INCREASED COMPETITION IN JAPAN

Is the pharmaceutical industry ready?

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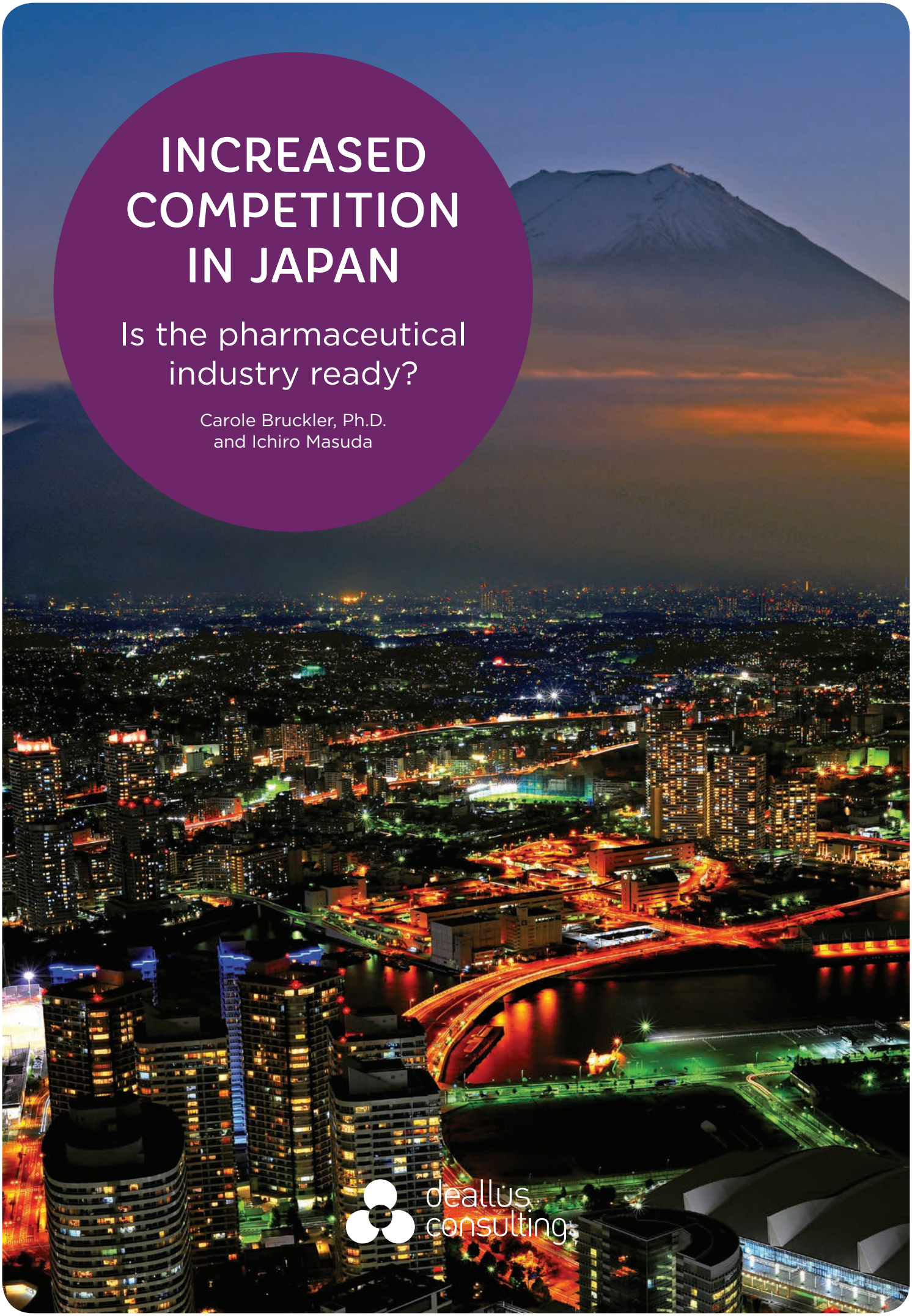

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JAPAN

A changing pharmaceutical landscape

Like many developed countries, Japan is facing new financial healthcare challenges. The strain of demographic changes, mounting expenses and a stagnant economy mean significant economic and healthcare reforms are underway to meet future needs. However, as new entrants and pricing reforms increase, and the generic market expands, is Japan's pharmaceutical industry ready for the impact that increased competition will bring?

