Shionogi/Purdue Strategic Discovery Alliance With Synchronicity And Serendipity—Case Study Of Open Innovation

By Eiichi Yamaguchi

Abstract:

The utilization of open innovation (Chesbrough, 2004[1]) for two companies will affect the long-term corporate strategies at both companies. Even prior to the term "open innovation," Shionogi & Co., Ltd. licensed MS Contin® & OxyContin®, from Mundipharma K.K., the Japanese affiliate of Purdue Pharma L.P. and developed a cancer pain market which did not exist in the mid-1980's in Japan. Due to the sales growth of MS Contin® & OxyContin®, Shionogi designated "Pain" as one of three R&D core therapeutic areas in their 2nd medium term business management plan in 2005. Shionogi chose an alliance strategy which has a synergistic effect and complementary one, rather than exploring closed innovation, so that the discovery alliance with Purdue was initiated in late 2005. While Shionogi was on the pioneering side of open innovation, Purdue's business conditions in 2004 and 2005 suited seeking a strategic partner to share the risk for their Discovery Research. Alliance health surveys are conducted annually between Purdue and Shionogi. The results reinforce a strong, healthy alliance. There is "synchronicity" and "serendipity" noted retrospectively related to the Discovery alliance between Purdue and Shionogi further reinforcing the benefits of open innovation.

Open innovation: "Open innovation is the use of purposive inflows and outflows of knowledge to accelerate internal innovation, and expand the markets for external use of innovation, respectively. [This paradigm] assumes that firms can and should use external ideas as well as internal ideas, and internal and external paths to market, as they look to advance their technology."

Henry Chesbrough

I. Introduction

In December of 2005, Purdue Pharma L.P. of Stamford, CT, USA and Shionogi & Co, Ltd. of Osaka, Japan entered into a multi-year agreement to develop and commercialize novel molecules for the treatment of pain. The research is focused on programs aimed at three different mechanisms within the human pain pathway. The research is jointly conducted at Purdue's Cranbury, NJ research facility and Shionogi's laboratories in Osaka, Japan. Under the terms of the agreement, Shionogi pays all research costs for the first three years of the collaboration, and provides additional payments to Purdue as the programs reach certain development milestones. Purdue in turn will make certain milestone payments to Shionogi based on sales once the products are commercialized. The companies will share the costs of clinical development and ongoing research costs after the initial three years. All analgesic medicines created through this research can be co-promoted by Purdue and Shionogi worldwide.

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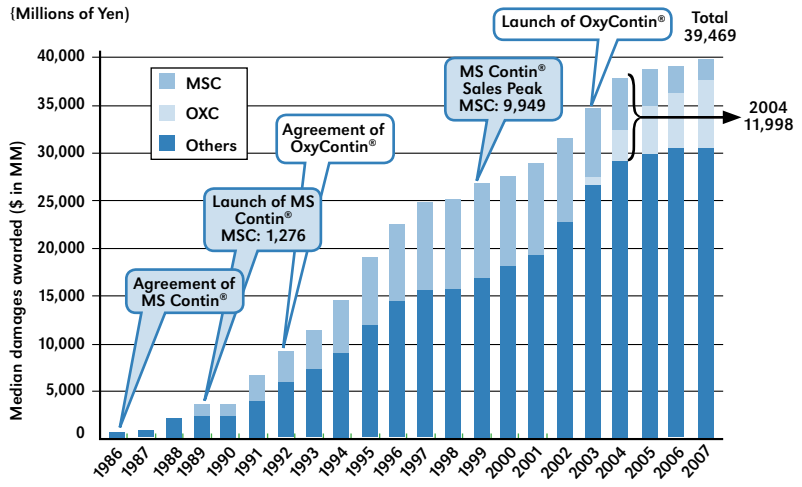
II. Shionogi's Influence on the Cancer Pain Market in Japan

Shionogi was established in 1878, and its head offices are located in Osaka, Japan.

Recent sales data from the fiscal year ending March 2008 was 164 billion yen, roughly equivalent to $1.6 billion. The ethical narcotic cancer pain market in Japan was practically nonexistent when Shionogi licensed MS Contin® from Mundipharma, Purdue Pharma's Japanese affiliate in 1986. Following Shionogi's contribution to the ethical narcotic market for cancer pain in Japan, it also licensed OxyContin® Tablets in 1992. The first year sales of MS Contin®, launched in 1989, was JPY 1,296 million, reaching peak sales of JPY 9,949 million eleven years after launch. The addition of OxyContin® in 2003 increased combined sales to JPY 11,998 million by 2004 as shown in Figure 1. This success was behind Shionogi's strategy for its 2nd medium term business plan that named "pain" as one of its core therapeutic areas. Shionogi's foresight to launch these products for the unmet needs of pain led the corporate strategy at Shionogi, although the success could not have been predicted at that time.

