tend to live in rural areas, rather than cities (ratio 1.1:1), where as in most developed countries it is urban areas where the Silvers mostly live.

It is not surprising that investors are aggressively investing in high-flying health care stocks, in line with the ageing population and the increase in medical spending. The Nikkei Stock Average’s health care sub-index has risen 14 percent since the end of 2011, compared with a rise of less than 0.5 percent in the Topix index of all first-section shares. The Nikkei ranked the stock price gains of 132 listed firms with a market capitalization of 3 billion yen or more from the end of 2011 through early November 2012. Many of the top performers are healthcare-related firms, but not companies that actually provide medical care services. The strong results of medical firms in general are due in part to Japan’s massive healthcare spends, which reached 37.42 trillion yen in fiscal year 2010, driven by the ageing of the population and advances in medical technology. The hope is that further innovation in the healthcare business, including the wider use of IT, will bring the surging costs under control.

Topping the list is NanoCarrier whose stock price had grown nearly fivefold through a series of tie-ups with large companies. For example, Shin-Etsu Chemical announced on October 26 that it would buy a stake in the cancer drug developer, becoming its largest shareholder through a third-party allocation of new shares. Shin-Etsu hopes to use NanoCarrier’s technology to develop its own cancer treatments. Another company that has worked with NanoCarrier is Nippon Kayaku, which uses technology licensed by NanoCarrier in a cancer drug that had entered the final stages of clinical testing in July. The conclusion of a joint research agreement with Eisai in May has also helped lift the stock price of NanoCarrier.

SMS, ranked number six, is expanding its staffing and e-learning business through measures such as the purchase of a social media site that counts 70% of all nurses in South Korea as members. The employment agency, which specialises in jobs for nurses and caregivers, predicts that its operating profit will rise for the ninth straight year this financial year.

At number 9, Medical System Network helps small pharmacies negotiate prices for medical products with wholesalers. It is also creating more “medical malls”, which gather clinics and pharmacies under one roof.

Daiken Medical makes plastic containers used to store blood and other bodily fluids in hospital wards and operating rooms. Its containers have a substance that immediately coagulates bodily fluids, making it easy to incinerate waste without spills. Its products also spare nurses from having to wash conventional glass containers for reuse. Daiken Medical recently entered the emergency medical treatment field by developing a...
tracheotomy tube that cools the throat of patients in cardiac or respiratory arrest, reducing swelling and improving the flow of oxygen to the brain. The company has applied for regulatory approval for the device.

With these dynamics, Japan is increasingly attracting the attention of overseas international players. In November 2012, Bayer confirmed they would invest 500 million euros, in its Japanese operations over the five years from 2013, mostly in clinical testing of new drugs. The German drug maker is targeting 7% average annual sales growth over the five years to 2017, to 330 billion Yen in 2017. Ten percent of the investment will go toward Bayer’s materials segment, a little more than 5% toward agrochemicals, and the rest toward Pharmas. The company is stepping up drug development for the circulatory system and will conduct some clinical trials in Japan.

One new major development focus, of ageing, heightened by a declining population, is that Pharma companies are taking a more comprehensive approach in targeting lifestyle-related illnesses, hoping to help patients who have not benefitted from existing treatments. Instead of addressing individual symptoms such as high blood pressure and excessive blood sugar levels, the new drugs aim to improve patients’ overall health.

For example, Takeda plans to release in Japan a drug that will help obese patients lose weight by curbing fat absorption from meals. Eisai will launch a medication that manipulates neurotransmitters in the brain to quickly curb appetite. The drug, which will debut in the US, is intended for use in combination with dietary and exercise therapy. An estimated 60 million US citizens will likely benefit from the treatment. Daiichi Sankyo is conducting a clinical trial on a new medication for high cholesterol. While conventional drugs lower the level of LDL, or bad cholesterol, by suppressing the function of certain enzymes, the new drug seeks to raise the level of HDL, or good cholesterol.

The market is also seen as attractive to new entrants, for example, Fujifilm who has in recent years established a leading role in the burgeoning supplements sector, is progressing with the development of two candidate cancer drugs that could become its first to enter into clinical trials. One of the drugs is an oral compound for the treatment of myelodysplastic syndromes, the name for a group of medical conditions related to low blood-cell production that can lead to leukaemia. Fujifilm plans to begin clinical trials in Japan next year and hopes to launch sales in 2018. The other drug is a treatment for pancreatic cancer and ovarian cancer, which the company aims to test in clinical trials in the US in 2014. Fujifilm estimates that the combined global market for these two cancer drug candidates will be 160 billion Yen.

Led by antibody drugs, the bioPharma market is forecasted to grow some 40% from 2010 to more than 150 billion dollars in 2016. Chugai Pharmas, a Japanese subsidiary of Switzerland’s Roche, will begin a full-fledged effort to license its technology for efficiently producing antibody drugs. Through trade fairs around the world, they will encourage companies manufacturing antibody drugs to license its mass production technology.