An urgent need for healthcare transformation

Japan has a large, well-developed pharmaceutical market and offers universal health coverage to its citizens. However its traditional low-cost healthcare model is now trending towards other developed countries.[1,2] This has been catalysed by major demographic changes. A low birth rate and low migration mean Japan's overall population is shrinking whilst the proportion of its elderly population grows. Higher life expectancy, advances in medical treatments and strong financial support are all increasing demand for healthcare services. However, as Japan's elderly population rises, the working population declines resulting in rising dependency ratios and shrinking taxation income.

In the absence of major healthcare reforms Japan will experience a funding gap of ¥19.2 trillion (~ $160 billion) by 2020 which is expected to rise to ¥44.2 trillion (~ $370 billion) by 2035. Increasing insurance premiums to fund the gap will increase labour costs and harm Japan's competitive position. Co-payment rates are already high at 30%, and an additional increase would undermine the concept of health insurance.[3-5] So, Japan needs alternative financial options.

The political will to shift gears in Japan's development has recently accelerated. Abenomics, based upon the "three arrows" of fiscal stimulus, monetary easing and structural reforms, are being implemented across Japan's industries to help aid economic growth.

This is having multiple effects on the Japanese healthcare system including; creating new markets (such as medical equipment), strengthening research and development capacity, offering preference for generics and biosimilars, providing market access to foreign companies and encouraging Japanese companies to become world players.[6]

Legal and regulatory changes have paved the way to a more open domestic pharmaceutical market and increasing deregulation has opened up opportunities for multinational pharmaceutical companies in Japan.

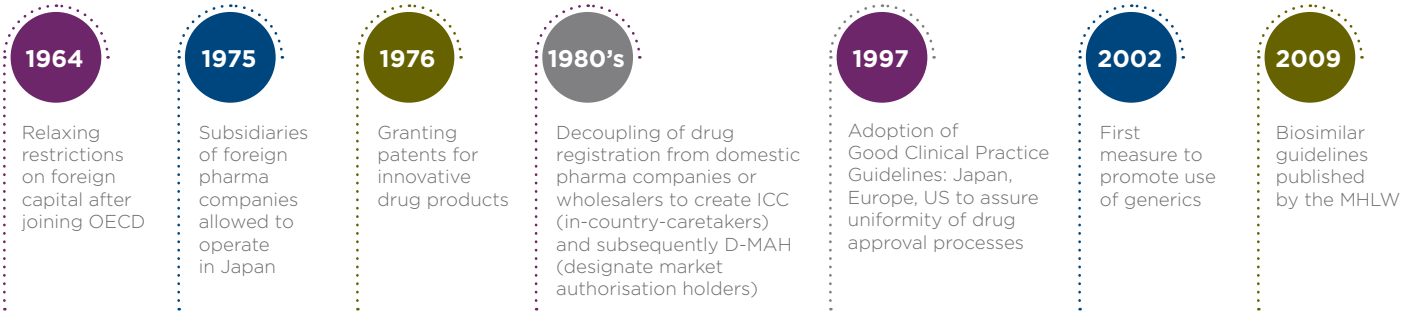


Figure 1: Japanese healthcare reforms over time[1,15,20]

A significant pharmaceutical player

The Japanese domestic pharmaceutical market is large and fragmented. It consists of over 100 companies despite some merger and acquisition consolidation for global investments.

52 domestic companies have significant research and development investments and 15 have annual sales in excess of ¥120.4 billion ($1 billion USD).[7]

