

Leveraging your biotech intellectual property

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Biotech companies can extract unexpected value from their patent portfolios to remove roadblocks on the path to commercialization and success.

For a biotech company, the ultimate goal of intellectual property (IP) is to protect the investment that goes into developing a commercial product. But as products are often many years away from commercialization, there are several ways IP can be exploited to get financing and complementary technologies needed for short-term survival. In this article, we discuss four ways (Table 1) that biotech companies can leverage value from an IP portfolio. Although these are the main strategies, they are certainly not the only ones for extracting extra value from patents.

Out-licensing

Out-licensing—the granting of an IP license from one company to another—is probably the most familiar form of IP leverage. The license may be exclusive, so that only the licensee can use the specified technology, or nonexclusive, so that the licensor can continue to use the IP and/or license it to others. It can be limited to a field, such as a particular indication, or to a territory, such as all of North America. A company might choose to license its IP—or limited rights to its IP—in exchange for upfront payments, milestone payments and royalties based on product sales. Some companies have successfully out-licensed IP apart from ongoing collaborations or sales of a product line, though many license deals arise in those contexts. IP may be out-licensed before a product is ready for clinical trials, particularly if positive results are found in animal studies and the market for the product is large. Also, many universities out-license early-stage discoveries in deals that include upfront payments and development obligations by the licensee.

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A highly desirable arrangement is for the patent holder to out-license some applications of its technology to generate revenues while reserving other aspects to commercialize itself. For example, CyDex Pharmaceuticals, of Lenexa, Kansas, has out-licensed its drug delivery system to larger pharmaceutical companies that have then incorporated their proprietary drugs into CyDex's system, which is designed to add value to such drugs by improving their solubility and stability. CyDex has received royalty revenues from this that have aided it in developing its own products based on off-patent drugs incorporated into its delivery system. The arrangement seems successful, and CyDex recently filed for a proposed initial public offering of \$50 million.

In another example of out-licensing, Advanced Cell Technology (ACT), of Los Angeles, granted Pharming Group, of Leiden, the Netherlands, an exclusive license to non-human use of ACT patents on the activation of oocytes. The agreement provides Pharming with exclusive rights in the field of transgenic technology. William Caldwell, chairman and CEO of ACT, says this allows his company's IP portfolio to be monetized in several ways: "Using this foundation as a basis for developing commercial therapeutics and entering into licensing agreements allows us to finance the company in profitable and nondilutive manners."

In addition to raising capital, another advantage to out-licensing a portion of a company's IP is that it can allow the company to narrow its focus. For example, in May 2007, ThromboGenics, of Leuven, Belgium, out-licensed antibodies against certain targets to the D. Collen Research Foundation, a nonprofit with some connections to ThromboGenics, so that the company could focus on other, more advanced programs. In return for this license, ThromboGenics received a lump sum payment equal to its total

investment in the programs and a 25% share of any future revenue that the foundation may receive from these programs.

Even so, companies are often fearful of out-licensing too early in the development of their technology. As a technology proceeds through development, various risks are reduced or eliminated. For example, the commercial potential for a drug product increases (becomes less risky) as the drug passes through preclinical testing and the various phases of clinical trials. As the risks go down, the value of the technology goes up. Obviously, a company will receive less for its technology at earlier, riskier stages than after its potential is more certain, so a company must balance its need for resources against the increased value at a later date.

When a technology is out-licensed, the licensee obtains some rights to develop and commercialize it. Effectively, the company is now joined with its licensee, and any missteps or mistakes by the licensee will redound to the company as well. Clinical trial failures and public relations gaffes by the licensee may (fairly or unfairly) affect the reputation and valuation of the technology and the licensor. In short, out-licensing may provide revenues in addition to, or in support of, a company's efforts at product commercialization, but the company should carefully choose its licensing partner and the timing of its licensing efforts.

