

Pharmaceuticals and Medical Products



The moment is now

Successful pharmaceutical alliances in Japan

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The moment is now: Successful pharmaceutical alliances in Japan

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The moment is now: Successful pharmaceutical alliances in Japan

Introduction

Alliances between Japan-based pharmaceutical companies and Western partners have a long history. Since the 1950s, domestic firms and multinational corporations (MNCs) have come together with big schemes and high hopes to pursue joint ventures, co-promotions, and other deals. But most alliances have ended in disappointment, with returns to one or both partners falling below expectations. Not surprisingly, several deals terminated early, as companies lost interest in the alliances and redirected their resources to more rewarding projects. Although Japan is now the second-largest pharmaceutical market, most MNCs have yet to capture the full opportunity there.

Recently, however, the industry has hit on a new alliance strategy for MNC originators that want to operate in Japan—the reverse co-promotion. As this paper will discuss, reverse co-promotions offer pharmaceutical companies appealing options for drug distribution, field-force detailing, and sales booking. Since these alliances are relatively new, limited information is available on their outcomes. But a review of five reverse co-promotions initiated over the last few years suggests that these deals produce greater benefits for both Japanese companies and MNCs than traditional alliances—and since both parties receive significant advantages, mutual commitment is easier to sustain.

Reverse co-promotions are particularly attractive now, as the changing pharmaceutical landscape is generating renewed interest in alliances. Virtually all major pharmaceutical companies are watching their revenues decrease because of weak pipelines, patent expiries, and the rise of generics in lucrative domestic markets. Japanese companies, which are experiencing these forces more severely than most, are now more open to alliances with large and midsize MNCs, and they are especially receptive to reverse co-promotions because of their benefits.

Like all partnerships, reverse co-promotions require diplomacy, negotiation, and carefully balanced interests; companies cannot simply sign a standard contract and hope for the best. Understanding the mechanics of the deal is important. Perhaps even more important is recognizing and accommodating the different motivations of the two companies involved. If the reverse co-promotion is well structured, both MNCs and their Japanese partners can achieve their major business goals. For example, the MNC can

obtain high contribution margins while its Japanese partner simultaneously books large sales in its home market—something that would be impossible under the structure of a traditional co-promotion.

Reverse co-promotions: A better option for Japanese-MNC alliances

Many traditional alliances have faltered because the deals were structured in a way that seemed to benefit one company to the detriment of the other. For instance, one alliance generated more than \$1 billion in annual sales of a Western blockbuster in Japan, but the partners fell out over the split of the profits. In another deal, an MNC received billions of dollars in revenues from a product originated by a Japanese company, but the partnership soured when the originator became dissatisfied because it received limited royalties under the terms of the contract.

But unequal profit sharing is only a symptom of a more fundamental problem. In most cases, when companies joined forces to develop, market, or promote new molecules through traditional alliances, the efforts failed because the partners had fundamentally different goals with respect to the following:

- **Domestic scale and contribution margins.** Top executives at Japanese companies value the scale of domestic operations, emphasizing revenue and growth over profitability. The Japanese press shares these preferences, and it often gives favorable coverage to companies that meet or exceed revenue targets. In comparison, MNCs tend to focus more on contribution margins than on revenue growth.
- **Size of the domestic sales force.** Japanese companies commonly have large sales forces; staff reductions are rare because of local employment customs and the fear of negative press. Even if the companies have few new products that require heavy detailing, they will retain representatives, rather than resort to layoffs. By contrast, MNCs have relatively small Japanese sales forces and have little desire to increase their size because new hires will decrease the productivity of any company for a time, even if they have prior experience.

- **Short-term contributions.** Japanese companies tend to be less concerned about the short-term contributions resulting from a partnership than MNCs because internal finance groups usually offer cheap rates (often 3 to 5 percent) when lending money to support the project. But MNC internal finance groups often set the cost of capital at 10 percent or more, making short-term contributions more important.

In a traditional deal, one company often has to sacrifice its interests in whole or in part to satisfy the other. As time passes, the company that capitulates may become even more dissatisfied and actively or passively withdraw support to the alliance. But a reverse co-promotion can eliminate this tension. Consider the following hypothetical alliances, old and new, involving two pharmaceutical companies—Company A (an MNC originator of a drug that is looking to enter the Japanese market) and Company B (a potential Japanese partner).

