L.E.K.

Special Report

How to Navigate the Challenging Japanese Pharma Market

Contents

Overview

Many pharmaceutical companies operating in Japan are facing a period of unprecedented pressure. Mounting challenges include price cuts, ongoing patent expirations, the increasing uptake of generics, and the seemingly immutable costs of a large, non-specialty sales force. Many pharma companies — small and large, local and multinational — will face considerable financial strain in the coming years as some struggle to reposition themselves for profitable growth or even long-term viability. However, those that can identify and focus on their true strengths, build value-oriented portfolios, and upgrade the analytics driving their operations will be best able to differentiate and win.

In this Special Report, L.E.K. Consulting proposes a range of tactics and strategies to help pharmaceutical companies in Japan navigate near-term profitability pressures; position themselves for efficient, profitable growth over the longer term; and potentially forge a path to market leadership.

Historical perspective

There was once a time when branded pharmaceuticals in Japan enjoyed a lengthy, graceful twilight following the loss of market exclusivity. Revenues for so-called long-listed brands — typically primary care-focused products — were historically resilient even when up against numerous generic entrants. For example, sales of the H2 blocker Gaster (famotidine) declined by only approximately 5% in each of the first two years following loss of exclusivity (LOE) in 2001, and sales of the statin Mevalotin (pravastatin) barely shifted after LOE in 2002 and the subsequent launch of 23 generics. Unlike in other markets, both physicians and patients in Japan have stubbornly refused to accept generics' claims of equivalence. Furthermore, until fairly recently, other actors in the supply chain have had little incentive to shift volume away from long-standing best-sellers. The result? As recently as 2008, generic penetration in Japan had reached only approximately 30% of substitutable volume — a fraction of generics' share in other major markets.

The far longer product life cycles in Japan benefited both the local pharma industry and subsidiaries of international pharma companies. Under these circumstances, non-specialty products remained important revenue drivers for companies operating in Japan, even as worldwide pharma shifted its attention to newer specialty drugs. With companies in Japan continuing to invest considerable amounts in the sales infrastructure required to support these long-listed products, it seemed the country's large, legacy sales forces would be spared the ravages wrought on their contemporaries in other major markets.

However, over this same period — and still today — Japan's economy has struggled. Together with this financial strain and the increasingly elderly population, a number of other factors have exacerbated the pressures on Japan's healthcare system, including diffuse delivery, archaic reimbursement, and the availability of innovative yet costly drugs. Given these pressures, the government has sought ways to reduce healthcare expenditures — and naturally has turned its sights on long-listed branded drugs, in turn burdening companies that derive a large proportion of their sales from these drugs.

Background: Economic challenges facing companies in the Japanese market

Government initiatives to encourage generic penetration began in earnest in the early 2000s with the introduction of higher fees payable to prescribers and dispensers of generics, as well as a redesign of prescription formats intended to sway physician's opinions. These measures gathered momentum over the next few years, with more frequent listings of new generics, requirements for physicians to opt out of substitution, and greater incentives to dispensers for substitution. The Japanese government also put forth a great deal of effort to shift physician and public opinion in favor of generics and to encourage overseas generics companies to enter the market in anticipation of growing demand. These efforts corresponded with a marked uptick in the substitution rate as the 2000s gave way to the early 2010s, with rates exceeding 60% by 2016 and seemingly on track to get close to or even meet the government target of 80% by 2018–2020.

In 2014, the government also introduced punitive pricing measures targeted at long-listed drugs that continue to maintain market share in spite of the availability of generics. Under what's known as the "Z2" rule, pricing for long-listed products is reduced by up to 2% every two years, in addition to cuts made under the R-Zone rule if generic replacement rates for that brand fail to reach 60% five years after the first generic listing.

Meanwhile, in response to growing generic competition in markets outside Japan, international pharma and the more global-minded Japanese pharma companies (most notably, Takeda and Astellas) were reinvesting in their pipelines. These investments are now bearing fruit, offering these companies new sources of revenue that will in due course replace declining sales from their long-listed products. More locally focused companies, however, erroneously assumed their businesses to be insulated from generic pressure and failed to make equivalent efforts to reinvent their portfolios. Today, they find themselves unhappily tethered to the increasingly pressured long-listed product model.