Cross-licensing

It may be surprising to some that having a patent does not mean that a person is free to make and sell the patented product. A patent merely gives its holder the right to exclude others from the claimed invention—but someone else may have a patent that excludes or blocks the patent holder from actually commercializing the invention. For example, one company may have a broad patent on

Table 1 The basics of leveraging your intellectual property portfolio

Method	Advantages	Disadvantages
Out-licensing	Raises capital Is suitable for early-stage technology Narrows company focus	Engenders fear of out-licensing too early Cedes some control over reputation and valuation of technology
Cross-licensing	Removes blocking patents Can allow collaboration	Requires giving up exclusive rights Can allow competition
Selling intellectual property (IP) or royalties owed on it	Raises short-term capital Narrows company focus	Requires demonstrable financial return Discounts value of IP
Lending secured by IP	Makes use of IP, which may be company's most valuable asset Raises nondilutive capital	Interest rates obtained do not generally reflect IP value Risks losing IP upon default

small interfering RNA (siRNA) products that silence a particular target, whereas another company may have a different patent on a method of treating a disease by using siRNA to silence that same target. In this situation, neither company would be free to market a siRNA product to treat that disease without infringing the other's patent. Those companies have blocking patents that prevent development of a promising treatment.

But a company might be able to leverage its own IP to remove that potential roadblock. With a strong patent portfolio, companies can often negotiate cross-license agreements with competitors that have a blocking patent or other IP in the same area. Cross-licensing requires both companies to give up some of the exclusive rights created by their IP, perhaps even allowing competition, but that might be preferable to the looming risk of a product being kept off the market entirely. A cross-license may even lead to the development of additional products or therapies. For example, AVI BioPharma, of Portland, Oregon, and Omaha, Nebraska-based Eleos entered a cross-license agreement to develop antisense drugs targeting the protein p53. AVI acquired rights to Eleos's patent portfolio, which encompasses a variety of molecules that target p53, for the treatment of most viral diseases. In return, Eleos obtained an exclusive license to AVI's antisense chemistry for the development of commercial p53 cancer products. Alan Timmons, chief operating officer of AVI, noted at the time that AVI would not have pursued p53-based treatments for cancer, but the deal provided access to a potentially broad area—p53-based treatments for infectious disease. AVI and Eleos are also sharing rights in other medical fields in which targeting p53 may be therapeutically useful.

Cross-licensing agreements also can allow companies to work together to develop new products. For example, bioMérieux, of Marcy l'Etoile, France, and NuGEN Technologies, of San Carlos, California, cross-licensed their

IP related to the amplification of nucleic acids, with bioMérieux acquiring nonexclusive rights to specific NuGEN amplification technologies that might enable bioMérieux to create and market *in vitro* diagnostic tests requiring amplification for expression analysis. In return, NuGEN gained access to bioMérieux's linear amplification technologies using chimeric primers, including extensive original equipment manufacturer rights for the research market. The companies also plan to integrate their technologies for the development of an entirely new product (an automatable microarray-based assay for cancer).

Although cross-licensing may provide a solution to the problem of a blocking patent, this solution may come with a hefty price tag. As mentioned above, a company loses some of the exclusivity provided by its IP, perhaps creating price competition with a rival product even while its patents remain in force. More commonly, the company will have to share its eventual royalties with its partner in the cross-license agreement. In short, cross-licensing may provide a solution to some near-term problems or concerns, but a company should be certain that its total price is not too steep.

Selling IP or royalties owed on it

When a company's IP covers products already on the market, the patents are especially ripe for leveraging and might be used to obtain short-term capital. In some cases, companies might be able to make outright sales of their IP. This may be especially desirable if the company has valuable IP that is outside its current commercial focus. An example is San Diego-based Cytori Therapeutics, which sold a surgical implant product line (and the IP related to that line) to bring in capital for its efforts with stem cell therapeutics. By selling a patent-protected product line outside its focus, Cytori leveraged its position and gained funds to support the development and commercialization of its core technology, adipose tissue-derived stem cell therapies.

