

The Challenge for Japan's Pharmaceutical Top Twenty:
Building on the Lessons of a Broken Model
Catenion

Prepared by: Christian Elze and Markus Thunecke

A. Introduction – Can the Japanese Pharmaceutical Industry Become Competitive?

With roughly \$60 bn in sales, the Japanese pharmaceutical market is the second-largest in the world. Regular price reductions across the board, as well as high clinical and regulatory hurdles for the introduction of foreign breakthrough drugs have kept the overall market size stagnant for the last decade. This has resulted in little incentive for local firms to innovate.

The Japanese pharmaceutical industry counts more than 1000 firms of which approximately 20 have annual sales of more than \$500 mn. It is a widely-held view in the West that the Japanese market is too large to let them fail and too small to generate sufficient profits for global expansion. As a result, many Western observers hold that the Japanese industry as a whole is not competitive given the small scale of its companies, a strictly home-grown management culture unfit for global markets and a lack of innovativeness highlighted by the belated investment in biologics. To make matters worse, Japan lacks the vibrant Venture Capital and biotech scene required to bottom-feed the pharmaceutical industry.

Yet for the last five years, the environment has been changing at an accelerated pace. In 2002, the Ministry of Health and Labour published a “Draft Vision for the Japanese Pharmaceutical Industry for Strengthening International Competitiveness”. The report defined four types of companies: “Mega-pharmas”, “Specialty pharmas”, “Generic pharmas” and “OTC pharmas” and stated that the formation of two to three mega pharmas would be “most appropriate” in light of the size of the Japanese market.

Since the publication of this report, the government has initiated a number of reforms aimed at creating a more supportive environment for the industry. Measures have included R&D tax credits, the uncoupling of marketing and manufacturing licenses, regulatory harmonisation with the EU and the US including the shortening of the historic approval lag between Japan and Western markets through bridging studies, and the negotiation of a new pricing scheme rewarding innovation expected to come into force in 2008.

In this Commentary, we discuss the strategic challenges and options for the top twenty Japanese pharmaceutical companies. This discussion comes at a time when the pharmaceutical industry in the West is struggling with a poor innovation track record and increasing regulatory scrutiny that will most likely lead to yet another round of consolidation. Therefore, we first take a look at the fundamental characteristics of the pharmaceutical business as it is operated outside Japan. A few crucial lessons for Japanese companies to heed can be derived from what has been called by some in the industry “a broken model”. In doing so, our focus will be on the subjects of innovation management and risk management in a strategic perspective.

We then proceed to establish a segmentation of the Japanese top twenty players. This segmentation is based on current dynamics, as well as a few key business and financial indicators and it differs from the one proposed by the Ministry. For each of the segments identified we list the specific challenges companies within them face and a few options for addressing them.

We conclude that there may well be room for a dozen or so flourishing Japanese pharmaceutical companies but they must be prepared to learn from the mistakes of the industry in the West. We argue that success requires them to resist the temptation to copy the business models and development paths of today's industry leaders. Rather, Japanese firms must innovate their business models and design strategies and organisational structures that successfully stimulate innovation and adequately deal with risk.

Finally we hazard a guess that some of the characteristics of the Japanese style of management may be ideally suited as elements of a specifically Japanese culture of innovation management embedded in collaborative community.

B. Innovation and Risk Management – Lessons from a Broken Model

What Went Wrong?

A quick review of the historical growth patterns of pharmaceutical companies shows that there almost invariably was a blockbuster drug at the beginning of a period of sustained growth. It was Zantac that launched Glaxo on its path to greatness and similarly Ampicillin for Beecham and Valium for Roche.

The funds generated by the product's sales were then invested in in-house R&D, in-licensing and take-overs of less successful competitors. Interestingly, with the possible exception of Merck & Co. in the seventies and eighties, not one of the world's leading pharmaceutical companies managed to set up a sustainable growth model driven mainly by internal discovery research. All but two of today's top ten made major acquisitions – the two exceptions being Eli Lilly and Merck & Co, who struggled to survive in the early 1990s and 2000s, respectively. UCB and Shire, two up-and-coming European bio-pharmaceutical players have used M&A to build their current positions, albeit with very different approaches.

