

Supreme Court boosts licensees in biotech patent battles

A US Supreme Court decision in January has left patent holders uneasy and licensees exploring opportunities to shed weighty royalty payments. The ruling could have wide-ranging effects on the biotech industry, where large profits come from a small number of patents. Furthermore, much of biotech intellectual property is based on incremental advances in science—patents often more prone to challenges from licensees.

In the past, before a licensee could sue to invalidate a patent, it usually had to breach its contract, often by halting royalty payments. But breaching a license agreement can bring on a lawsuit, monetary damages and loss of rights to make a product—risks most licensees aren't willing to take. In its 8-1 decision in *MedImmune v Genentech*, the Supreme Court took away that risk for licensees, saying they can sue patent holders even as they continue paying royalties.

"You take a license because you don't want a lawsuit," says Tom Kowalski, a partner at the law firm Frommer, Lawrence & Haug in New York. "That fine tension is what has kept the biotech industry running." Being able to protect against infringement by getting a license while retaining the right to contest the patent means "licensees can have their cake and eat it too," he says.

Patent holders may be able to offset the court's decision by adding protective clauses to new contracts. But power has certainly shifted

to licensees, and the impact of the Supreme Court's decision will depend on how broadly lower courts interpret it in upcoming lawsuits.

The most likely targets for litigation are patents that are weak, carry high royalty fees, cover platform technologies and are non-exclusively licensed, experts say. Licensees whose royalty fees outweigh the cost of suing to invalidate the patent—which can often run more than \$10 million for big cases—may have the most incentive to sue, especially if they have a product near or on the market. Stanford University in Stanford, California, and the University of California, San Francisco, for example, licensed their now-expired Cohen-Boyer patents more than 400 times, but dodged litigation largely by charging licensees less than \$10,000 per year in royalties.

It is clear that *MedImmune v Genentech* has already touched some pending cases. A lawsuit between Melbourne, Australia-based Benitec, and Horsham, Pennsylvania-based Nucleonics was on appeal in the US Court of Appeals for the Federal Circuit, and the day after the *MedImmune v Genentech* decision was announced, that court asked both parties to respond with new briefs.

The *MedImmune v Genentech* case centered around Genentech's ubiquitous Cabilly II patent (Table 1). Genentech, based in S. San Francisco,

had sent threatening letters to MedImmune, of Gaithersburg, Maryland, saying it must pay royalties for Cabilly II. This patent covers a process in the manufacture of human antibodies, and is involved in the production of MedImmune's main product, Synagis (palivizumab), a treatment for respiratory infection. Sales of the drug account for nearly 80% of MedImmune's profits—a tremendous amount of business to gamble. So the company paid the Genentech fees, documenting that it was doing so "under protest." The Supreme Court declared the situation an overt controversy between the two companies, giving MedImmune grounds to sue to invalidate the patent.

Licensees with a similar documented controversy will likely bring the first lawsuits, experts say. "If there's sufficient economic incentive and if the underlying facts fit, they will take advantage of this," says Giulio DeConti, a partner at the Boston-based law firm Lahive & Cockfield.

The priciest licenses are usually the exclusive contracts, which provide sole rights to a technology. Companies with such contracts may shy away from litigation because invalidating the patent would open them up to competition, say experts. But an exclusive licensee whose product is way ahead of its competitors may find filing a lawsuit in its interest. For example, if a licensee is about to launch a product and its competition



Table 1 Biotech patents of note

Patent holder	Patent name and no.	Technology
Amgen (Thousand Oaks, California)	Fenton (5,599,690)	Inhibition and promotion of norleucine in recombinant gene products
Cambridge Antibody Technology (Cambridge, UK)	Griffiths (5,885,793; 6,521,404; 6,544,731; 6,555,313; 6,593,081; 6,582,915)	Production of anti-self antibodies from antibody segment repertoires and displayed on phage
Centocor; New York University (New York)	Le (5,919,452)	Method of treating diseases using anti-tumor necrosis factor antibodies
Chiron (Emeryville, California)	Houghton (5,885,799; 5,712,145; 5,371,017)	Hepatitis C virus protease
Columbia University	Axel (6,455,275)	DNA constructs for producing an antibody in Chinese hamster ovary cells (CHO)
Dyax (Cambridge, Massachusetts)	Ladner (5,223,409; 5,403,484; 5,571,698; 5,837,500)	Methods used in displaying three-dimensional structures on cells, spores or viruses
Genentech	Andya (6,267,958)	Lyophilized formulations
Genentech	Basey (6,417,335; 6,489,447)	Purifying antibodies using cation exchange
Genentech	Cabilly II (6,331,415)	Methods of producing immunoglobulins, vectors and transformed host cells
Genentech	Chen (5,856,179; 6,180,401)	Methods for producing a protein in animal cells by using controlled osmolarity and glucose
Genentech	Presta (6,737,056)	Antibodies having one or more alterations in the Fc region
Immuno AG/Baxter	Reiter (6,100,061)	Methods for producing a recombinant protein in a CHO cell that is stable for 40 generations or more in serum
PDL (Fremont, California)	Queen (5,585,089; 5,693,761; 5,693,762; 6,180,370; 7,022,500)	Antibody humanization techniques
Stratagene (La Jolla, California)	Wigler (5,780,225; 6,479,243; 6,635,424)	Methods for making antigen-binding molecules using primer-based PCR
Suntory	Furukawa (5,976,833)	Culturing recombinant CHO cells at one temperature then shifting to a lower temperature
Xoma (Berkeley, California)	Robinson (5,618,920)	Secretion of heavy and light chains