Despite clear economic imperatives, Japanese companies have struggled to "right-size" their costly commercial infrastructure to match the diminished revenue outlook for their leading brands. The most innovative companies are striving to adapt in both focus and skill to the sales requirements of specialty-driven portfolios. Labor laws and cultural norms in Japan make it very hard to trim sales capacity quickly. Public opinion frowns on redundancies, and newspapers and other mass media channels are quick to condemn restructuring efforts, which reflect poorly on the organization in the eyes of customers and contribute to moral quandaries for management. Redundancies are typically viewed as legitimate only when accompanied by large payoffs, yet these often offset the underlying economic rationale for such layoffs.

In order to scale down commercial organizations, companies in Japan typically face a finite set of options: Either they bite the bullet and provide redundant sales reps with sizeable payoffs (thus compromising the economic benefit of down-sizing), or they maintain their sales forces and repurpose more versatile reps to cater to specialty call points, while relying on retirement to whittle down excess capacity. Companies in Japan cannot even rely on frequent turnover to contribute to necessary scaling down; employees, even in sales professions, tend to change jobs infrequently (although younger people have begun to think differently in this regard). Nor can pharma companies rely on reducing headcount because of poor performance as sales forces have historically operated on the basis of seniority rather than meritocracy, leaving managers with no rationale for dismissals.

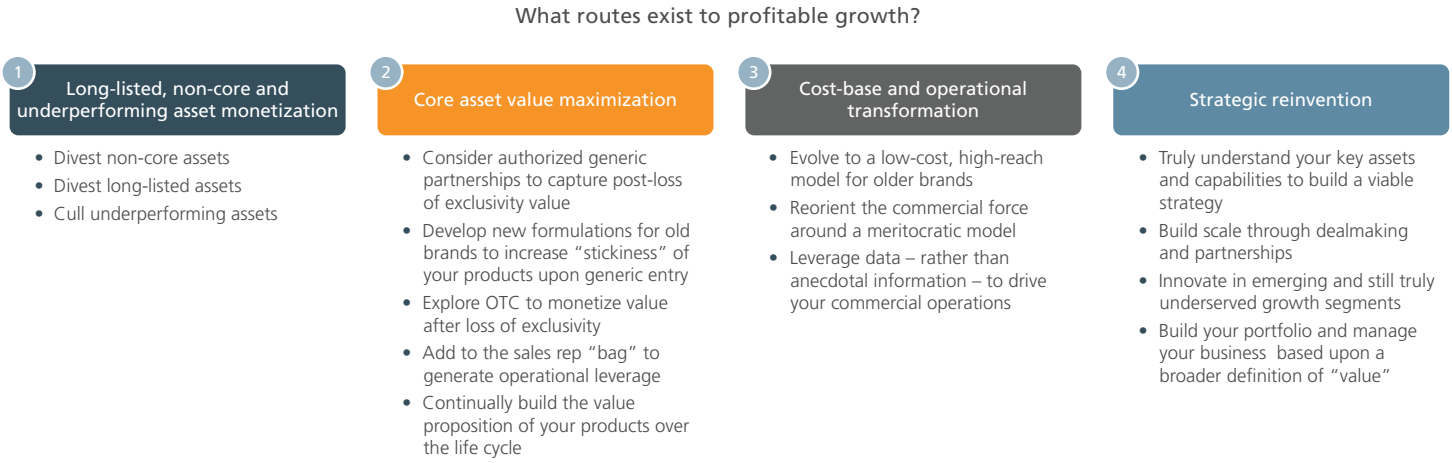
As a result of these dynamics, many pharma companies, both foreign and domestic, are facing increasing pressures on profitability.

Although robust pipelines promise brighter days ahead, many foreign companies operating in Japan — and the larger, more innovative local companies — should anticipate near-term pressure on profits. The challenge for these companies is two-fold: First, they need to identify the immediate tactics that will prop up sales and shed sales capacity. Second, they need to establish the capabilities that will help them differentiate and achieve enduring success in increasingly competitive growth segments.

The future looks bleaker for smaller, locally focused companies that were caught unawares by government efforts to promote generic substitution and apply pricing pressure on long-listed brands. Many lack a strategy that will either help them navigate the urgent, critical threat to their profit drivers or steer them toward long-term growth. For these companies, the challenge is existential.