M&A – A Key Driver of Growth

Today's Pfizer is a result of the mergers and take-overs of the following companies: Pfizer, Warner-Lambert, Parke-Davis, Agouron, Pharmacia, Kabi, Carlo Erba/Farmitalia, Upjohn, Searle, Sugen, Rinat and many more – what's next?

Today's Sanofi is a result of the mergers and take-overs of the following companies: Sanofi, Sterling-Winthrop, Synthelabo, Rhone Poulenc, Rorer, Pasteur-Merieux, Connaught Labs, Hoechst, Marion, Merrell Dow – what's next?

Two up-and-coming European bio-pharmaceutical companies have used very different strategies to position themselves as global specialists:

- Shire took over nine smaller companies between 1999 and 2007
- UCB forged ahead in three steps in the span of three years: Take-over of Celltech in 2004, divestment of non-pharmaceutical business in 2005 and take-over of Schwarz Pharma in 2006

Why, one wonders, has investing in in-house R&D not been enough for any company to grow in the long term? Why haven't the billions of dollars spent on R&D been sufficient to ensure the next blockbuster would be ready once the patents of the previous one expired?

In Catenion's view, the industry faces two fundamental problems for which it has not yet found an answer; these problems are firstly, an inadequate approach to managing innovation and secondly, a profound misunderstanding of the nature of risk and consequently poor risk management.

An Inadequate Approach to Managing Innovation

The industry's poor innovation track record is shown by the statistics of drug approvals by the FDA. There has been a long-term trend of a decrease in the number of NCEs and NBEs despite rapidly increasing R&D budgets. A recent study by Czerepak and Ryser published in Nature Drug Discovery shows that for the period between January 2006 and December 2007, barely 35% of the drugs approved by the FDA originated in the pharmaceutical industry. Less than half of these qualified for the label “novel drug and new chemical structure”.

Industry critics have used statistics such as these to argue that Big Pharma is shying away from “true” innovation and pursuing mostly me-too projects. A quick look at company pipelines shows this to be a wrong conclusion: There is an abundance of exciting, highly innovative projects and risky science going on at most companies.

While some industry observers and investors continue to hope there might be an innovation backlog in the wake of unprecedented progress in molecular biology, disease understanding, lab technologies and novel drug formats, others are more pessimistic.

In an interview with the Financial Times on December 11th, 2007 Dr. Moncef Slaoui, newly-appointed head of R&D at GSK had this diagnosis to offer: “The science is overridden by managers...we should move away from industrialised R&D”.

Dr. Slaoui is not the first industry executive to notice something is going wrong. Indeed his predecessors at GSK boldly decentralised R&D in 2002 to instill a level of entrepreneurship into the organisation. Novartis and recently Roche have followed suit with new organisational approaches to R&D and in a way so has the industry as a whole. "Disease Biology", "translational medicine", "biomarkers" and "proof of concept" are but a few of the concepts the industry hopes will reignite the stalled internal innovation engine.

The lack of internal innovation has led to escalating competition for in-licensing deals with the cash cost of partnering now arguably exceeding in-house cost – viz talk of the "\$100 mn IND". With patent expiries and a decreasing flow of innovation resulting in only slow if any growth of pharmaceutical markets, consolidation through M&A remains the most viable route to growth for many companies.

At Catenion we maintain that the real problem sits deep down at the level of culture and operating models: The way Western companies manage R&D – Dr. Slaoui calls it "industrialized R&D" – is fundamentally at odds with the requirements of breakthrough innovation which can be gleaned from successful innovators across industries and academic research institutes.