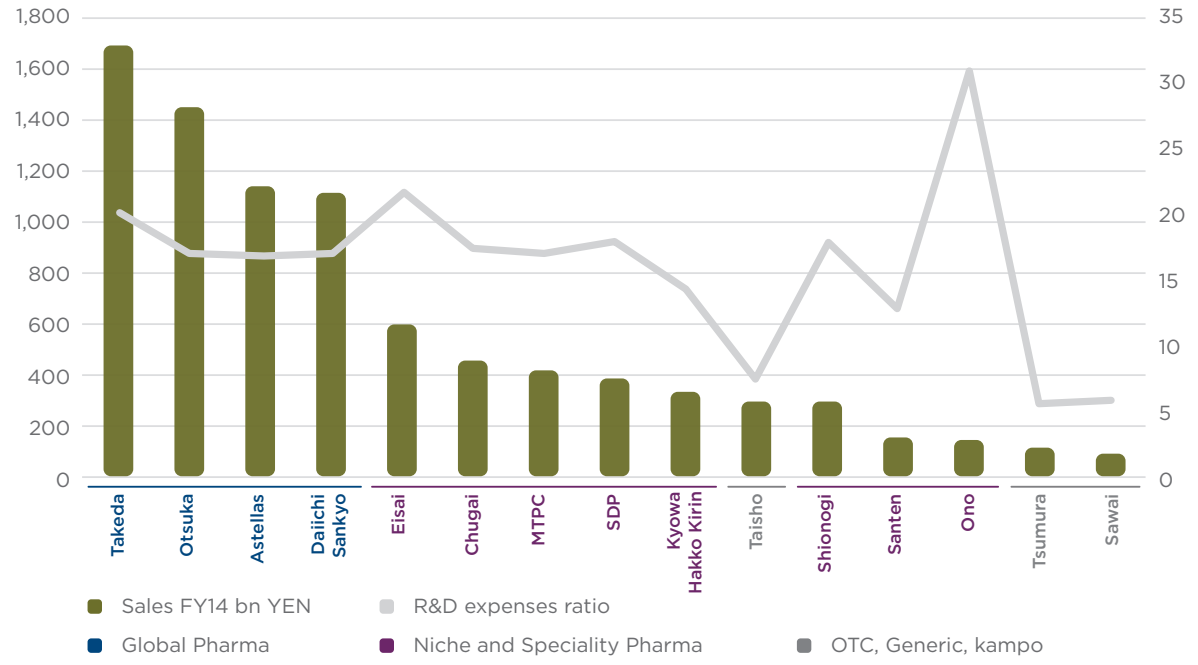


Figure 2: Comparison of Japanese Pharma sales and R&D expenses[7]

Despite flat economic growth, Japan's position in world pharmaceutical sales is projected to remain significant. The market in Japan is projected to grow 17% over the period 2011–2020 (based on constant exchange rates).[8]

The Japanese pharmaceutical industry is self-sufficient. Many domestic companies thrive on local innovation and Japanese pharmaceutical research and development are the source of many global blockbusters. Some Japanese collaborations with multinational partners such as BMS with ONO, and Janssen and Novartis with Mitsubishi Tanabe Pharma are based on royalty payments in ex-Japan markets. These have resulted in the multinational partner accruing most of the value of the innovations, not the Japanese originator. However, where there has been co-promotion and development, Japanese companies have benefited financially. Successful examples of this include collaborations of Pfizer with Eisai, BMS with Otsuka and AstraZeneca with Shionogi.[9] So, with domestic demand plateauing, should Japan start to reach further afield?

Brand	Generic	FDA Approval year	Peak sales (bn USD)	Peak sales year
Aricept	donepezil	1996	3,883	2009
Abilify	aripiprazole	2002	9,512	2013
Crestor	rosuvastatin	2003	7,881	2011
Gilenya	fingolimod	2010	3,813	2018 E
Invokana	canaglifozin	2013	2,305	2020 E
Opdivo	nivolumab	2015	6,993	2020 E

Figure 3: Global blockbusters based on Japanese innovation[7]

Three emerging market trends

1. Increased intensity of new entrants

New drugs are reaching the Japanese market faster and in larger numbers than ever before. The last decade has seen an increasing volume of drug approvals processed. Review times at PMDA are now shorter for new drugs (just 6.5 months for priority-review and 11.5 months for standard-review.) 50% of approvals are for multinational pharmaceutical originated products, so the effects of acceleration are equally distributed, although multinationals have a broader catch-up need.[10]

Clinical trial deregulation has simplified clinical development strategies by clarifying requirements for Japanese market entry. Clinical trial execution is now also associated with lower cost and barriers.