Key tenets for near- and longer-term commercial success in Japan

With these challenges in mind, we have identified a series of levers that pharma companies operating in the Japanese market can consider in order to optimize near-term profitability; direct their commercial organizations toward a leaner future; equip themselves with capabilities that enhance competitiveness; and pave the way to viable, lasting strategies. Although some of these levers may be obvious to certain readers, our experience indicates that companies operating in Japan generally are not exploring these tactics in earnest and may gain from having a better understanding. Other levers, especially those around the use of analytics to enhance commercial operations and expanding brand value propositions to encompass economic considerations, will interest the majority of our readers.



1. Long-listed, non-core and underperforming asset monetization.

   - **Divest non-core assets.** Divestment of non-core assets, such as manufacturing capabilities or brands in non-core disease areas, may inject much-needed cash that can be redeployed to more advantageous ends, bolster financial metrics, and create value as new owners invest additional time and resources in managing these assets. Takeda was able to generate $1.3 billion by selling its chemicals business to Fujifilm. Similarly, AstraZeneca entered into a deal worth up to $770 million with Aspen for AZ's non-core anesthesiology business, including its sizeable Japanese business.

   - **Divest long-listed assets.** For diversified pharmaceutical companies that enjoy successful in-market brands, divestment of long-listed brands can generate the cash to promptly secure breathing room throughout the wait for promising pipelines to mature. While the net present value (NPV) basis of such decisions is sometimes questionable, the immediate impact on earnings can soothe anxious investors, assuming the strategy does not suggest desperation or mismanagement. For example, Novartis Japan's deal with Sun Pharma appeared to be a win-win, with Sun gaining scale in the marketplace to help its burgeoning Japanese generics business, and Novartis generating cash from old assets. Mitsubishi Tanabe also benefited from this deal, agreeing to provide its commercial capabilities (and thus soak up some of its excess sale capacity) to help Sun promote its suddenly expanded business.

- **Cull underperforming assets.** Companies operating in highly competitive yet underwhelming drug classes (e.g., SGLT2s for type 2 diabetes) are likely faced with challenging P&Ls that offer at best a cloudy outlook for improvement. Other companies seeking to establish a foothold in the marketplace may be willing to acquire such assets, as well as any associated commercial infrastructure, for the strategic purposes of developing a platform in a disease area for future drug launches. In such cases, divestment can be a valuable means of shedding both low-performing assets and costly commercial capacity.

2. Core asset value maximization

- **Capture value after LOE through authorized generic partnerships.** Authorized generic (AG) deals allow branded pharma companies to participate in value created after loss of exclusivity that they would otherwise miss out on.

By awarding AG rights to a generic partner, originators permit the earlier entry of a generic competitor to the brand in return for milestone payments and, potentially, royalty streams from the generic. The generic company benefits from the opportunity to build a strong volume position prior to entry of its competitors and from the perception of high quality that comes from being first to market. However, originators must design deal terms that result in net value creation by weighing the value of the deal against the impact of the generic's early entry on branded sales.

- **Develop new formulations for old brands.** Investment in new proprietary dosage forms prior to LOE can increase "stickiness" of products and complicate substitution upon generic entry. For example, Shionogi has developed an oral disintegrating form of Crestor (rosovastatin) in an effort to protect Crestor sales after patent expiry in late 2017. Similarly, product design can achieve subtle points of differentiation among drug devices — without notable clinical impact — that may result in patient preference for the long-familiar delivery device over the bioequivalent generic newcomer.
- **Explore OTC to monetize value after loss of exclusivity.** The over-the-counter (OTC) channel offers well-established pharmaceuticals the chance at a second life of sorts. While the OTC regulatory path has proven challenging in the past, the MHLW (Ministry of Health, Labor and Welfare) is endeavoring to lower entry barriers for well-known, safe drug classes such as PPIs (Proton Pump Inhibitors). While the commercial potential of branded OTC drugs is far lower than is typical for prescription counterparts, the target customer segment for an OTC formulation is often distinct from that for the prescription formulation; the licensee often tends to assume most of the responsibility for regulatory approval and initial safety monitoring, thus resulting in little downside or incremental expense for the licensor. Depending on the partner, OTC deals may also result in swift, sizeable cash payments that would be otherwise forgone.
- **Add to the sales rep "bag" to generate operational leverage.** Another approach that could reverse declining sales and commercial overcapacity is to simply add brands to the portfolio. However, with so many companies chasing quality assets for strategic purposes and paying premiums for global rights, there are generally few attractive, reasonably priced candidates that would be appropriate