As we have argued elsewhere, breakthrough innovation cannot be managed with short-term plans, budgets, balanced score cards and incentive systems. It involves by nature bottom-up and cross-boundary idea generation throughout the R&D value chain, is often serendipitous, requires long-term effort and works best in an environment where project teams are empowered as innovation cells. (For more details cf. the Catenion Commentary on Recombinant Innovation Management).

What we see at Big Pharma is a mismatch between the intent of using risky science and highly innovative approaches to address unmet need on the one hand and an operating model that emphasises process efficiency (industrialized R&D) at the expense of quality on the other.

All too often companies get stuck in a vicious circle where ambitious short-term productivity goals backed up by incentives lead to reduced resource allocation per project with an ensuing loss of quality and increase in attrition. To counterbalance increased attrition, the productivity-driven manager sees a need for more projects in the pipeline, resources are spread even thinner and in the end most of the few projects that make it through to the market are in the low innovativeness/lower risk category.

Janelia Farm's Six Principles to Manage Innovation

When designing the Janelia organisation, HHMI looked at the MRC Laboratory of Molecular Biology in Cambridge, AT&T's Bell Laboratories in Murray Hill, New Jersey and a few other leading research institutes. For details cf.: <http://www.hhmi.org/janelia/forebears.html>

Six principles were distilled:

- Individual research groups were small to promote collaboration and communication between groups, as well as good mentoring.
- Group leaders were active bench scientists – this was true even for Nobel Prize winners and department chairs.

- Research was internally funded – all research funding was provided from internal sources at a dependable and generous level. Outside grant applications were not permitted.
- Excellent support facilities and infrastructure were provided – this enabled individuals and small groups to function effectively and to focus on creative activities.
- Staff turnover was high and tenure limited – many scientists were at an "early career stage," and moved on to university positions after 5–10 years.
- Originality, creativity and collegiality were valued and supported.

Similar principles led to the foundation of the Kaiser-Wilhelm Society in Germany in 1911, later renamed the Max Planck Society.

Successful innovators manage a target innovation mix, stating explicitly how much breakthrough vs. me-too R&D they want to pursue. They have found a way to grant autonomy to their scientists and engineers without giving up on challenging their assumptions and premises. Some companies like Google and Genentech practice a “loose-tight” management style. Dr. Slaoui calls for “deep science, passionate people and ownership”.

Importantly, the cross-boundary aspect of many breakthroughs requires open, collaborative partnerships with universities and biotechs. A recent greenfield approach to building a best practice research institute by the Howard Hughes Medical Institute (HHMI) produced a number of interesting insights from benchmarking the world's leading research institutes. These confirm our analysis and draw a very different picture from what can be found inside Big Pharma.

Poor Risk Management

Turning to the second issue we have identified, the pharmaceutical business is a risky business *par excellence* but the nature of risk is often not fully appreciated by operators. Of course pharmaceutical executives know the scientific, technical, regulatory and commercial risks of their business. They spend a lot of their time devising and executing risk mitigation activities for these risks at the operational level. The argument we wish to make here is that there is too little awareness that risk must be managed properly at the strategic level as well. Such strategic risk management requires more sophisticated methods than those generally used in the industry today.

There are three major points to our argument, covering the nature of risk itself, correlated risk in the R&D pipeline and the degree of risk diversification at the corporate level.

1. The Nature of Risk

At its most basic, the problem begins when success probabilities are viewed as additive. To begin with a familiar example, how often do you have to throw a dice in order to get one six? Most people would say: Six times, which is the right answer in the long run, when the experiment is repeated many times. But for the first round, six throws will give you at least one six with 66 % confidence only.

If you want to be reasonably sure (say with 95 % confidence) of getting at least one six in a sequence of throws, you will need an astonishing seventeen throws of the dice!