Under a traditional co-promotion scheme, A distributes its product into channels, but the sales forces from both A and

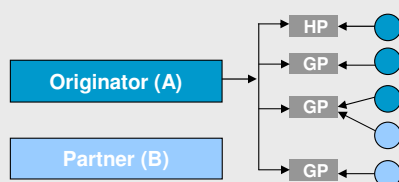
B detail target accounts. Since Company A conducts some details, it is able to build customer relationships in Japan. However, it does not need to increase the size of its sales force significantly because Company B's representatives cover many accounts. Company A “owns” the accounts, meaning that it compensates B for its details but books all sales. While A may obtain high contribution margins, this fee-for-detail arrangement deprives B of its goal of booking large sales in its home market of Japan.

By contrast, in a reverse co-promotion, A delivers its product to B at an agreed-upon supply price (the transfer price). As in the first example, both companies detail target accounts. But B is the sole distributor and “owner” of the accounts—the opposite of the traditional deal. This arrangement allows B to reach its goal of booking large sales in Japan while A achieves a high contribution margin because of the attractive transfer price. As in a traditional co-promotion, this arrangement allows Company A to build customer relationships through detailing while eliminating the need to hire new representatives. Exhibit 1 summarizes the differences between traditional and reverse co-promotions.

Exhibit 1

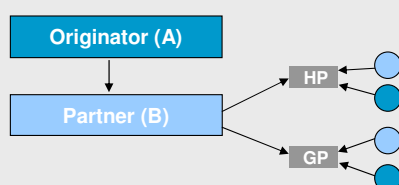
Reverse co-promotions differ from traditional co-promotions in several key areas.

Distribution patterns in traditional co-promotion (example)¹



- Medical representatives for A and B detail target accounts to hospital physicians (HPs) and general physicians (GPs); B receives compensation for detailing
- A distributes the product in channels and owns accounts
- **A books sales**

Distribution patterns in reverse co-promotion (example)¹



- A delivers product to partner at agreed-upon price
- B solely distributes products
- Both A and B MRs detail target accounts
- **B books sales**

¹ In both traditional deals and reverse co-promotions, companies may divide sales coverage in different ways. For instance, both companies may detail the same customers, or they may each be assigned specific accounts that reduce or eliminate overlap.

Given the advantages of reverse co-promotions, several pharmaceutical companies have adopted this model since 2009:

- The Japanese pharmaceutical giant Astellas entered into reverse deals with AstraZeneca for Symbicort, Pfizer for Lipitor, and NBI for Micardis; it also recently changed a traditional co-promotion with Pfizer for Caduet into a reverse co-promotion.
- Merck Sharp & Dohme (MSD) has partnered with Santen on a Cosopt reverse co-promotion.
- AstraZeneca recently signed a reverse co-promotion deal with Daiichi Sankyo for Nexium.

We believe that more pharmaceutical companies will pursue reverse co-promotions in the future, and many industry leaders share our positive view of these deals. In a recent speech, Katsuro Yamada, the senior corporate executive at Astellas, noted that reverse co-promotions “are the best method to maximize product value” and added that they “contribute to our company’s top-line growth.”

The appendix lists all of the reverse co-promotions of the past few years, as well as other partnerships formed between MNCs and Japanese companies since 2006, to illustrate industry trends related to alliances.

How to make reverse co-promotions work

Although reverse co-promotions offer many advantages, they are not simple to implement, nor do they guarantee that the MNC and its Japanese partner will be satisfied. As with any alliance, careful oversight and the close involvement of both companies are important during the planning, negotiation, and postdeal phases. The following factors can help increase the likelihood of success.

Strategic planning

Before approaching a potential partner, the MNC originator must clarify its objectives. What capabilities does it seek? Does the Japanese company have important assets that it could leverage? Without clear goals, it will be difficult or impossible to select the best partner.