Even when a company has already licensed its IP and will receive future royalties, the company may wish to leverage its IP to meet an immediate need for capital. Many license agreements provide for payments of royalties on product sales over the course of many years. A company can use this long-term royalty stream to get short-term capital by selling or 'monetizing' the royalty stream. InNexus Biotechnology, of Vancouver, Canada, sold a royalty interest in two cancer products to New York-based Royalty Pharma, which also purchased shares of InNexus for \$1 million. Royalty Pharma paid \$2 million for the first royalty interest and holds an option to purchase a royalty interest in a second product for another \$2 million. The total purchase price for the royalty interests may be increased by up to \$30 million for the two products if certain conditions are fulfilled, allowing InNexus to use the proceeds for developing one of the cancer products.

Other firms that purchase royalty streams include Paul Capital Partners, of New York, and Drug Royalty, in Toronto. In August 2006, Cambridge, Massachusetts-based Dyax and Paul Royalty Fund Holdings II entered a royalty interest agreement in which Dyax received \$30 million in cash upfront in exchange for a specified percentage of the net royalties (initially up to 70%) receivable by Dyax under its phage display program. Dyax plans to use the payment to continue advancing product candidates, such as DX-88 for hereditary angioedema, through clinical trials. The agreement also provides for annual guaranteed minimum payments to Paul Royalty, starting at \$1.75 million through 2008 and eventually escalating to \$7 million for the years 2015 through 2017. Selling a royalty stream in this way can raise immediate capital to fund research, clinical studies or facilities.

Opportunities to sell IP or royalty streams tend to be limited to situations in which a product is already being commercialized or the company is at least receiving some

demonstrable return on its IP. Generally a purchaser will be interested only if a financial return on the IP is immediate, quantifiable and virtually certain over the foreseeable future. Moreover, such opportunities provide funds in the short term while sacrificing some long-term value, because purchasers of IP or royalty streams will seek a discount for making current payments based on the expected value of the asset.

Lending secured by IP

Finally, a company may get capital using its IP as security for loans. In a secured agreement, a borrower puts up an asset or assets as security for a loan. If the borrower is later unable to repay the loan, the lender will have some rights to the asset that was put up as security. In this way, a company may be able to leverage its IP by using it as security to borrow funds.

In September 2007, Rockville, Maryland-based EntreMed obtained a \$20 million loan from a syndicate of lenders to strengthen its cash position and fund anticipated clinical development expenses into 2009. The loan collateral includes a royalty stream that EntreMed acquired when it sublicensed commercial rights for thalidomide to Celgene, of

Summit, New Jersey, in return for royalty payments on thalidomide sales. The thalidomide molecule originally licensed, now called Thalomid by Celgene, is approved by the US Food and Drug Administration, based in Bethesda, Maryland, to treat leprosy, but it is used widely on an investigational basis for the treatment of multiple myeloma and other cancers.

Other examples include Monogram Biosciences, of South San Francisco, and SeraCare Life Sciences, of West Bridgewater, Massachusetts, both of which obtained \$10 million worth of revolving lines of credit from Merrill Lynch Capital by offering, among other things, a number of patents as collateral. Monogram put up 38 patents or pending applications as security for its obligations. SeraCare, which emerged from bankruptcy in May 2007, put up two issued patents acquired when it purchased Celliance in 2005 and a pending application as security for its obligations.

Many lenders require a security interest in a company's assets as a condition for providing a loan, and for many biotech companies, their most valuable assets are their IP. Leveraging this wisely may put the company in a better position to obtain loans on good

terms. Another advantage to this method is that a loan may enable a company to move its product development forward when additional capital is needed but a stock offering is not practical.

The capital received from a lender is attractive to shareholders because it does not dilute their ownership in the company, but it must be repaid—with interest. A disadvantage of borrowing funds secured by IP is that the value of the IP is typically not reflected in the amount, interest rate and other terms of the loan. Instead, the interest rate is typically set based on the market and the company's credit rating. Moreover, if the company defaults on the loan agreement, the lender may foreclose on the IP assets.

Conclusions

The ways of leveraging IP listed in this article are not exhaustive. Creative executives, financiers and lawyers may find other ways to obtain short-term value from a company's IP. But a broad and diverse patent portfolio, combined with flexibility and ingenuity, can provide unexpected leverage to remove roadblocks on the path to commercialization and success. 