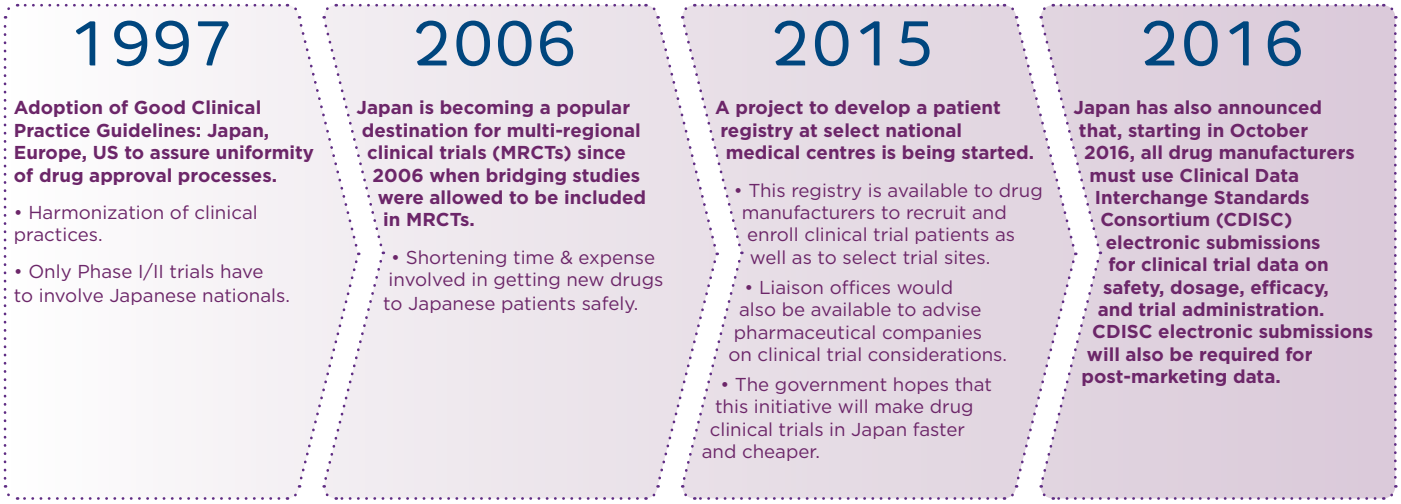


Figure 4: Japanese clinical trial reforms[21,22,23]