Early in the process, MNCs should keep their options open. In addition to possible alliances, they should consider

organic strategies—among other benefits, this will help them to establish their baseline growth potential. When screening partners, MNCs should consider several candidates and objectively assess their capabilities before reducing the list to two or three front-runners. However, MNCs should remain flexible and not set strict priorities, since information that becomes available during later negotiations may change their perspective.

Deal negotiation

Four steps are essential in a successful deal negotiation.

1) Conduct a due diligence. MNCs must conduct a due diligence on all potential partners to understand their capabilities. This process involves interviews with staff at many levels, including the sales and marketing team at headquarters, branch managers, and members of the field force. The goal of the interviews is to gain a deeper understanding of internal governance and infrastructure, the positioning of the co-promoted product against other brands, and other topics. In many cases, the partner’s detailing capacity will be the subject of intense focus, since this often has the greatest influence on a product’s success.

Exhibit 2 provides an example of a due diligence that an MNC conducted on two potential partners, X and Y. Although the MNC originally felt that Company X was superior in most areas, the due diligence highlighted the greater benefits of Company Y, which demonstrates the importance of remaining flexible during the negotiation stage.

2) Align on strategic intent and joint operational control.

All too often, alliances fail because the MNC and its partner do not align on goals during the negotiation phase—perhaps the most critical step in the process. The lack of unity inevitably leads to frustration, as the two companies try to force the alliance in different directions or find themselves at an impasse during commercial meetings. To avoid such problems, MNCs should begin working on strategic alignment as soon as they select a partner. For instance, both companies should agree on a business plan and budget before the deal is signed, and they should also discuss their market-share aspirations for the co-promoted product. Among other benefits, the open exchange of information will help the MNC and its partner build mutual trust.

While business-development groups are responsible for drafting alliance contracts, commercial staff should be involved in strategic negotiations, since marketing and sales will be a joint effort. Commercial teams should

Exhibit 2

Conducting a due diligence helped a multinational corporation choose between two potential partners.

Strategic factors	Preferred company	Rationale
Presence in the franchise	▪ Company X	▪ Company X has a strong presence and promotional experience in the therapeutic area, while Company Y has no major product in this category
Risk mitigation in limited approval	▪ Company X	▪ A strong presence in this category is critical because the brand lacks a full indication
Details of capacity	▪ Company Y	▪ Company Y has more flexibility in capacity management, given that the portfolio mostly has Y's original products, while Company X holds significant partnering products
Internal governance capability	▪ Company Y	▪ Company Y has better control over details, as headquarters provides guidelines for weight and capacity per medical representative ▪ Company Y has a better wholesale management structure that is closely linked to the sales force
Positioning of the brand	▪ Company Y	▪ There is no particular issue for Company Y, but uncertainty exists for X — Company X's ability to promote another brand is unclear (cannot directly control because of competition law)
Operational complexity	▪ Company X	▪ Company X has less complex operations, but the partner would be required to handle 2 Company X sales teams, as well as another company ▪ The multinational would have to handle 3 partners for Company Y
Benefit beyond the brand	▪ Company Y	▪ Another Company Y brand is a strong strategic fit and is available for a quid deal. A reverse co-promotion with a quid deal offers greater benefits

also understand and align on the key principles of joint operational control before the deal closes. For instance, in one reverse co-promotion, commercial groups from both companies discussed territory-based sales tactics and agreed on a governance strategy for all branch managers in the field before the contract was signed. Their cooperation continued throughout the negotiation phase, as well as postcontract.

3) Secure the partner's commitment. For an alliance to be successful, MNC originators and their partners must remain committed. However, it is not uncommon for one company to fail to fulfill funding or resource obligations. Given the risk of such complications, MNCs should be careful to secure a partner's long-term commitment to a deal, being explicit about both financial and nonfinancial requirements in a contract. For example, the MNC may want to specify what the partner will provide with regard to audited details, reimbursement for gross sales and marketing expenses, and recruitment of patients for postmarketing surveillance. It could also note penalties that the partner will incur if it does not meet its obligations—for instance, fines for insufficient sales details or termination of deal rights in response to continual underdelivery.