Figure 1. Sales of Ethical Narcotic Cancer Pain Products Including MS Contin® & Oxycontin®



Median damages are adjusted and represented in 2007 U.S. dollars.
 Source: IMS JPM March MAT 1978-2008.

III. External Factors Analysis Behind Licensing MS Contin®

In Japan in the 1980s, the cancer pain market was almost zero and a pervasive negative perception existed in Japan regarding narcotic medications. Figure 2 depicts a timeline of critical historical factors that guided Shionogi's decision-making processes.

As early as A.D. 500, the Japanese letter "医" meaning "medical treatment" for pain relief had become the root of medical treatment in Japan. (Akiyoshi, 1998[2]) In 1982, Dr. Fumikazu Takeda, Director, Saitama Cancer Center began introduction of the WHO three step analgesic ladder for the treatment of cancer pain in Japan in an attempt to bring Japan's treatment of pain up to Western standards. Shionogi's belief in pain treatment as the root of all medical treatment, along with Dr. Takeda's message, were the motivating factors behind the high-risk licensing of MS Contin® from a Purdue affiliate in 1986. This was further strengthened during the First Ladies Summit, held in conjunction with G7 Summit in 1986 in Tokyo, when First Lady Nancy Reagan met with Mrs. Nakasone, wife of Mr. Nakasone, Prime Minister of Japan, concerning the utility of ethical narcotics for cancer pain relief. Shortly after this acknowledgement by the Prime Minister's wife, clinical trials of ethical narcotic analgesics and subsequent approval were rapidly accelerated in Japan. The decision in 1992 to license a second product, OxyContin®, further increased the sales of ethical narcotics and stimulated growth of the pain market in Japan.

IV. Synchronous Partner & Open Innovation

Once Shionogi designated pain as a core therapeutic area, the need to support drug discovery research for pain became critical. Since internal drug discovery seemed inadequate to populate the pain pipeline, Shionogi sought a partner to enrich its internal pain portfolio. The criteria for a partner included an established franchise in the pain market, similar discovery targets of pain in terms of mechanism of action and therapeutic indication, and complementary expertise of research technology. Additionally, similar corporate cultures and company size were favored characteristics in a research partner. Purdue had all the factors needed to meet these requirements. Purdue had a reputation as a leader in the pain market, as well as significant intellectual property and several years of research advantages that would foster Shionogi's business model to sustain its pain research program. Additionally, Purdue had proprietary computational combinatorial medicinal chemistry expertise. The hope for Shionogi was that the collaborative arrangement with Purdue would strengthen

Figure 2. External Influences in Japan Related to the Licensing of MS Contin® by Shionogi

500 A.D.	医 (Medical treatment) meant an origin of pain treatment.
1982-1986	G7 Ladies Summit Tokyo: influencing on adopting an opioid analgesic for cancer pain treatment.
1986	WHO three step analgesic ladder guideline introduced by Professor Takeda.
	Shionogi licensed MS Contin® Tablets (Morphine Sulfate Controlled Release) for cancer pain from Purdue's Japanese Affiliate (Mundi Pharma K.K.).
1992	Shionogi licensed OxyContin® Tablets (Oxycodone Hydrochloride controlled release) for cancer pain from Purdue's Japanese Affiliate (Mundi Pharma K.K.).

Source: Fumikazu Takeda, Cancer pain relief. Yasashikuwakaru Toyo Igaku, 2005, Kanji Denrai 2006.

Shionogi's franchise in the pain management field.

Purdue's corporate headquarters are located in Stamford, CT, USA. The current owners acquired the company in 1952, and through 1995 the business was built upon over-the-counter products such as Senokot® and Betadine® and other small Rx products until the launch of MS Contin® Tablets in 1984. In 1995, OxyContin® was launched and U.S. sales grew to over $2 billion by 2003. In 2004 and 2005, ongoing patent challenges necessitated some strategy changes within the company. Due to these changes, Purdue sought a partner to share the cost and provide infrastructure lost during the company downsizing.

Shionogi was an established partner with Purdue through the independent associated company, Mundipharma K. K.'s earlier licensing of MS Contin® Tablets and OxyContin® to Shionogi for the Japanese market. Shionogi's culture is very similar to Purdue's as both companies are family-owned businesses. The complementary aspects in laboratory and scientific synergy were apparent through interaction of the scientists during the due diligence process. Finally, Shionogi's ability to finance Discovery Research for three years in exchange for joint ownership in certain patents relating to the treatment of pain was the ultimate selection factor.