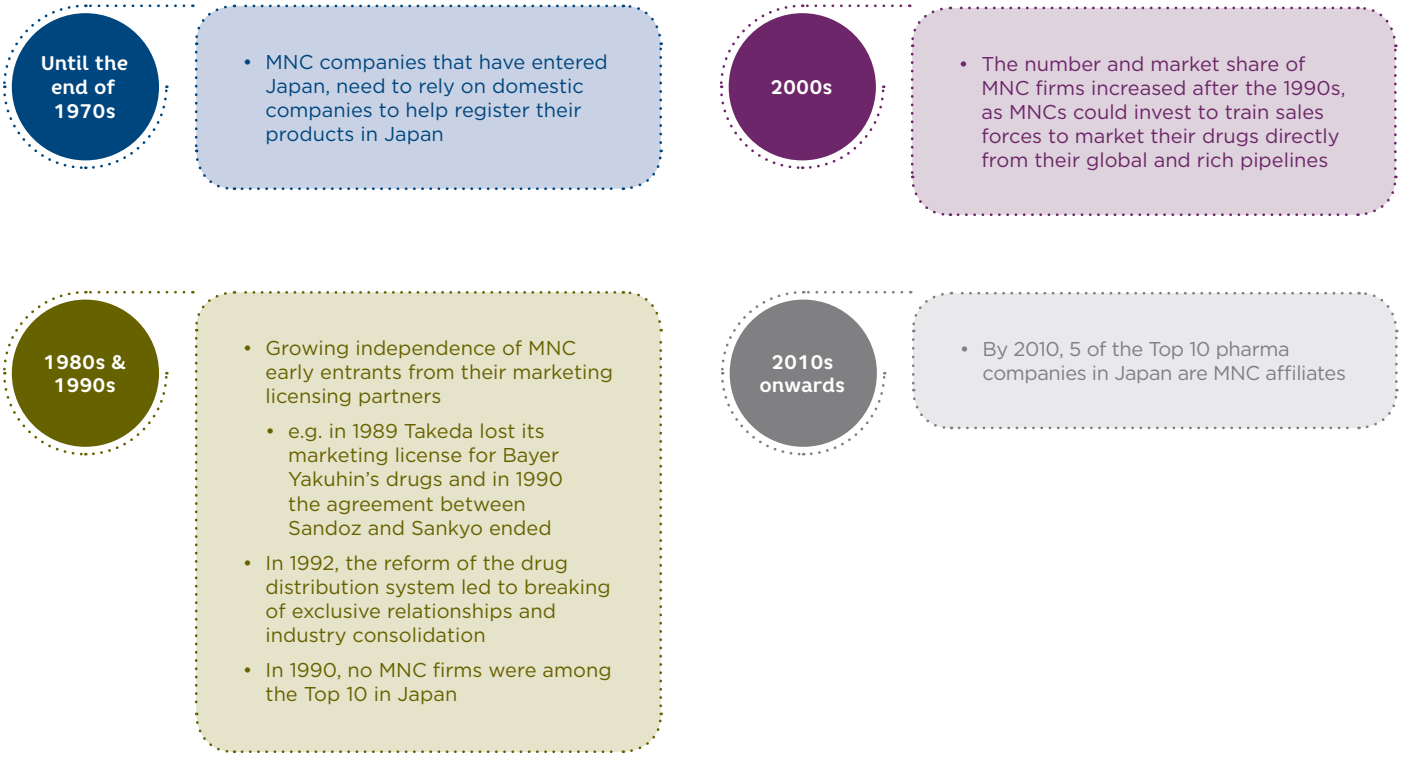


Figure 5: Accelerating entry of MNCs into Japan[7,24]

These reforms are also having an impact on multinational entrants who are now able to set up and operate freely without legal or channel hurdles, nor involvement of domestic pharma companies.

Until the end of the 1970s, multinational pharmaceutical companies needed to rely on domestic companies to help register their products in Japan. During the 1980s and 1990s there was a growing independence of the early multinational entrants from their marketing licensing partners, for example in 1989 Takeda lost its marketing license for Bayer Yakuhin's drugs and in 1990 the agreement between Sandoz and Sankyo ended. During this time no multinational firms were amongst the Top 10 in Japan.

In 1992, the reform of the drug distribution system led to the breaking of exclusive relationships and industry consolidation. The 2000s have seen a rapid change as the number and market share of multinational firms has dramatically increased. They have been invested in training sales forces to market their drugs directly from their global and rich pipelines. By 2010, five of the Top 10 pharma companies in Japan were multinational affiliates.[11–13]

2. Increased leveraging of buying power

Buyers are increasingly leveraging their buying power to manage budgets and costs through controls and policy reforms.

Strict Price Controls

The Ministry of Health, Labour and Welfare (MHLW) already has a tight control over the National Health Insurance (NHI) price of new drugs. For example in 2014 only 24% of new drugs evaluated on efficacy and 29% of drugs evaluated on cost received a positive premium.[14]

Further forces such as biennial price revisions, prescription drug price reductions, generic price capping and additional price cuts are also pushing NHI prices further down after initial price setting.

In April 2014 revisions were announced where generic prices would be lowered to 60% of the originator drug price (this was previously 70%). Additionally once 10 generics are approved, further generics are to be capped at 50% and there is a possibility that all generics will be capped at 50% by 2018. Additional price cuts were also implemented for existing generic products of 1.5–2.0% if the drug is less than 60% cheaper than the originator. For off-patent branded drugs there were cuts of up to 25% if annual sales double the forecast and cuts of 1.5–2% if generic substitution rates are too low. This rule particularly impacts domestic companies which are heavily dependent on long-listed products which have had traditionally a slow rate of generic erosion.

Three further consecutive pricing revisions are expected in 2016, 2017 and 2018 with a proposal to make price revisions annual deferred to 2019 and beyond.[7,15,16]

Progeneric Policies

The Japanese government has been implementing increasingly assertive progenerics policies at all levels in the value chain. Targets for generic substitution rates are accelerating and are on track to be met. The first target was set in 2007 to achieve 30% generic substitution by March 2013. Since April 2013 a 60% target deadline was set and has recently been brought forward to March 2017. There is now a new target of 80% generic use by March 2021 under discussion.[7,17]

Health Technology Assessments (HTA)

HTA is on the horizon in Japan with a greater emphasis on the cost-effectiveness of new products. This strategy has implications for pharmaceutical companies including:

- Greater focus on cost-effectiveness of new products
- Higher planning burden on companies with a less clear return on investment or likelihood of success
- Lack of staff with appropriate expertise in the HTA field

In 2014, the government announced a plan stipulating the trial rollout of cost-effectiveness assessments in 2016. Discussions have been gaining momentum in recent months although there are still several areas which require greater clarity such as the framework of how MHLW will incorporate the HTA into NHI price calculations, whether refusal of reimbursement will become an option and the practicalities of cost and timelines for executing and evaluating HTA submissions.[18]

3. Growing generic and biosimilar market

The need for cost restraints is opening the market for increased use of generics and biosimilar products. Japan's existing domestic generic industry will need to consolidate in order to fund the investment required to keep pace with the rapid expansion of the multinational generic market.