In parallel, as the government moves to contain health care costs, the approval process has become more stringent for new drugs lacking strong demand from the medical community. Pharma companies are thus developing new treatments by incorporating requests from physicians and others in a bid to reduce their dependence on off-patent drugs.

“The burden of older citizens increasing in numbers...” is a phrase that echoes in the halls of government and businesses. The tendency to see the economic aspects of an ageing population in a negative light is widespread. It is also an uninformative narrative of potential that has yet to be released. Global leadership and expertise in robotics can be leveraged to solve health-related labour shortages looming large in Japan. By 2015 the government of Japan will have subsidies in place for the use of healthcare robots in homes and in elder-care centres. With appropriate human and cultural design adaptations, what Japan is developing for itself will be globally useful. Japan is not alone in robotics innovation or applying it to healthcare. What is unique is the Japanese demographic engine which is delivering this ‘elder trend’ faster and more poignantly than the rest of the world. Japan stands in its current situation that is the future for the rest of the first world.

What is currently viewed as a set of intractable problems can be a national catalyst driven by cultural necessity, to create what will inevitably be the next wave of high value exports from Japan. This initiative to enhance global competitiveness simultaneously holds the potential of raising healthcare standards for mankind. It should come naturally as Japan’s post-war economic achievement illustrates: Without natural resources Japan is without parallel and the level of adaptability has been an inspiration to many countries. In the same way, Japan’s leaders need be clear about their strategic intent and share their goals and aspirations for 2050. In particular, how improving the well-being of the people of Japan can also be a platform for future economic growth – and better collaboration with other nations. This is a natural progression of post-modern societal development driven by necessity, in a country which has long been recognised for its ‘Creative Class’ (Richard Florida’s writings). This may be viewed, by some, as part of the journey to ‘singularity’ as most popularly expressed by Ray Kurzweil, who in December 2012, became Google’s Chief Engineer.

In the fall of 2011, researchers at RIKEN and Toikai Rubber Industries (TRI) of Japan have developed the new robot that can lift a patient up to 80kg in weight off floor-level bedding and into a wheelchair, freeing care facility personnel of one of their most difficult and energy-consuming tasks. In early 2013, a team of researchers at Osaka University’s School of Medicine will begin offering transplants of nerve tissue from the noses of paraplegics to help restore their damaged spinal cords.

As part of the rehabilitation, patients will wear the HAL robotic suit on their lower bodies to relearn how to walk. The suit was developed by University of Tsukuba professor Yoshiyuki Sankai and is manufactured by Cyberdyne. HAL can detect the minute electric signals transmitted by the brain when people try to move their arms and legs. The motorised suit is designed to
assist with those movements. Since 2008, Osaka University has conducted nerve transplants on four patients with damaged spinal cords in clinical trials. The university says the patients have seen improvements in their daily lives and are able to roll over in bed and work seated at a desk for extended periods.

In a broader sense, medical technology is seen as a broad new area that from Japan’s perspective offers much potential locally and a vehicle for reinvigorating value add exports and global presence. Indeed, it is seen as offering the potential of arresting the country’s decline in global scientific influence. Tight regulations have long stifled innovation in clinical medicine in Japan. This has been compounded by the fact that few Japanese Pharma firms, except Takeda, have accelerated their growth and global footprint by mergers and acquisitions. Indeed, between 2003 and 2007, Japan was the world’s number three publisher of academic papers on basic medical research, behind America and Germany. However, Japan ranks a mere 18th in the number of papers on clinical medicine, and the country runs an annual trade deficit of over $12.3 billion in medical products and equipment.

There are signs of major breakthroughs ahead for Japan’s medical care industry. Kenji Yamada, Nomura Research Institute, explains why: “The Japanese medical industry is undergoing radical change due to the ageing of the nation’s population and the growth of emerging markets.” A number of different Japanese technologies can help to build this industry? Naturally there is a focus on cancer treatment where radiation is the most favored alternative to intrusive surgery and chemotherapy, which often causes severe side effects.

They include:

1 Focused Chemotherapy 1
Fujifilm’s diversification is also into drug discovery, where they are developing a group of Pharmas called armed antibodies. An antibody is something that bonds with an antigen, or disease-causing agent, and inhibits its activities. Fujifilm has added a radioactive substance to an antibody that attacks cancer cells. The armed antibody is thought to be effective in treating cancer-attacking, difficult-to-reach organs like the lungs and pancreas. Cancer patients in the US will start receiving armed antibodies in 2013.

2 Focused Chemotherapy 2
Japanese researchers are developing something called boron neutron capture therapy (BNCT). BNCT radiation therapy uses two components – a stable isotope of boron that can be concentrated in tumor cells and a beam of low-energy neutrons. Stella Pharma and Sumitomo Heavy Industries in Q4 of 2012 began the world’s first clinical trial of BNCT. Stella Pharma is the only company in the world that can mass-produce the boron compounds used in the therapy. The role of Sumitomo is fundamental to translational success. They have shrunk the equipment needed to produce neutrons, making hospital installation possible.