Shionogi visited Purdue's Discovery Research facility in New Jersey in December of 2004 for an initial due diligence meeting. In October 2005, a final term sheet was agreed upon. The collaboration agreement was executed in December 2005.

The final deal included three separate pain targets in one contractual arrangement. In exchange for the research funding, Shionogi gained joint ownership in portions of Purdue's pain patent portfolio. As the two companies work together to create products, any patents that evolve from the joint research will outlive the collaboration and may continue to affect corporate strategy of both companies. This and other examples of open innovation are seen throughout the alliance.

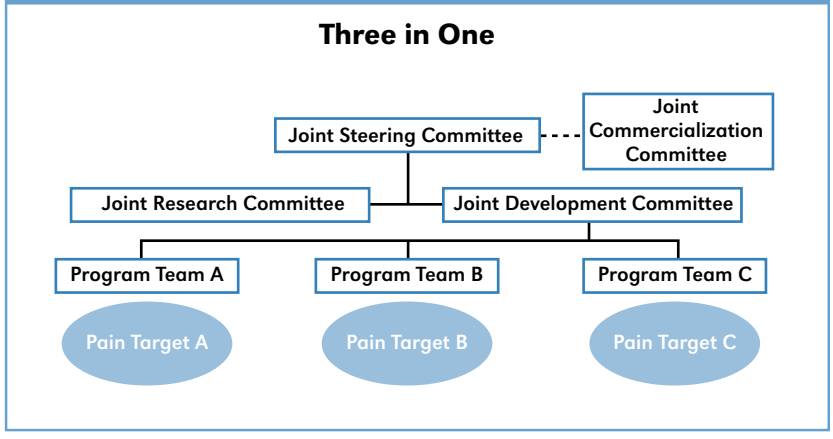
V. Governance & Role of Alliance Management

Traditional governance committees were formed to oversee and operate the complexities of research for the three programs. The Joint Steering Committee is the most senior governing body charged with oversight of all aspects of Research and Development. In order to provide oversight to the operational aspects, additional working committees were formed with plans to continually evolve as projects reach success milestones along their pathways to ultimate commercialization. A Joint Commercialization Committee will be formed to oversee the commercial aspects. All committees include equal representation by the partners. Alliance managers continuously monitor the state of the collaboration by ensuring communication is consistent and transparent between the partners and to resolve potential disputes before escalation is necessary. However, all team members that interact between Purdue and Shionogi have established best practices for working together, and these efforts have created a practically seamless team on all fronts. The research teams consistently use brainstorming techniques to isolate potential issues that are then proactively addressed, not only with standard business practices, but also scientific issues as well. Outcomes of the brainstorming sessions and lessons learned are used to train new members as they are brought into the alliance. The partners use SharePoint Internet sites to communicate and share documents. Additionally, real-time scientific data is made available to both partners via custom database hardware and software created at Purdue.

VI. Alliance Health Survey

The Alliance Managers coordinate a formal alliance survey on an annual basis. The 2007 survey was distributed to a total of 44 participants. Selected participants include colleagues at all company levels who interact through governance committees, program teams and supporting teams. The 2007 survey was implemented via a Web-based survey tool man-

Figure 3. Governance Structure Between Purdue and Shionogi



aged by Purdue's Human Resources Organizational Development group. The survey statements were mutually agreed upon by the Alliance Managers with choices of either English or Japanese language. Shown below in Table 1 are the survey statements and the percentage of favorable (strongly agree or agree) and unfavorable responses (disagree or strongly disagree). Typically, unfavorable responses less than 15 percent are ignored, but since the outcome of the survey was so positive, the areas with the least favorable responses are highlighted.

Figure 4 compares the alliance survey results for 2006 and 2007. The results from 2007 suggests that overall, improvements were made within the year. This has been largely attributed to specific steps implemented by the research managers at both companies following a year-end brainstorming meeting that focused on tangible ways to improve the chance of success and the quality of the relationship.

At the end of the first year of the collaboration, the research managers from both companies met to brainstorm further about the strengths and weaknesses observed to that point in the relationship. The goal of the meeting was to devise tangible actions for the remaining years of the collaboration that might improve the relationship, scientific progress, and the efficiency of the collaboration. Meeting planning and management, proper distribution of resources needed to achieve desired annual goals, and improved efficiency of chemists through better utilization of technologies were each targeted as strategic initiatives for both research groups, and departmental objectives were created in both companies.