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Box 1 A problematic effect on academic licensing?

It is impossible for a university to fully prosecute patents for the hundreds of discoveries its scientists make each year. They must focus on later-stage inventions, and leave the more nascent technologies with minimal patent protection. Thus, university patents may be more challengeable than those created by industry, leaving them a target under *MedImmune*. At the same time, licensing early-stage inventions may give universities some leverage. There are a lot of unknowns in contracts for early-stage science, and licensees often find that things change after they've signed an agreement, forcing them to go back to the university to try to amend it. This may present an opportunity for universities to negotiate some anti-*MedImmune v Genentech* clauses. EW

is years behind in clinical trials, it may see little reason to continue paying high rates for exclusive access, says Sigrid Volko, a portfolio director in the tech transfer office at Johns Hopkins University in Baltimore, Maryland.

Nonexclusive patents are usually cheaper to license, but there are exceptions. In the antibody world, for example, Genentech, Immuno AG/Baxter of Vienna/Deerfield, Illinois, Strategene of La Jolla, California, and Suntory of Osaka, Japan, all hold widely licensed patents with fairly substantial royalty rates. Patents that cover basic drug production technologies can stir grumblings among their hundreds of licensees, as did Cabilly II and New York-based Columbia University's Axel patents. "If you have a base technology, you should spend some time figuring out if people are going to sue you," says Elaine Jones, a partner at Euclid SR Partners in New York.

MedImmune v Genentech may be most problematic for universities, who may not have sufficient funds to fight a lawsuit (Box 1). Licensees could use the threat of a lawsuit as leverage to demand major concessions, such as lowering royalty rates and waiving milestones, says Volko. "Most universities would likely succumb to the licensee's pressure," she says. For the generic industry, *MedImmune v Genentech* provides a new tool to challenge brand-name companies, and it is likely that one or more of the large generics will soon bring a lawsuit to test it out.

Indeed, the Supreme Court's decision may seem like a fortuitous occasion to sue one's way out of royalty fees. But it will come at the high cost of severing a relationship. Companies that license more than one patent from a source will have to think very carefully before suing. And companies that have cross-licensed their patents may be too intertwined to even think about bringing litigation, say experts. "Licensing is not an isolated event," explains Jones. "You have to see these people over and over. A lawsuit puts a chill on everyone involved."

But for *MedImmune*, it was worth it. Cabilly II expires in 2018, and the royalties *MedImmune* would have to pay to produce

Synagis over the life of the patent outweigh the costs of suing Genentech to invalidate it, says Bill Bertrand, senior vice president of legal affairs at *MedImmune*.

For new deals, negotiation times will surely increase as partnering companies try to balance their interests and powers under the new ruling. Patent holders will find themselves corresponding with licensees very cautiously, making sure not to create an overt controversy that would give licensees grounds to sue. Some may decide to go to court up front.

Patent holders are already preparing new clauses in contracts to protect themselves. Legal experts recommend that companies demand higher up-front fees and lower royalty payments, reducing licensees' incentives to sue later. Some suggest adding termination clauses, which say that if the licensee sues, the contract ends. This type of protection has worked in Europe, where companies can sue without breaching their contracts. US courts, however, may find such a clause unenforceable. Companies could also add language that forces the licensee to agree not to sue to invalidate the patent. But most experts say this type of language will be struck down by US courts.

With the uncertain enforceability of these new protections, some companies are getting creative. Vitae Pharmaceuticals in Fort Washington, Pennsylvania, is considering clauses that say if the licensee successfully invalidates a patent, it must still pay some sort of royalty for know-how of the technology, says Alex Howarth, chief business officer at Vitae. The company may also ask that disputes be reexamined by the US patent office, rather than the courts, and that a licensee hand over in advance the rationale for its claim.

As a last resort, some patent holders could opt not to license at all. "I hope it won't come to a point where I have a license and I can turn around and sue," says Ivana Magovcevic-Liebisch, an executive vice president at Dyax Corporation in Cambridge, Massachusetts. "I don't think people will be willing to license patents if that's the case."

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