Now let us apply this finding to a question on the pharmaceutical strategist's agenda: Let the benchmark probability of a development candidate to reach the market be 10 %. How many new development candidates are required annually to launch at least one product every five years? The intuitive but wrong answer to this question is two per year. A correct answer using the Bernoulli formula for sampling with replacement yields six development candidates per year to get to a 95 % confidence level. That is three times more than the intuitive answer would have it.

2. Risk Correlation

Not only are correct success probabilities non-additive, they should also take into account the fact that risk can be and often is correlated across projects. Risk correlation can be found at the level of target, chemical space, disease, Therapy Area, drug format and the organisation. If the front-runner for a novel target fails, the likelihood of the followers to make it to market diminishes. If the same physician designs all your trials in Therapy Area X, the risk is higher than if different people with diverse backgrounds design the trials. What this means is that when risks are correlated, it is a mistake to simply use the same success probability for each compound in a given group, eg.: all targeting the same disease. In an industry with high overall attrition, most companies experience a negative effect from correlated risk. Only a few have benefited from the positive effects of risk correlation – an example is Genentech betting everything on monoclonal antibodies at the right time. Deep science and culture surely played a part, too.

3. The Corporate Risk Profile

Now let us take a look at the third and final point of our argument concerning the management of risk. The 1990s saw the rise of the shareholder value ideology in the US and Western Europe, which postulated that value creation for shareholders was the only legitimate goal for public companies.

The interests of other stakeholders such as employees and local communities were to be disregarded, as was the long-term survival of the corporation itself. In this context, professors Prahalad and Hamel published a hugely influential article in the Harvard Business Review in 1990 arguing that business strategy should be built on “The Core Competencies of the Corporation”. A focus on core competencies – and core businesses – was increasingly seen as an indicator of competitive health and value potential. Thus, pharmaceutical companies divested other businesses or were spun-off from their holding companies. The high margin/high growth pharmaceutical sector became a star of the stock markets.

But what was good for investors turned out not to be so good for most companies. Investors do not care about the longevity of the companies they are invested in – they can balance risk across their portfolio of stock holdings and in fact often stand to gain when companies are taken over.

The newly focused companies had significantly worsened their risk profiles (increased the likelihood of the catastrophic risk of kinks in their sales and earnings curves). Those with more cash on hand and a little more luck with in-licensing and R&D were forced into buying up their less lucky competitors in order to keep growing. In a nutshell, essential parts of corporate risk management were outsourced to the markets.

What we have seen is a clear-cut case of market failure. Markets were not and are not able to value early pipelines with long timelines and to deal with the near-impossibility of delivering R&D success in steady annual increments inherent in the risk profile of the industry. Aggressive in-licensing and M&A thus have become the main drivers of stock market success with few signs that the companies that disappeared were in any way structurally less capable of producing long-term growth than the survivors. Interestingly, a few companies bucked the trend and survived as part of diversified corporations.

The Fate of the Pharmaceutical Interests of Diversified Corporations

Conglomerates which divested their pharmaceutical business

- ICI – spun out Zeneca in 1994 and AstraZeneca later spun out agro business into Syngenta
- BASF – sold Knoll in 2000 to Abbott
- Dupont – sold its pharma business in 2001 to BMS
- Kodak – sold Sterling Winthrop in 1992 to Sanofi
- Akzo Nobel – sold Organon to SP in 2007
- Dow – spun out Merrell Dow into Marion Merrell Dow in 1989
- 3M – sold its pharma business in 2006
- Procter & Gamble – stopped in-house pharma R&D in 2007

→ Outside Japan, only Solvay, Merck KGaA, and Bayer continue to operate in both chemicals and pharmaceuticals

Pharmaceutical companies that divested their non-healthcare business interests

- Hoechst and Rhone Poulenc – divested chemicals in the 1990s, before merging in 1999 to form Aventis and later spinning off agro business to Bayer; Aventis in turn was taken over by Sanofi in 2004
- Sandoz – spun off its chemicals business in 1995 and merged in 1996 with Ciba Geigy to form Novartis; Ciba’s chemicals business was spun off shortly afterwards
- Schering – spun off its agrobusiness into Agrevo in 1994
- Roche – spun off its non-healthcare businesses in 1990s
- Pharmacia – spun off Monsanto in 2002 before being acquired by Pfizer in 2003