3 Focused Chemotherapy 3
In 2010, Mitsubishi Heavy Industries introduced a radiation device with the world’s first technology for real-time tracking of carcinoma lesions, which are in constant motion as a patient breathes. Like a sniper, the device fires focused bursts of radiation. Mitsubishi is exporting the device to North America and Europe to treat early-stage lung and other cancers.

4 Supercomputer calculations
There are an estimated 350 disease-causing proteins and around 30 million compounds that have been identified as potentially effective in treating them. That means 10.5 billion combinations must be tested to find possible treatments for particular ailments. Fujitsu and the Riken research institute, have built one of the world’s fastest silicon brains; the K supercomputer. It is currently using its considerable numbers-crunching might to reinvent the way drugs are developed. K’s power holds the key to the success of a joint project launched by nine Japanese drug makers at the end of Q3 of 2012, which could change drug development fundamentally.

5 Growing new skin
Japan Tissue Engineering (J-TEC) produces JACE autologous cultured epidermis; in other words – sheets of regenerated skin. The sheets are the only regenerative product eligible for coverage by Japan’s national health insurance. The government approved the sheets for production and sale in 2007, and they became eligible for insurance coverage in 2009 for patients with serious burns over more than 30% of their body. J-TEC expects much more demand for another of its regenerative products – JACC autologous cultured cartilage. This is regenerated in much the same way as the skin product but shaped into three-dimensional forms after about four weeks of growth. Athletes and accident victims whose cartilage has been damaged will benefit most from this product. The government approved it for production and sale in July, and J-TEC expects sales to start in the next fiscal year.

6 Growing a new jaw
As J-TEC cultures skin from cells, 3-D Matrix Ltd produces materials to promote cell regeneration; the peptide that promotes the regeneration of alveolar bone. The firm has exclusive license to use technology developed by the Massachusetts Institute of Technology to recombine human amino acids into peptides. The peptides are already in clinical trials in the US; commercial application could come in three years and allow for dental implants in patients with a weak alveolar bone.”
Healthcare 3.0 has to be on all our agendas – connecting professionals, patients and people

Paradoxically, there is often a tendency to overestimate how much things will change in the next two years, and also, a tendency to underestimate how much things will change in the next decade. We need to understand “what is” but have a passion and enquiring mind for “what can be”. The need for fundamental change is clear but it is also clear that three major Information Age advances are helping to drive the Imagination Age of new Healthcare with marcoms playing a central role empowering individuals.

The world needs Healthcare 3.0: it demands enlightened thinking and deployment. Without such leadership we will face Francis Fukuyama’s scenario at the “end of history”, when “the world-wide ideological struggle that called for daring, courage, imagination and idealism [has been] replaced by economic calculation, technological problems, environmental concerns and the satisfaction of consumer demands.” Marketing has perhaps its greatest opportunity in the next decade.

The Role of M&A in the Healthcare Revolution

Innovation and effective provision of healthcare services have been the characteristic of the global healthcare business sector. Innovation can originate anywhere but history suggests that drug discovery is co-located with the main markets and sources of funding. Meaningful innovation demands commercialisation, otherwise it remains simply ‘of interest’. The globalisation of innovation is as important as the discovery and development. It is important that innovation wherever it originates has access to the means to effective commercialisation, whether by a licensing agreement, or through an M&A deal. These are standard ways of ensuring the distribution of healthcare services. There are good deals and bad deals and one way of minimising the risks associated with these events is to use professional transaction advisors. Conducting international transactions with Japanese companies adds additional complexity, but again risks can be alleviated by using professional advisors with experience of successfully working with Japanese clients and counterparties. Rh

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5 The importance of new companies for drug discovery: origins of a decade of new drugs. Nature Reviews Drug Discovery 9, 867-882 (November 2010), Robert Kneller
About the author

Chris Beaumont is Regional Director, North Asia for Results International, based in Tokyo where he has resided for over 20 years. His broad experience includes strategic roles in Marketing consultancy with Coopers & Lybrand Europe; an academic career at London Business School; as well as regional leadership roles in marcoms, in Asia, with McCann World Group and the Grey Group.

At different times he has been on all possible sides of an M&A transaction; indeed was Results first client in Asia!

His healthcare experiences are likewise varied; including a seminal study on Morbidity and the Environment for the DOE in the UK, the purchase of a healthcare agency to enhance his advertising group in Japan, and his current Chair at The University of Tokyo, where he is a Professor in their Global COE, Centre for Medical System Innovation. Recently, he co-authored a leadership, business case series, for Stanford Business School based on the strategic options facing Takeda.