How Not to License a Drug into Japan

Doug Berger, M.D., Ph.D,
Pablo Ruano, Ph.D., M.B.A., Douglas Eames, Ph.D.

I saw a ballet the other day and it struck me that the better dancers were good on their toes. This gave me a hint on improving one aspect of our pharma consulting business: to broker a deal to license a candidate drug into Japan, or get venture capital and start your own company with a candidate drug, you need to stay on your toes.

* First, you need to look for candidate drugs from overseas. Everyone wants to be your friend until you tell them their drug cannot make it in the Japan market. They will have good preclinical data, maybe PI data, but no proof of concept, and maybe skeletons in the closet you haven't found out about yet -that is why they have not yet sold it to a Japanese company and are talking to you. You need an experienced licensing person on your team. Keep on your toes.

* Find out *why* they have not been able to sell the drug in Japan. Did a drug with a similar action already fail development somewhere in the world? Did it perform worse than other competitors in development? You need a competitive intelligence person on your team to get the information. Keep on your toes.

* Try to get the licensor to invest in the equity of the development in Japan by holding onto rights or making a joint venture with you. This will help them get some Japan experience and will go a long way to create trust among the potential investors in Japan. This scheme can also function to keep the licensor honest and working hard for your Japan interests. The Japanese might say, "*tatami wo tatakeba hokori ga deru*", or "you won't know how much dust is in the *tatami* mat until you hit it". Keep on your toes.

* Usual licensing costs for the Japan rights are about 20% of the estimated Japan peak sales (usually considered to be 10% of global peak sales). Some licensors expect you to fork-up the whole 20% upfront *before* PII ("proof" -actually semi proof- of concept in humans) is even completed abroad. No company in Japan will pay the full licensing amount upfront unless the drug is clearly going to be a big hit or already has great sales overseas. Orphan indications or minor entry indications without a clear high-potential revenue life-cycle management program will also not fly. Don't waste your time or the time of your buyers or financers. Also confirm the patent and freedom-to-operate status in Japan. You need a business intelligence person on your team to get a realistic estimate of the medical use of the drug in Japan (i.e., its positioning in medical use) and the Japan potential peak sales based on disease demographics and present and future local competition. Keep on your toes.

* Have a realistic idea of how much it will cost to develop, market, and follow the safety reporting of a drug on the market. It is not simply a matter of the licensing costs. You need to compare the sales minus all these costs with the income you would get from having the cash invested along with an inflation factor. This is a calculation of a discounted cash flow called NPV (net present value). You need an experienced finance person on your team. Keep on your toes.

* A drug may be a great idea abroad but may not get past the Japanese Authority (PMDA) to enter into man in Japan. The nature of the drug composition, i.e., using specific biologic materials (virus vectors, bovine materials), the nature of the mechanism of action (i.e., MAOI action), the nature of the indication (i.e., one that requires treatment with stimulant or opioid activity), etc may make development in Japan a regulatory or clinical feasibility (recruitment) impossibility even though it may be approved in dozens of countries already making your licensor think Japan is a sure bet. You need an experienced clinical development person on your team to keep your regulatory reality in check. Keep on your toes.

* You are all excited because the candidate drug may be a new and innovative way of delivering an old standard drug into the body, e.g., patch, intranasal spray, injection pen, etc. The licensor conveniently did yet not tell you that the device part has still not completed development, nor did you check with the Japanese authorities what you need to do in Japan to get approval of a drug that also uses a device for delivery. Don't begin a huge evaluation project before confirming whether the drug can even get inside the human body. You need an experienced CMC (formulation and manufacturing) person on your team to keep your drug specification reality in check. Keep on your toes.

* Be creative. See if the licensor and investors are willing to jointly go so far as to the first PMDA consultation with an agreement in place for full licensing if the PMDA evaluation is favorable. It is a low financial risk to go only as far as the first PMDA meeting but a great way to find out where the future road map for Japan leads. You may need a choreographer on your team. Keep on your toes.

* The drug may actually have good potential for Japan but your strategy for licensing doesn't work for the licensee. Make sure the milestone payment schedule makes sense with the progress of development abroad (i.e., an FDA letter allowing progress to PIII in the US means much more than "good" PII results reported by the licensor). The pharma or venture capital company you want to make a deal with may meet with you, but they do not have the time to sit down and work-out what to do with your candidate. It is your job to make a licensing strategy that is win-win for all parties. Remember, venture capital companies are essentially investors and they need an exit plan to sell the stock they have bought from your start-up company. Get expert advice if you don't know what to do. Keep on your toes.

* You need to make a contract with the licensor before you present your new great drug candidate to any local pharma company stating your commission and that only you can be the go-between between the licensor and the pharma you speak to. Your information may be on the next email from that company's licensing department to the licensor's business development window on their home page if you don't. Keep on your toes.

* How will you set your fees vis-à-vis the licensor? If your fee is too high they will not want to have you as a go-between. If your fee is too low, you will have low motivation to help them. Make sure they understand that. You can structure a flat success fee, or a lower success fee plus per-hour fees. If you want, you can have a pure per-hour fee and function only as their in-country consultant. See what other people in the industry say works for them. Keep on your toes.

* You need to make a contract with any venture capital company before you present your new great candidate drug to them stating they must keep your information confidential and cannot present or engage in licensing this drug into Japan with anyone other than yourself. Your information may be on the next email from the venture capital company to the licensor's business development window on their home page if you don't. Keep on your toes.

* Even if you are successful in getting venture capital funding, do not expect a venture capital company to throw a big salary at you. You will need to work hard from humble beginnings and have personal back-up savings already in the bank in case there is bad weather ahead. Try to get a few candidate drugs on board from the start to decrease your chances of failure. Keep on your toes.

Now with this article in hand, you are ready to assemble your team and start looking for your compound for Japan. Make sure you have some other source of income while you try to make this enterprise fly, it may take a long time. You can always take ballet lessons if you find you have a lot of free time.

Questions? Please ask us for help:
doug(at)japanpsychiatrist.com
We will be sure to keep you on your toes.

Douglas M. Berger, M.D., Ph.D., and Associates.
Japan Pharmaceutical Consultants
www.japanpsychiatrist.com/DrugDev.html

Drs Berger and Eames are Pharmaceutical consultants in Tokyo, and Dr Ruano formerly in Pharmaceuticals in Japan for many years, now works in the EU.