1. Meeting Management

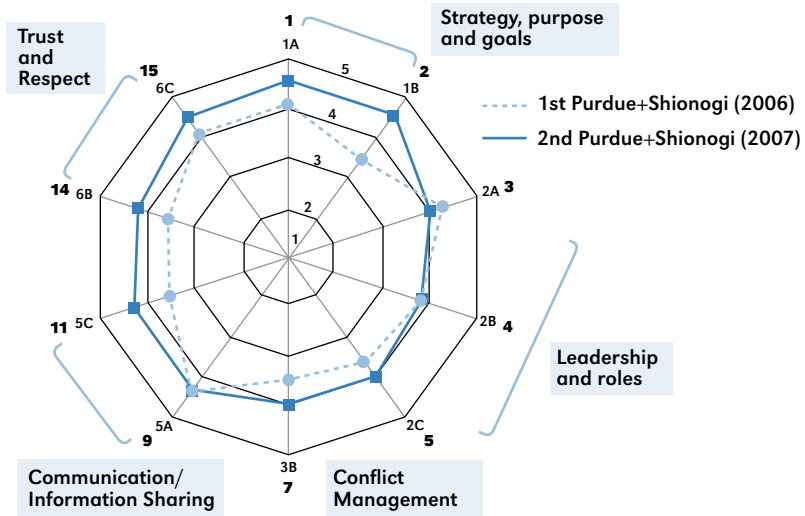
Like many other discovery research operations in pharmaceutical companies, the project team leaders in Shionogi and Purdue are typically selected from a

Table 1. Shionogi/Purdue Alliance Survey 2007

Question	Favorable%	Unfavorable%
1. Our partner commits to the Discovery/Development/Alliance strategy.	97.7	0.0
2. We understand and agree on our purpose and the goals we need to accomplish.	95.5	4.5
3. Our responsibilities are clearly defined.	88.6	11.4
4. Appropriate and adequate resources are assigned based on the assigned roles and responsibilities.	81.8	13.6
5. The governance structure in place supports teamwork and minimizes barriers to accomplish our goals.	84.1	11.4
6. We confront and deal openly with differences of opinion.	88.6	9.1
7. We have an agreed upon process to resolve conflict.	84.1	11.4
8. We have an agreed upon procedure for making decisions and we follow it.	86.4	11.4
9. Information is actively exchanged between partners.	97.7	2.3
10. Our partner is responsive to our requests.	97.7	2.3
11. Our meeting frequency is sufficient to meet our goals.	97.7	2.3
12. Our meetings are productive and worthwhile.	88.4	7.0
13. We trust our partner.	97.7	0.0
14. Our partner trusts us.	95.3	2.3
15. We demonstrate a high level of respect and openness for our partner.	97.7	0.0
16. Our partner demonstrates a high level of respect and openness for us.	97.7	2.3

% Favorable = % Strongly Agree + % Agree
% Unfavorable = % Strongly Disagree + % Disagree
Total may be less than 100% because of N/A response.

Figure 4. Shionogi/Purdue Alliance Survey 2006-2007 Overall Results



pool of lead scientists, rather than from professional program managers. Since the Purdue group had recently been restructured, and since the Shionogi group was new to the pain research field, the team leaders from both sides were somewhat new to program leadership, particularly relating to sharing resources with another company on the opposite side of the globe, and where the scientists communicate in a different language.

Through formal training and ongoing mentoring from senior managers in both companies, team leaders were coached in areas related to planning agendas, managing meeting time and discussion, consensus building, and decision making. In addition, certain practical steps were taken to account for differences in meeting culture and language. These included deliberate and frequent pauses in the discussion to ensure mutual understanding of the issues, and ending each meeting with joint preparation of a written summary of the discussed points of agreement and future required actions. SharePoint sites were developed to provide easy access to all slides and related meeting materials for all scientists. In addition, an extended version of the Purdue CCMC (Computational Combinatorial Medicinal Chemistry) informatics system was implemented in Shionogi, allowing real-time access to chemical and pharmacological data, further facilitating rapid and data-driven decision-making on the teams. These actions significantly improved the focus and effectiveness of the team meetings, improved the relationships between the scientists by providing a mechanism for more detailed live discussion, and improved the decision-making effectiveness of the teams.