Expectations should be stated explicitly in contracts, even when companies appear to share the same goals, because priorities may shift over time. For instance, a partner may lose interest in a co-promoted drug because it wants to allocate more resources to a newly discovered compound with higher sales potential. Without a written agreement that obligates both companies to provide a certain level of ongoing financial and staffing support, the alliance might falter.

As noted, detail coverage often represents the greatest source of contention. There have been instances in which partners attempted to get a “free ride”—they accepted the benefits of a co-promotion but provided limited sales details. In another case, a partner's headquarters tried to fulfill the terms of the alliance but provided little guidance and oversight to the field, resulting in inadequate detail efforts for the co-promoted product. In one deal, the MNC eliminated the potential for such problems by specifying in the contract penalties that the partner would incur if it missed a certain percentage of audited details. If the contract had only specified sales goals, the MNC would not have achieved the same degree of commitment. For instance, unexpectedly strong demand could have allowed the partner to meet or exceed sales goals with little effort.

MNCs may also want to secure commitment by introducing performance incentives, but they should weigh their benefits carefully. Will the incentives truly increase commitment to the alliance, or do they represent an unnecessary expense? What incentives would the partner most value? If MNCs elect to provide incentives, they can choose from a wide range of options. For instance, MNCs could specify that their partners will be rewarded financially for hitting a sales milestone early or on target.

4) Consider other types of deals. In conjunction with a reverse co-promotion, MNCs should consider so-called quid deals that give them rights to market one of their partner's compounds inside or outside of Japan. Creative deals that cross therapeutic areas, business lines, and regions are particularly compelling. For instance, an MNC could enter into a reverse co-promotion for a drug from its primary-care business unit and also arrange a quid deal for one of the partner's specialty-care drugs. Alternatively, the reverse co-promotion could focus on the Japanese market, but the quid deal could give the MNC rights to market one of the Japanese partner's "long listed" drugs in an emerging market.

Quid deals may represent an MNC's best opportunity for an "outbound" alliance, as Japanese companies have become disillusioned with the out-licensing deals that they previously favored when attempting to expand their global presence. Although out-licensing minimized the amount that Japanese companies had to invest in global infrastructure, it also transferred most of the value to their MNC partners—an arrangement that is no longer acceptable, given current revenue pressures. Since many Japanese companies are eager to increase their presence and capabilities in emerging markets, quid deals involving these countries may be particularly attractive.

Postdeal management

Once a deal is signed, the MNC and its partner must continue to work together closely, holding joint meetings of key functions and refining the business strategy and plan as needed. Such close cooperation is essential because MNCs have limited control over their partners' operations during a reverse co-promotion, making these deals more difficult to manage than joint ventures, mergers, and acquisitions. If companies agreed to the principles of joint operational control suggested for the negotiation phase, postdeal management will be less problematic.

Benefits of reverse co-promotions: Why the opportunity should be pursued now

After years of failing to capture optimal value from alliances—sometimes leaving hundreds of millions of dollars on the table—both Japanese companies and MNCs may be wary of tying the knot. But recent changes in the pharmaceutical industry make this an ideal time for reverse co-promotions that involve an MNC originator and a Japanese partner.

Benefits to MNCs

MNCs usually confront several barriers when attempting to enter the Japanese market. First, the Japanese focus on domestic sales leads them to employ large field forces that provide extensive coverage, posing a challenge to pharmaceutical companies with a smaller local presence. In addition, wholesalers manage 95 percent of distribution in Japan—a much higher percentage than in most other countries—and they have a stronger relationship with domestic players than MNCs. The close ties allow Japanese companies to leverage the wholesalers' promotional forces, granting them further access to physicians. In consequence, representatives at Japanese firms are more efficient in accessing physicians than those employed by MNCs, leading to greater "reach" (Exhibit 3).

Japanese companies also have an advantage over international competitors because their representatives have developed close, long-term relationships with local physicians, and they tend to score highest on physician surveys that rank sales-force quality. Since physicians are generally more receptive to their calls, Japanese field forces are more likely to reach or exceed their sales goals than MNC field forces.