→ With the exception of Roche, which has a large diagnostics business, all of these companies have disappeared

Pharmaceutical Businesses that have been successful as part of conglomerates

- J&J – healthcare only
- Roche – healthcare only
- Novartis – healthcare only
- Bayer – chemicals, agro and healthcare
- Merck KGaA – fine chemicals
- (in 2003, Fresenius set up a small specialty company Fresenius Biotech)

Note that this analysis is far from exhaustive; most pharmaceutical businesses, including Merck & Co. and Eli Lilly were highly diversified at some stage of their life cycle, especially in the 70s and 80s, when diversification was synonymous with “good management”. Some continue to be active in related healthcare businesses but on a relatively small scale, eg.: GSK in consumer healthcare and BMS with Mead Johnson in nutritionals.

Against this background, it is illuminating to study the fate of the once flourishing German industry: the survivors were shielded from short-term stock market pressure by diversification (Bayer), private ownership (Boehringer Ingelheim, Grunenthal) or both (Merck KGaA), while those who followed the logic of focus and hence were fully exposed to the risk inherent in the ethical business have all disappeared (Hoechst, Knoll, Schering AG).

Conclusion: Risk Management and Strategy

Taken together, the two factors of **non-additive success probabilities** and **correlated risks** can lead to a **dramatic under-estimation of the risk of overall failure**. Traditional metrics, including the risk-adjusted expected value reflect pipeline value based on average industry success rates. They fail to capture the impact of risk correlation and the significant likelihood of the distribution of actual project results significantly deviating from the average. In other words, they hide substantial catastrophic risk and can create a false sense of security in management and investors.

Adding in the third factor of full exposure to the stock market without sufficient corporate risk diversification provides a convincing answer to the question of why no company has been successful through in-house R&D alone. **In a nutshell, you need too many projects and the risk of complete failure (or catastrophic risk) is too high for a smooth growth path of a company focused exclusively on ethical pharmaceuticals.**

Western pharmaceutical companies have developed sophisticated approaches to deal with the scientific, technical, regulatory and commercial risks inherent in their business. Their track record of strategic risk management is distinctly less impressive.

At Catenion, we believe this analysis provides a few insights that can help Japanese companies in their development:

We believe that whatever their current size and strategic position, Japanese firms would be well-advised to consider these lessons learnt in the West when designing their future strategies and organisational set-ups.

1. Strategic goals should be based on explicit trade-offs of the target innovation mix and the corresponding risk profile the company finds acceptable; on this basis:
 - a. **Quality comes first.** Adequate resourcing of key projects is more important than freeing funds for a few additional ones;
 - b. **Correlated risks** should be made **transparent** and **actively managed**, without too much focus in terms of targets, indications, drug formats, etc;
 - c. Risk should be further **diversified** by **partnering** to spread bets and gain access to projects with different risk profiles from the internal ones.
2. To encourage cross-fertilisation and creative solutions, companies need to create a culture of collaboration
 - a. Internally between functions and Therapy Areas and by **empowering project teams** to develop project strategies;
 - b. Externally with academia, biotechs and other pharmaceutical companies by encouraging **joint project work** with the partner whenever possible.
3. The experience of senior line management is best brought to bear by accompanying such a culture of collaboration by a **stringent R&D portfolio management process that ensures:**
 - a. **Full transparency** of project strategy options, all scientific, technical, regulatory and commercial risks, as well as approaches to risk mitigation;
 - b. **Tough challenging** of project teams on proposed actions;
 - c. **Clear rules** for project prioritisation and resource allocation;
 - d. **Adequate metrics** to capture the distribution of risk and value for each project and for alternative portfolios.
4. At the **corporate level**, companies should consider complementing the ethical portfolio with a **significant share of revenues** from **businesses** with a **different risk-profile** in order to:
 - a. Cushion the effects of temporary “bad luck” with the ethical pipeline;
 - b. Obviate the need for consolidation or expensive in-licensing driven purely by financial need, rather than by opportunity.