for opportunistic Japan-focused deals. Moreover, when Japanese rights are available, competition is fierce among the many Japanese companies that have long made local commercialization a key part of their domestic strategy. Adding biosimilars to the portfolio (as discussed further below) lends an alternative flavor to this strategy, and this maneuver is attracting a lot of attention among larger local and international pharma companies with excess commercial capacity. Yet we caution companies about pursuing such tactics solely to offset the fixed cost of a large sales force in legacy disease areas. Unless a sales force is of strategic value and required for commercialization of promising pipeline programs, it seems counterintuitive that "innovative" pharma companies should be pursuing such deals simply to prop up these oversized relics. A more suitable line of attack would be actively seeking to scale down or reallocate capacity to disease areas and brands that are clearly core to the strategy.

- **Build the value proposition of products over the life cycle.** Companies should continually look to build the value proposition of their products over the full life cycle of the drug to maximize access, patient share and price, and potentially to broaden the label of products and subsequently extend the life of their products. This requires a strategically minded medical affairs team to scope and execute small-scale studies and retrospective analyses that are supportive of commercial goals. These efforts can be directed at physicians, but should also focus on the government payer, which — with the advent of health technology assessments and prescriptive, government-issued usage guidelines — will become an increasingly important arbiter of price and access. Analyses of real-world data sets (derived from claims, electronic health records (EHRs), post-marketing surveillance data sets, and so forth) are critical inputs to these activities. Both medical affairs and pricing and access teams must be sufficiently skilled to understand these resources and to scope analytics that will bolster product value propositions in the eyes of prescribers and payers.

3. Cost-base and operational transformation

- **Evolve to a low-cost, high reach sales model for older brands.** Many older brands in well-established drug classes where much of the competition has already yielded to generics do not necessarily require skilled and costly medical reps to maintain sales. Tapping more efficient alternatives to the traditional MR-led detail may allow older brands to maintain brand awareness among physicians and sustain prescription volumes. For example, syndicated sales forces such as those offered by CMIC Ashfield enable pharma companies to share sales reps with other noncompeting companies that address a similar call point, thus preserving reach while improving rep productivity, which may translate to savings relative to the MR model. Virtual sales forces (such as those offered by EnTouch) that rely on a flexible staff of former MRs to deliver details via a web-based platform present another alternative to the

traditional model. Scheduling time slots in advance rather than snatching opportune moments in a physician's day renders the typical virtual detail both longer and more able to engage with doctors who are free of distractions. Moreover, the virtual MRs are paid only for the time they spend scheduling and detailing, not for time spent traveling or waiting for physicians to become available. A service rep

model represents an even greater departure from the norm; these employees are not MRs at all, but rather experienced salespeople from adjacent industries (e.g., consumer goods) who concentrate on maintaining awareness among physicians rather than focusing on scientific details, and who cost a fraction of the typical MR.

- **Reorient the commercial force around a meritocratic model.** As mentioned earlier, sales forces in Japan rely on seniority rather than merit to guide promotions and salary increases. This norm has long prevailed, and efforts to implement a performance-based model akin to that seen elsewhere in the world are indeed up against a challenge, given how ingrained the seniority model is in Japanese corporate culture. However, a performance-based sales model has multiple clear benefits: It rewards and helps retain top performers, puts top performers in positions where they can be most impactful, creates a desirable "metabolism" in the sales force, and can contribute to organic attrition among sales reps whose interests are not best served under a meritocratic model. Nevertheless, companies need to design such a system thoughtfully to ensure performance is indeed measured accurately and appraisals are based on fact. Furthermore, companies need to comply with local laws as well as communicate and manage change tactfully throughout the organization in order to navigate what can be a highly controversial shift in management practice.
- **Leverage data — rather than anecdotal information — to drive commercial operations.** Both local and global pharma companies in Japan are still relatively undeveloped in their use of data and analytics to maximize the efficiency and effectiveness of their commercial ops. Large data sets such as claims and EHR data are not routinely used by commercial organizations as they are in the U.S. and Europe. To the extent these data are used, the emphasis is often on health economics or adverse event tracking rather than measuring commercially relevant KPIs. However, the opportunities to use a plethora of data to enhance commercial operations will increase as patient journeys evolve and become more nuanced (for example, due to the advent of companion diagnostics and personalized medicine), as influence over treatment decisions becomes diluted across a greater number of stakeholders, and as the range of data available to support commercial operations develops. Moreover, as growth segments such as immuno-oncology, IBD and respiratory become increasingly competitive, companies that struggle to differentiate around product characteristics alone may be able to achieve wins through commercial excellence — by proactively adopting sophisticated analytics to guide commercial activities.