If an MNC can convince a Japanese company to enter a reverse co-promotion, it could gain access to a large network of skilled representatives—a compelling benefit in a detail-driven market like Japan. To gauge the size of the opportunity for MNCs, consider that very few companies have a gross market share in Japan that equals or exceeds their global market share. MNCs that close this gap could capture significantly more sales and revenue—an important benefit, since they are all facing, to some extent, revenue pressures

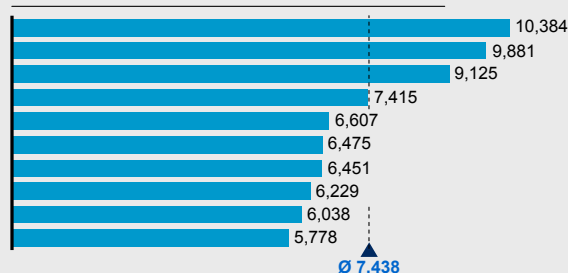
Exhibit 3

Leading Japanese firms show greater medical representative (MR) efficiency than MNCs.

MR¹ efficiency (Japanese firms)

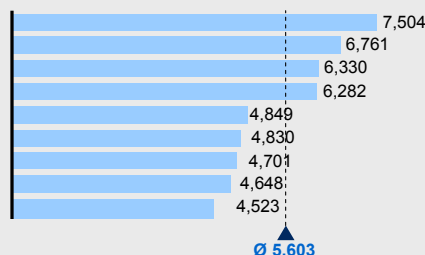
Ono
Tsumura
Otsuka
Eisai
Takeda
Dainippon Sumitomo
Shionogi
Kyowa Hakko Kirin
Daiichi Sankyo
Astellas

Physicians reached per MR² 2011



MR efficiency (MNCs)

Nippon Boehringer
Sanofi-Aventis
AstraZeneca
GlaxoSmithKline
Bayer
Roche (Chugai)
Novartis
MSD
Pfizer



1 Number of MRs for AstraZeneca, Dainippon Sumitomo, and Otsuka as of 2010 by Mix.

2 Calculated by reach rate multiplied by number of practicing physicians.

Source: Yakugyo Jiho; Mix; Ministry of Health, Labour, and Welfare (Japan)

resulting from reduced R&D productivity, patent expiries on branded drugs, and the rise of generics.

Reverse co-promotions will also help MNCs deal with another trend: the dwindling number of potential acquisition targets in Japan. In recent years, many Japanese companies have become sizable through consolidations and thus are unlikely to enter into an equity deal with an MNC (for example, Daiichi and Sankyo joined to become Daiichi Sankyo, Yamanouchi and Fujisawa became Astellas, and Mitsubishi and Tanabe formed Mitsubishi Tanabe Pharma). Reverse co-promotions, which Japanese companies find more compelling than other deals, will help compensate for the reduction in targets.

Benefits to Japanese companies

All pharmaceutical companies are confronting multiple forces that decrease revenue, but Japanese companies are under more severe pressure than most, making them very

open to deals that will strengthen their portfolios. Three areas present challenges:

- **Pipeline decreases.** Japanese companies have an impressive record of innovation and have introduced many blockbuster drugs over the years. But of the major Japanese players, only Takeda has five or more new active compounds in Phase III trials as of May 2011, and only Shionogi has five or more in Phase II. With troubled pipelines, Japanese companies are unlikely to launch many new drugs over the next three to five years.
- **Patent expiries.** Many blockbuster drugs will soon go off patent, depriving companies of a major revenue source. Of the largest Japanese companies, many now receive a substantial portion of their domestic revenue from products that will lose patent protection between 2012 and 2016. In several cases, these sales total \$1 billion to \$2 billion annually, meaning that companies will need to take drastic action to fill the revenue gaps.

- *Threats from generics.* Although generics penetration has occurred more slowly in Japan than in other markets, the Japanese government is now undertaking an initiative to increase the use of generics. This will pose a serious threat to Japanese pharmaceutical companies, most of which are currently earning 30 to 65 percent of sales from long-listed drugs (for example, Takeda's Takepron and Astellas's Gaster).

Since Japanese companies have historically focused on domestic sales, they are receptive to alliances that allow them to maintain their scale in Japan. As discussed, a typical alliance with an MNC drug originator would not significantly help a Japanese company reach its domestic goals, since the

MNC would book most sales. But a reverse co-promotion could play an important role in keeping local sales strong, despite the challenging pharmaceutical environment.