C. Structure of the Japanese Top Twenty Pharmaceutical Companies – Four Groups with Distinct Strategic Challenges

Overview of the Top Twenty

As mentioned above, the industry environment in Japan has changed over the last few years – and so has the industry itself. Foreign firms have staged a few take-overs (eg.: Merck Banyu) or have entered into close alliances backed up by shareholdings (eg.: Roche-Chugai). There has been a spate of consolidations among local players, leading to the formation of Astellas, Daichii-Sankyo, Kyowa Hakko Kirin and to the entry of Fujifilm into the industry through its alliance with Taisho/Toyama. In general, companies have begun to do their homework in terms of restructuring domestic Marketing and Sales operations, redesigning R&D strategies, process re-engineering and beginning to develop long-term visions and strategies.

As a group, Japan's pharmaceutical top twenty share a few characteristics that are often overlooked by Western observers and bode well for their future:

- A proven track record of blockbusters, among them pravastatin, donepezil, aripiprazole, levofloxacin, rosuvastatin – to name but a few;
- Strong balance sheets with between six months' and 1.5 years' worth of equity with no significant debt (with the exception of Eisai);
- A shield against stock market volatility and pressure through the controlling interest of a conglomerate or a family or by having implemented poison pills, as seems to be the case with Eisai;
- A long-term management perspective deeply embedded in the country's culture which is well-suited to the requirements of an R&D-based pharmaceutical business;
- Lower susceptibility to the latest management fad by Japanese managers as a whole in comparison to some of their Western colleagues.

On the basis of size, current business dynamics and profitability, we have identified four groups of players among the top twenty that face distinct strategic challenges.

Group 1: Potential Global Mega-Players

The first group is made up of the three “Potential global mega-players” Takeda, Astellas and Daiichi Sankyo. While classified as “mid-sized” in the global industry, these three companies have broad portfolios of marketed drugs in a mixture of primary care and specialty businesses and strong in-house R&D for small molecules and biologics. Having achieved a significant share of total sales in global markets of around 50 % and sporting excellent margins, they essentially face the same issues and dilemmas as their Western competitors. Based on our analysis of the nature of risk in this business, one might expect further mergers either within this “pharmaceuticals-only” group or with Western companies. Alternatively, they could opt for a portfolio diversification approach to better manage their respective risks or try and develop innovative business models building on the lessons outlined in the previous chapter.

Group 2: Potential Global Niche and Specialty Players

The second group we would call “Potential global niche and specialty players”. This is a somewhat heterogeneous group which, however, shares a few key characteristics: Smaller in size than the three companies in Group 1, these companies have a proven track record of innovative R&D, are mostly invested in biologics, enjoy benchmark operating margins of 20 % or more, are debt-free and seem well positioned to expand and grow globally despite currently marginal international operations. We would count Ono, Shionogi and Santen, as well as three larger companies Eisai, Otsuka and Chugai in this group.

Eisai is the largest firm in the group with 40 % of sales generated abroad. The company has followed the received wisdom of the industry and built up an infrastructure, portfolio of marketed products and pipeline focusing on oncology and CNS. It has wisely used the profits it has earned with Aricept and is the only company of the top twenty to have raised debt for an acquisition (MGI) aimed at countering the effect of patent loss of its blockbuster in 2010.

Following in Eisai's steps, Otsuka Pharmaceuticals has built an international infrastructure on the back of Abilify. In contrast to the other companies in this group, the company's pharmaceutical business is embedded in a vast conglomerate of businesses, with the profitability of the pharma business and mid-term growth perspectives unclear and intransparent to the outside observer.