4. Strategic reinvention

    - **Truly understand your key assets and capabilities.** Viable strategies are built on a foundation of valuable, elusive assets and capabilities; leveraging these points of differentiation enables companies to create value. Although many pharma companies in Japan consider themselves innovative, they often derive the vast majority of revenues from either long-listed products or generics, and lack the capabilities required to truly innovate. Only a select group of top-tier, globalized and second-tier Japanese pharmaceutical companies can realistically claim to be R&D-driven; the resources required to enter and maintain membership in this group are beyond the reach of many other companies. This delusion goes a long way toward explaining the ongoing reliance of these smaller companies on long-listed products despite the clear imperative for change, and to some degree prevents them from developing viable strategies as the basis for future growth. Not everyone can be an innovator; focusing on innovation alone may cause these companies to overlook other routes to value creation and long-term viability.

Pharma companies operating in Japan need to focus on their strengths and on the growth vectors surrounding their particular points of differentiation. For some companies, strong distribution and sales capabilities present

opportunities beyond marketing solely groundbreaking pharmaceuticals. Takeda, for example, has entered into a joint venture that marries its sales prowess and distribution relationships with the manufacturing scale of Teva, one of the world's largest generics companies. Similarly, Daiichi Sankyo has partnered with Amgen to combine its commercial scale with Amgen's emerging biosimilars portfolio in the Japanese market. Maruishi, a smaller Japanese company, focuses its energies on a finite set of hospital call points along the surgical continuum, where it has a market-leading position in anesthesia and post-surgical pain. Maruishi leverages this targeted commercial scale and expertise to become a "partner-of-choice" for innovators lacking such infrastructure, as evidenced by its Japanese commercialization partnership with Faron Pharmaceutical for Faron's acute respiratory distress syndrome asset, Traumakine.

- **Build scale through dealmaking (AP) and partnerships.** Companies with largely generic and long-listed portfolios, faced with increasing competition (including the renewed presence of large, international generics companies with a highly efficient cost structure) and pricing pressure, will need to build scale to remain viable. Japan's pharmaceutical market is notoriously fragmented, with some estimates suggesting approximately180 companies marketing drugs locally. Although this fragmentation creates precarious operating conditions for many of these companies, it also presents considerable opportunities for those willing to build and leverage scale. Recognizing this, scaled global generics players have entered the market, albeit with varying levels of success due to challenges around local distribution and the slow maturation of Japan's generic market. Local generics companies remain relatively passive in this respect, and despite clear economic imperatives that have long suggested the need for consolidation, the market remains fragmented. Nevertheless, we see an attractive opportunity for well-resourced players and/or those with strong relationships with lenders and investors, to roll up the more attractive and willing of its generics competitors and build a home-grown, scaled generics player that could potentially leverage its newfound scale to compete outside of Japan as well.

  Companies that are differentiated by their focus on a particular disease or care continuum should augment this through addition to their product portfolio, expansion of commercial capabilities, and other distinguishing moves to solidify their position and surge ahead of the pack. Ayumi Pharmaceuticals, for instance, has acquired a portfolio of both novel and long-listed drugs and developed a commercial platform targeted at rheumatic and orthopedic pain, and is seeking now to develop its presence in the space through the licensing of biosimilars.