The domestic industry faces the dual challenge of maintaining reliability of supply and quality whilst facing reducing margins due to downward pricing. Meanwhile the global scale of multinationals are already adapted to such an environment and are ready to expand.

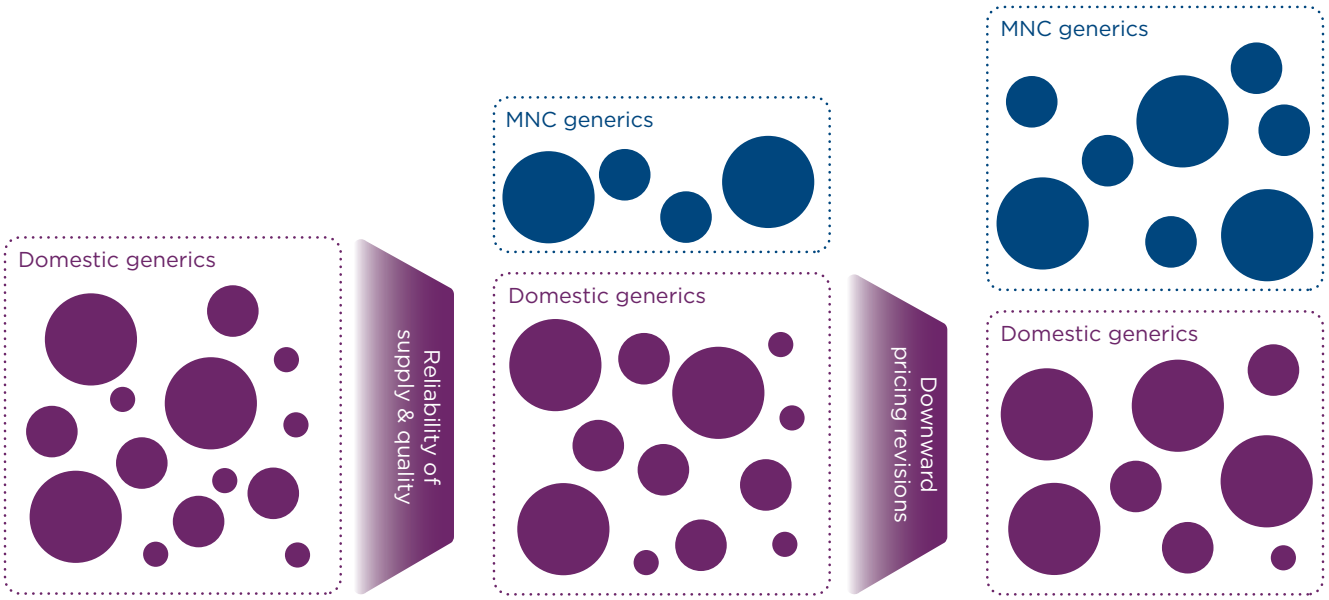


Figure 6: Multiple Challenges are reshaping the Japanese Generics Market

The biosimilar market in Japan was created in 2009, following the European lead on guidelines. To date, these guidelines have favoured market penetration, in conjunction with a multinational, to leverage global clinical trials. Guidelines were published by MHLW in 2009 to establish safety, quality and efficacy of biosimilars in Japanese patients for pharmacokinetic and pharmacodynamics data (PK/PD). If a clinically relevant PD markers exist linking the PD data of the biosimilar in Japanese patients to efficacy data in other populations, this may be sufficient.

The biosimilar field is associated with significant cost, requires manufacturing expertise and budget to execute efficacy trials. Additionally, to remain profitable, discounting versus the originator drug cannot be too aggressive. So far only a small numbers of domestic companies have been willing, or able, to enter the market.

The advantage of scale favours multinational companies or partnerships in this field. In fact 5 out of first 7 biosimilars approved in Japan were developed by multinational companies with global scale expertise and the appetite for risk.[7,19,20]

How will these trends impact the industry?