Finally there is Chugai, historically the biologics leader amongst the Japanese firms. The company faces an unusual strategic conundrum: The alliance with the Roche Group and the richness of their pipeline mean Chugai will have to massively invest in the domestic development and marketing of a string of global blockbusters. Whether or not its financial position and theoretical independence under the agreements with Roche will allow it to become an independent global player driven by its own in-house R&D and with commercial operations in major markets outside Japan remains to be seen.

Companies in this group face similar challenges as Western up-and-coming players, like Shire, UCB, Celgene and Ammiral. They must succeed on the basis of focused, excellent R&D with an innovation mix containing a significant share of potential breakthrough projects addressing high unmet need, albeit for smaller populations and resulting in compounds of sufficient commercial value to invest in global growth. In order to do so, they have to venture selectively into novel technologies, complement sales and pipeline portfolios through targeted M&A of small companies with an edge and broadly pursue in-licensing and partnering. The position of a global player requires the build-up of small but significant infrastructure in foreign markets for niche and specialty indications with high unmet need.

If luck strikes big, there is a chance to move up into Group 1. If bad luck hits, they will be take-over targets for the ever-hungry majors or they will have to retreat into a domestic play and join Group 4, that is unless they have achieved a level of corporate risk diversification that shields them from temporary mishaps in their ethical pipeline.

Group 3: Subsidiaries of Japanese Conglomerates

The "subsidiaries of Japanese conglomerates" form a third group of companies sharing essential characteristics and challenges. Mitsubishi Tanabe, Dainippon Sumitomo, Kyowa Hakko Kirin, Japan Tobacco and of late Fujifilm-Taisho/Toyama all have much smaller pharmaceutical businesses than companies in Group 1 and show poor profitability compared with their peers in both Groups 1 and 2 with the exception of Mitsubishi Tanabe. None of the companies in this group has built a significant international infrastructure but their pharmaceutical operations are all shielded from stock market volatility by virtue of having a diversified majority shareholder. R&D track records look diverse, with Kyowa Hakko Kirin and Japan Tobacco having built a comparatively strong basis in biologics.

The situation of Mitsubishi Tanabe and especially Dainippon-Sumitomo is delicate. Sub-standard industry profitability of largely primary care-dominated portfolios contributes significantly to the operating margins of their respective holding companies. One sees a danger of a repeat Kodak-story lurking. Kodak, it may be remembered, bought Sterling-Winthrop for \$5.1 bn in 1988 and let it manage itself for a few years. Five years later, a decision was made to split the company up and divest its businesses to a number of companies – among them Sanofi.

Whatever their future plans, all companies in this group must build competitive R&D machines to fulfill the leadership visions of their holding companies. Me-too R&D will not suffice to achieve this end. The key strategic question to answer is whether the aim is to ultimately position the company in the group of potential Japanese mega-players or build a global specialty business – two very different strategies requiring fundamentally different business models. Just as importantly as for the players in Group 1, innovation at the business model level should be a major topic for the companies in this group. Whichever option is pursued, it is fair to predict that most of the Group 3 companies will be involved in major M&A transactions sooner or later, either building or divesting.

Group 4: Smaller Japanese research-oriented companies

Finally, there is a number of “Smaller Japanese research-oriented companies” which we would assign to a fourth group. Most prominent among them are Kyorin, Mochida and Nippon-Shinyaku. With sales well below \$ 1 bn, slow mid-term growth and operating margins around 10 %, these companies are smaller in size and notably less profitable than those in Group 2. Also, they tend to run their pharmaceutical businesses as part of a larger healthcare business portfolio, eg.: Mochida with Mochida Siemens Medical Systems.

R&D budgets of these players are comparatively small. For these companies, there would seem to be room for a strategy of profitable growth in the domestic market fuelled by occasional R&D success.

Given their size and available resources, these companies would be well advised to target their innovation mix more towards improving on established, de-risked areas and to pursue potential breakthrough research with limited resources.