  It is worth noting that the bold strategic moves — especially where acquisitions and partnerships are involved — are inherently risky, however, with several companies having been "burned" by large acquisitions that did not deliver the anticipated return; deals involving Daiichi Sankyo/Ranbaxy and Shionogi/Sciele are good examples. Careful diligence is critical in such cases, including a realistic, disinterested appraisal of the operations and commercial potential of targets and the strategic rationale behind the deal. Also essential is serious, careful consideration of the likelihood

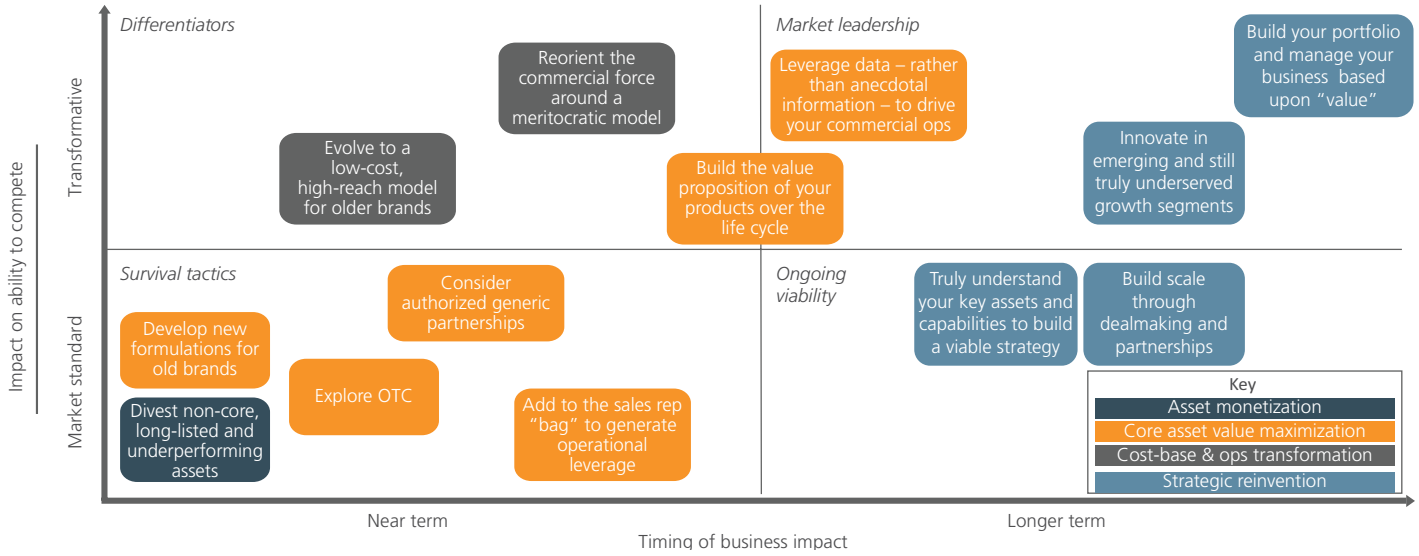
and implications of downside scenarios, and of how to best integrate targets that are often located overseas and inhabit a corporate culture very different from that of the acquirer.

- **Innovate in emerging and underserved growth segments.** We see many local, innovative pharma players drawn to the same diseases as their peers in Japan and other major markets — chiefly oncology, but also immunological and metabolic disorders. The barriers to entry in highly invested disease areas, especially oncology, are great, and it is likely too late to build a de novo presence in these marketplaces that, luck notwithstanding, would be anything but value destructive. Smarter companies are looking to build positions in emerging and less-obvious growth segments, orphan and rare diseases, critical care, and (over a longer period) antimicrobial resistance. Attractive growth segments such as rare diseases may still be poorly understood. The market need may still be emerging as with antimicrobial resistance, provider financial accountability and quality. And market orthodoxy may still inform an inability to envision the world differently; for instance, the biosimilar opportunity may be discounted due to skepticism about willingness to adopt, despite clear alignment with economic reality and tailwinds from growing acceptance of small-molecule generics in Japan. But consider these challenges from an innovator's perspective: Industry interest is similarly nascent, the barriers to entry are still modest, and the possibility of value creation is still present.
- **Build the portfolio and manage the business based on a broader definition of "value."** With Japan's pricing and access landscape changing rapidly (see our recent report on *New Realities of Drug Pricing and Access in Japan*), we believe there is an emerging opportunity for companies that can develop drugs with demonstrable value — both clinical and economic — to differentiate and win. This means learning from the European and, increasingly, U.S. experience in terms of how development programs are prioritized and how trials are designed to include not just direct clinical benefits as understood by the physician, but also consideration of systemwide economics and patient-oriented outcomes such as HRQoL (Health-Related Quality of Life) that can inform cost-utility analyses. From a portfolio standpoint, companies should understand in granular detail the range of stakeholders involved in access and clinical decision making as well as the criteria these stakeholders use to make decisions, and should incorporate this understanding into business case assessments and portfolio prioritization decisions. From a clinical development standpoint, companies that