The implications of these trends mean that the Japanese pharmaceutical industry now has four strategic options to consider:

1. Consolidate domestically through mergers and acquisitions
2. Expand overseas
3. Optimise and prepare for changing domestic dynamics
4. Plan for global product development

1. Consolidate domestically through mergers and acquisitions

Large scale domestic consolidation through mergers and acquisitions has already been actively happening over the past decade across Japan. Further consolidation would be beneficial at company and industry level as this would allow for opportunities of scale to drive investment in research and development, enabling market expansion.

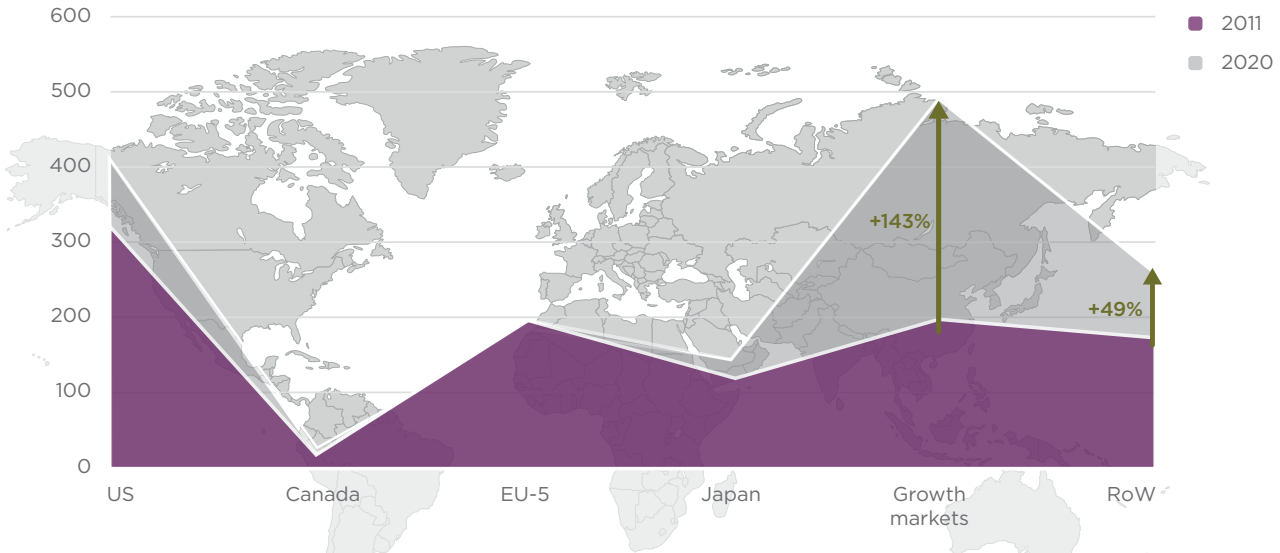
In the near term there are limited expectations of further consolidation however it is an option to consider seriously for small or medium sized enterprises that want to build up scale for further investment.

Year	Merging companies	Resulting company
2004	Dainippon Pharmaceutical and Sumitomo Pharmaceuticals	Sumitomo Dainippon Pharma
2005	Sankyo and Daiichi	Daiichi Sankyo
2005	Yamanouchi Pharmaceutical and Fujisawa Pharmaceutical	Astellas
2007	Tanabe Seiyaku and Mitsubishi Pharma	Mitsubishi Tanabe Pharma

Figure 7: Pharmaceutical merger and acquisitions[8]

2. Expand overseas

The growth opportunities outside of Japan and the developed markets are significant for those companies who are poised to access them.



Growth markets include in descending order China, Brazil, Russia, India, Mexico, Turkey, Poland, Venezuela, Argentina, Indonesia, South Africa, Thailand, Romania, Egypt, Ukraine, Pakistan and Vietnam.

Figure 8: Global Growth Market Opportunities to 2020[8]

There are different routes available for overseas market entry during a product growth cycle. The option pharmaceutical companies choose are driven by the strategic intent of the expansion, the ability to invest and expectation on financial returns.

Out-licensing - In less attractive markets, where local production is required, out-licensing the product at the out-set may be preferable, as the set-up costs may make market entry otherwise cost-prohibitive.