Out-licensing global rights of candidates having achieved proof of concept and in-licensing domestic rights to globally successful compounds for the Japanese market forms part of Kyorin's explicit strategy of being a “Global Drug Creation Company” – a strategy which looks sensible as long as the risks inherent in drug creation are well managed by diversification at the project portfolio and corporate levels.

In addition, there is ample room for consolidation with struggling companies in the next tier below, as well as for growth by building contiguous businesses and healthcare brands.

D. Conclusion – Sustainable Competitiveness Must Be Built with Innovative Business Models

Beyond differing scopes for long-term strategic positioning, all Japanese companies face the underlying challenge and opportunity of achieving a step-change in innovativeness and risk management.

In fact, our quick review of company websites and publications has produced two unexpected findings:

- Most leading Japanese pharmaceutical companies have so far not followed the Western example of the uniquely focused, non-diversified, public firm;
- Surprising examples of Japanese companies applying elements of a novel approach to innovation management.

Suffice it to mention Shionogi's Finds initiative (Pharma Innovation in Drug Discovery Competition Shionogi) and the company's "collaborative" Innovation Center for Drug Discovery on the campus of Hokkaido University. The Kaspac Institute of Dainippon Sumitomo at Karolinska Institute for Alzheimer's research and Astellas' joint venture with Kyoto University, the Innovation Center for Immunoregulation Technologies point in the same direction. The open floor design to further communication at Astellas' new research facility in Tsukuba and a high-level global clinical project management function reporting directly to the CEO at Eisai take up other insights into the dynamics of breakthrough innovation.

At the strategy level, it is Ono that most clearly goes beyond the usual but rather meaningless mantra of "first in class and best in class". The company states it aspires to, "develop first-in-class drugs that do not exist anywhere and that no one has dealt with before", focusing on the "motivation of individual scientists". Shionogi is managing risk with its global but targeted co-discovery, development and commercialisation alliance with Purdue in pain.

At Catenion we are newcomers to the Japanese market and its players. Our long experience with Western companies, however, has trained us to spot some of the fundamental short-comings of the established approaches to innovation management and risk management.

We are also naturally sensitive to differences in the Japanese approach to management. Top-down, short-term strategies and decision-making as practiced in the West are fundamentally at odds with the requirements of breakthrough innovation. Could it be that the principles of *nemawashi* – consensus building – and *ringi-seido* – shared decision-making – might serve as a basis to a specific Japanese culture of innovation management embedded in collaborative community?

The skeptics will argue that breakthrough innovation always has to go against the established consensus. We leave it to our Japanese readers to judge whether there might be a grain of truth to this intuition or whether this is just another misperception of Western observers about things Japanese.

Whatever the answer, [simply copying the business models of the West](#) will not do for Japanese companies to fulfill the Ministry's vision, except through sheer luck. To many observers, the country's industrial genius lies in imitating and improving on Western models, as exemplified by the success stories of the Japanese electronics, ship-building, machine tool and car industries. We hope to have shown in this Commentary that [establishing sustainable positions of competitiveness in the global pharmaceutical industry will require more than incremental innovation](#).

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Berlin · Headquarters

Catenion
Hausvogteiplatz 12 · 10117 Berlin
Germany
phone: + 49 30 20 63 996 – 0
fax: + 49 30 20 63 996 – 22

Dr. Markus Thunecke · Senior Partner
phone: + 49 163 850 91 53
email: markus.thunecke@catenion.com



Dr. Matthias Krings · Partner
phone: + 49 163 850 91 54
email: matthias.krings@catenion.com

Arno Heuermann · COO
phone: + 49 163 850 91 51
email: arno.heuermann@catenion.com

London

Catenion
211 Piccadilly · London W1J 9HF
United Kingdom

Christian Elze · Senior Partner
phone: + 44 7044 008 009
email: christian.elze@catenion.com

www.catenion.com