wish to embrace this trend should design trials that include QoL endpoints, consider healthcare utilization for subjects over the course of trials, and conduct supporting health economic analyses to support access and pricing discussions. Moreover, Japan's fast-changing market landscape may offer opportunities for forward-thinking companies to explore risk-sharing agreements. Companies that develop programs attentively and that collect and analyze real-world data to understand the systemwide economic impact of their product may feel sufficiently confident to take on risk in return for favorable pricing and access, at the expense of their more ill-prepared or timid competitors.

Implications for pharma companies operating in Japan

What impact will these levers have on a pharma company's ability to compete and win over time?



Global pharma and top-tier Japanese pharma companies should seek to lead. Many larger pharma companies are facing immediate challenges in Japan that will undermine profitability and provoke irritation among investors. The levers mentioned suggest several ways for these companies to optimize local operations and support profitability and cash generation in the near term. Renouncing complacency and shedding commercial capacity, while necessary for many, will be tough and culturally challenging, although novel approaches to reduce capacity — such as transferring MRs to CSOs (Contract Sales Organizations) or bundling MRs with asset divestments — may soften the blow. Shifting commercial organizations away from seniority-based to meritocratic remuneration and promotion will support efforts to reduce and reorient capacity in the near future while also serving to enhance the quality of the commercial organization over a longer time horizon.

We believe that this segment's most promising strategies — on developing and commercializing existing pipelines, and building further scale in focused disease areas — will be supportive of long-term success. However, given how crowded the innovative growth segments are likely to become, it may take more than compelling products alone to win in the marketplace. Two broad elements suggest future success in the Japanese pharma market:

1. Chiseled, value-oriented product profiles that differentiate both the launch and the in-market portfolios
2. Lean, focused and smart commercial organizations that support both effective engagement with stakeholders and capture of patient volume

Both scenarios demand enhanced analytics that enable collection and analysis of the data required to build underlying value propositions and to generate the insights that will elevate commercial organizations.

Other top-tier and second-tier Japanese pharma companies should build on their strengths, innovate selectively, and prepare to make difficult decisions. Large local pharma companies, which have lagged behind their more innovative peers, may benefit from diversification into emerging growth areas where their development skills and commercial scale will serve them well. They also should look to envision themselves as a local partner of choice for smaller foreign biopharmas, and to reinvigorate their pipelines through focus on disease areas with credible prospects of generating value rather than on areas that are overinvested and that offer only limited value creation at this time. For those in this group whose businesses are more heavily weighted toward generics, viable growth vectors likely exist in biosimilars and in building greater scale in small-molecule generics.

These companies may also need to make tough decisions about commercial capacity that, historically, they have been reluctant to make due to prevailing cultural norms. If new revenue streams cannot be generated to support the legacy sales force, and if unwieldy R&D organizations continue to yield little, then top-tier and second-tier companies will need to aggressively pare costs to maintain financial sustainability.

Smaller Japanese pharma companies urgently need a fundamental strategic rethink. Smaller companies must accept that they can no longer rely on long-listed products to support their businesses. These firms need to take a frank look at their core assets and capabilities and at the resources available to them in order to understand where the market is headed and develop strategies accordingly. To do nothing is implicitly choosing either to be acquired or to go bankrupt. Bolder organizations may be capable of building compelling scale in either manufacturing or specific disease areas that will stimulate longer-term viability — or at least maximize their value when the time comes to exit. However, these companies need to act with urgency. The simple reality of fast-declining market share and price will make survival increasingly challenging.

Why Pharma Companies in Japan Must Rethink Growth Strategies was written by **Patrick Branch,** Principal, and **Ray Fujii,** Managing Director, in L.E.K. Consulting's Tokyo office.

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