2. Resources and Technologies

The initial collaboration was created to work jointly on three research-stage programs. In the first year, chemistry progress was slower than expected for a number of reasons. Of course, medicinal chemistry is a process of trial and error, so it is never possible to guarantee improvements by managerial initiatives alone. However, certain areas of weakness were identified and targeted for improvement as one approach to improving the overall chance of success in the collaboration. One initiative was the proper training and required utilization of parallel purification systems (since purification can be one of the rate limiting steps in any chemical synthesis). Another initiative involved limiting the number of medicinal chemists drawn into scale-up activities that support late-stage *in vivo* experiments. Although these experiments are critical, keeping the most creative medicinal chemists focused on advanced structure-activity relationship (SAR) studies and developing new intellectual property (IP) is more effective in the long term. The more routine scale-up can often be accomplished by junior chemists, specialized supporting groups within the company, or by a suitable contract research company. A further initiative involved the proper training and maximal utilization of computational, informatics, and data visualization tools to maximize the efficiency of the chemists in the laboratory. For example, in silico studies performed in advance can help chemists prioritize the synthesis targets they will work on in the laboratory, making it more likely that the molecules with the best overall chance of success will be made early.

A major contributor to the success of the research alliance between Shionogi and Purdue is the ongoing open and honest discussion and brainstorming between the research managers in both companies, and their willingness to implement specific initiatives and processes that better support the needs of the teams. Administrative improvements were derived from training and coaching team leaders in areas of meeting logistics, planning, and communication.

Scientific improvements were obtained by allowing the medicinal chemists to focus mostly on new SAR and new IP, rather than redundant scale-up. Moreover, efficiency in the laboratory was enhanced by enabling certain types of automation. These latter concepts further contributed to improved quality and numbers of molecules synthesized, which in turn led to major breakthroughs in the second year of the collaboration.

The mutual willingness of the scientists in both companies to learn new things and adopt good practices from each other has created a creative, efficient, cordial learning environment for both research groups. Our scientists' motivation and hard work has ultimately led to success in the alliance, and has also supported the perception that they are working together for a single purpose, and that there are many opportunities for professional satisfaction and advancement.

VII. Discussion and Conclusion

As both companies reflect back on the initial three years of the collaboration, some examples of serendipity and synchronicity can be noted. Definitions of these two terms (Merriam-Webster's, 10th edition) are provided below.

syn-chro-nic-i-ty: the quality or fact of happening, existing or arising at precisely at the same time.

ser-en-dip-i-ty: the faculty or phenomenon of finding valuable or agreeable things not sought for.

The examples of synchronicity for Purdue included Shionogi's willingness to contribute to the research effort with both people (to replace those that had been lost by downsizing) and funding. Although Shionogi was not the only company in negotiation with Purdue for these pain assets, the timing of the negotiation process worked in Shionogi's favor enabling it to benefit from the business dynamics happening within Purdue.

Synchronous events for Shionogi included Purdue's strong patent portfolio that fit well with Shionogi's innovative strategy to strengthen its pain research. Additionally, Purdue's scientific expertise in the pain research area, along with its strong U.S. market presence, was important for Shionogi.

The Alliance Managers also noted some serendipitous events that they believe make this alliance unique. The previous relationship between Purdue and Shionogi was a factor in bringing them together, but the synergy exhibited between the partners may be unrelated to the former ties. This synergy in itself is extraordinary, as it is not critical to a successful relationship, but in this instance adds to the potential for success. Even though Japanese and American cultures are different, the similarities in the scientific integrity and company culture appear to be practically identical. During the intensive due diligence process, Purdue recognized a synergy with the Shionogi scientists and this enhanced the other complementary aspects of the alliance. Along these lines, both companies have worked together to create an exciting pipeline of new therapeutic agents. Along the way, both groups have improved their understanding of each other, have learned from each other, and have improved themselves by keeping an open mind and sharing a passion for high quality science.

In conclusion, the main points that demonstrate how open innovation has shaped both Purdue and Shionogi are listed below:

- Both Purdue and Shionogi have continued their discovery pipeline in the field of pain, which is critical to both companies.
- Through this ongoing relationship, there is a potential to expand into other products and areas that may be outside the initial scope of the collaboration.
- Several Shionogi scientists have temporarily relocated to New Jersey, providing an invaluable experience to both partners.
- Working together has been so rewarding that plans are currently underway to extend the research phase of the collaboration.
- Finally, the investment involved in collaborating with another company in this manner will have lasting benefits.

Innovation is a collaborative process; the secret is to foster your relationships to create a seamless connection between the two parties. Two separate companies, in the same field, from opposite sides of the globe, having very different languages and cultures, can successfully join together to create a seamless operating body in spirit. ■

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