Agency – This can be an option when exporting of finished products is a viable option. If low market knowledge is available in addition, then the use of a local agent can be a pragmatic and cost-effective choice.

Foreign Direct Investment (or JV) – In attractive markets that require local production, manufacturing investment can provide additional value for the long-term presence.

Marketing Affiliate – Once local market knowledge has been established, a marketing affiliate is a good option to grow further in a promising market as it opens channels.

The right route to market for each company ultimately depends on their expected outcome from the overseas expansion.

3. Optimise and prepare for changing domestic dynamics

This is important for all domestic marketing companies and the Japan affiliates of multinational companies. Pharmaceutical companies should optimise performance in the domestic market by preparing for generic penetration into successful brands. They must assume steeper sales erosion curves in the coming years due to increasing generic substitution targets, incentives and requirements of all healthcare market players. Therefore, they should also be proactive in preparation to support their products as they are approaching the end of patent/data exclusivity. This Loss of Exclusivity (LoE) planning is already established in US and European market through activities such as building brand loyalty programmes, however the urgency of this dynamic shifting in Japan is unprecedented and some companies are likely to be caught unprepared.

When planning for the Japan domestic market, pharmaceutical companies should also include global product development within their plans. They should anticipate the multinationals future intentions and the role they will play as competitors prior to and at market entry and have strategies in place to aid rapid decision making.

The implications for pharmaceutical companies will be adopting new business planning processes, improving investment in competitor analysis and to preparing for upcoming LoE dynamics and new entrants. Pharmaceutical companies could also consider using 'War game' strategic tools to prepare for competitor product launches. This can be an effective way for organisations to practice strategic decision-making in a risk free environment before having to commit to real life decisions.

4. Plan for global product development

It is essential to start considering global clinical strategies from the earliest stages of drug development. Pharmaceutical companies should consider the following from the outset:

- Does the product meet a need on a global level or Japan only?
- Can we develop it ourselves or should we partner or out-license?
- Should we consider early global commercialisation strategies?
- Does this product fit into the corporate ex-Japan market development strategy?
- Could this be a cornerstone product which is part of a regional expansion plan with associated long-term investment?
- Will out-licensing with royalties be the best strategy?

The implications for pharmaceutical industry include the need to adopt new business planning processes, anticipate changes in global pricing and reimbursement as well as market access dynamics. Pharmaceutical companies also need to have a good understanding of the global competitor landscape and market opportunities. This is critical for medium-sized domestic companies if they wish to retain a greater share of the innovation value that they have created.

Conclusion

The Japanese healthcare landscape is undergoing a period of transformation catalysed by demographic change and a stagnant economy. Despite flat economic growth, Japan remains a significant and innovative pharmaceutical presence in the global market. Japanese economic healthcare reforms to drive growth have resulted in a significant increase in new entrants, pricing and reimbursement revisions and a growing generic and biosimilar market. These trends have many implications for the industry. However, domestic and multinational companies with Japanese affiliates can ensure they are ready for the increased competition by being prepared with strategies in place.

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Carole Brückler is the COO for Deallus globally and Head of the Deallus Consulting Japan and Asia-Pacific operations, based in Singapore. Previously she led the established European business. She has extensive experience in leading client engagements developing regional or global product strategy.

Carole's clients assignment have enabled business decisions reflecting market evaluations of new products and acquired assets, pricing and reimbursement challenges, generic and biosimilars entry and landscape assessments to validate opportunities present existing portfolios. Carole's experience covers multiple therapy areas, particularly Vaccines, CNS, CVM and respiratory fields.

Carole has also lectured at multiple Pharma industry conferences on the challenges of conducting research in the vaccines area, in Europe, US and China. Prior to joining Deallus, Carole worked in preclinical R&D, both in a synthetic organic setting, as well as an analytical setting in support of asthma treatments at GSK.

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He spent 21 years at Eli Lilly Japan in progressively senior sales, marketing and product management roles, before he moved to the consulting industry. At IMS Health Consulting, he worked in the Commercial Practice, delivering market optimisation, resource allocation and marketing training projects. At ZS Associates, he developed the area of strategic market research in ZS Tokyo and worked on forecasting and business development assignments, while managing business development and client engagements. Ichiro is a graduate of Kyoto University in Economics, a nationally registered management and certificated healthcare management consultant, as well as a native Japanese speaker.

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About Deallus Consulting

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