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Pharmaceutical companies are facing more revenue and growth pressures than ever before, increasing interest in alliances. Reverse co-promotions, with their unique deal structure, will benefit both MNC originators and their Japanese partners to a much greater extent than traditional alliances, provided that they follow best practices when planning, negotiating, and managing such deals.

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Appendix

■ Reverse co-promotion

A number of co-promotion deals involving multinational corporations were established in Japan from 2006 to 2010.

Deal year	Product	Company A (originator)	Company B (partner)	Type
2010	Equa	Novartis	Sanofi-Aventis	Co-promotion
2010	Nexium	AstraZeneca	Daiichi Sankyo	Reverse co-promotion
2010	Biosimilar of herceptin and remicade	Celltrion	Nippon Kayaku	Co-development and co-marketing
2010	Cosopt	MSD	Santen	Reverse co-promotion
2010	Stogar	UCB	Taicho	Co-promotion
2010	Micardis family	NBI	Astellas	Reverse co-promotion (extension)
2010	Velcade	Janssen	Takeda	Co-promotion
2010	Reminyl	Janssen	Takeda	Co-marketing
2009	Biologics for lysosome diseases	GSK	Japan Chemical Research	Co-development and co-promotion
2009	Aricept	Pfizer	Eisai	Co-promotion (renegotiation) ¹
2009	Lyrica	Pfizer	Eisai	Co-promotion
2009	Caduet	Pfizer	Astellas	Reverse co-promotion
2009	Symbicort	AstraZeneca	Astellas	Reverse co-promotion
2009	Avolve	GSK	Taiho	Co-promotion
2009	Botox (ophthalmology)	GSK	Wakamoto	Co-promotion
2009	Dermovate, Kindavate, Zovirax	MSD	Pola Pharma	Co-promotion
2009	Tykerb	GSK	Nippon Kayaku	Co-promotion
2009	Renivace, Lipovas	MSD	Mylan	Co-promotion
2009	Sprycel	BMS	Otsuka	Co-promotion
2009	Lucentis	Novartis	Alcon	Co-promotion
2009	Fosamac	MSD	Hisamitsu	Co-promotion

¹ To continue in the United States and European Union, but to end in Japan in December 2012.

Deal year	Product	Company A (originator)	Company B (partner)	Type
2008	Dapagliflozin	BMS	AstraZeneca	Development and co-marketing ²
2008	Eyevinal	Banyu (Merck)	Meiji Seika	Co-promotion
2008	Zevalin	Bayer	Fujifilm RI Pharma	Co-promotion
2008	Desmopressin	Ferring	Kyowa Hakko	Co-promotion
2008	E Keppra, Cimzia	UCB	Otsuka	Co-development and co-marketing
2008	Glucobay	Bayer	Mitsubishi Tanabe	Co-marketing
2008	Edirol	Chugai (Roche)	Taisho Toyama	Co-development and co-marketing
2008	Selexipag	Actelion	Nippon Shinyaku	Co-development and co-promotion
2007	Erbitux	Merck Serono	BMS, ImClone Systems	Co-development and co-marketing ³
2007	LU-AA21004, LU-AA24530	Lundbeck	Takeda	Co-development and co-promotion
2007	Gonapure, HMG	Merck Serono	Aska	Co-promotion
2007	Cymbalta	Eli Lilly	Shionogi	Co-development and co-marketing
2006	Pletaal (dialysis)	Otsuka	Chugai (Roche)	Co-promotion
2006	Ibandronate	Chugai (Roche)	Taisho	Co-development and co-marketing
2006	Golimumab	Janssen	Tanabe	Co-development and co-marketing
2006	Patanol	Alcon	Kyowa Hakko	Co-promotion
2006	Myslee	Sanofi-Aventis	Astellas	Co-promotion
2006	Differin	Galderma	Shionogi	Co-promotion

² AstraZeneca to conduct development from Phase II.

³ Co-marketing by Merck Serono and BMS.

Source: Press articles; Asu no Shinyaku

