

## **Therapeutic Antibodies: Top Three Intellectual Property Issues**

Therapeutic antibodies have become big business. Twenty-one antibodies are now approved by the FDA for marketing and annual sales have reached well past the billion dollar mark. Companies operating in this space must pay careful attention to intellectual property issues, which can dramatically affect potential development and profitability. The Top Three IP issues are freedom-to-operate, patent lifecycle management, and the changing legal landscape.

### ***Freedom-to-Operate***

A patent does not grant the patent holder the affirmative right to practice the patented technology – a patent conveys only the *right to exclude others* from practicing that technology. It is a real possibility that in making, using, or selling patented technology, companies may unwittingly infringe a separate patent of a third-party. In fact, the tremendous growth in the therapeutic antibody market has created a minefield of third-party patents which must be carefully navigated as a company seeks to commercialize its proprietary antibody technologies.

If a company proceeds with commercializing its own antibody technology in blind disregard to, or even ignorance of, potentially dominating third-party patents, that company may wind up in the unenviable position of being forced to accept onerous third-party licenses or being kept off market on the eve of commercial launch.

Avoid or minimize the likelihood of this scenario by conducting an appropriate freedom-to-operate search of third-party patents early in the development process. Critical for any antibody company regardless of size, many venture capitalists now view freedom-to-operate as important as a strong patent portfolio when assessing the future of an early stage company.

It is far better to address what has been called the "monoclonal maze" early on, with a proper freedom-to-operate analysis in hand to guide decisions, than to blindly move forward and run the risk later of being shut down or having to accept onerous licenses due to third-party patent issues.

### ***Patent Life-Cycle Management***

Many of the therapeutic antibodies launched in recent years are the result of groundbreaking technologies first developed a decade or more ago. Antibody humanization techniques, the phage display technologies, and the technology for producing fully-human antibodies in mice were all critical to making therapeutic antibodies the multibillion dollar business it is today.

However, as the use of these technologies becomes more common, and their broad applicability becomes increasingly apparent, they are no longer considered groundbreaking – their use becomes more of an industry norm. Consequently, the argument for patentability of the products of these technologies has become more difficult. In a sense, companies that develop these technologies can be the "victim of their own success."

Companies can address this by adopting a well-planned filing strategy that seeks to time the filings of new applications so as to minimize the threat posed by their own prior patents, while at the same time maximizing patent term for potentially blockbuster products. Companies should also continue to innovate during the product development and clinical trial phases. Insights which were not apparent early on can often result in patents to novel pharmaceutical formulations, dosage regimens, methods of administration, combination therapies, etc. that add to the patent protection for the core antibody and extend the patent protection closer to the commercial life of the therapeutic product. By crafting a careful patent life-cycle management strategy, companies can continue to obtain patents to new innovations surrounding a valuable antibody product.

### ***Changing Legal Landscape***

The legal landscape in which antibody patents are procured and enforced is constantly being reshaped by Congress and the courts. In particular, several recent decisions by the U.S. Supreme Court may affect the patentability of recombinant antibodies, as well as the very right of patent holders to effectively license their technologies or to exclude others from practicing them. These include:

- *KSR v. Teleflex* – In this 2007 case, the U.S. Supreme Court clarified the standard for determining when an invention is nonobvious. Under the new standard, a patent examiner may utilize a reasonable degree of common sense in applying what is well-known in the art instead of a rigid test. Most relevant to the recombinant antibody industry, an invention may be considered obvious if it is the mere result of applying a known technique to a known starting material ready for improvement to yield predictable results. It is currently unclear how the *KSR* decision will impact the patentability of novel humanized Abs produced from murine antibodies according to known humanization methods.
- *eBay Inc. v. MercExchange* – Concerning using patents to prevent others from entering the marketplace, the Supreme Court applied an equitable balancing test for determining when injunctions are appropriate in this 2006 decision. Subsequent lower court decisions have generally established that infringers in direct competition with the patentee upon entry into the marketplace are more likely to be enjoined than are infringers who are sued by a non-practicing patentee. The decisions have also established that public interest concerns are deemed relevant by courts when deciding the injunction issue in cases impacting the public health.
- *MedImmune v. Genentech* – In this 2007 case, the Supreme Court held that a licensee who has not breached the licensing agreement nonetheless has standing to bring a declaratory judgment action (a lawsuit brought by a potential defendant seeking a declaration that a patent is invalid and/or not infringed) against the patentee provided that an actual controversy otherwise exists between the parties. Later that year, the Court of Appeals for the Federal Circuit applied the *MedImmune* standard to the pre-agreement licensing negotiation process in *SanDisk Corp. v. STMicroelectronics, Inc.* where a potential licensee was deemed to have standing to bring a declaratory judgment action in a situation where the patentee had presented a detailed infringement analysis during meetings even though the patentee had provided assurances that it had no intent to file a suit for patent infringement. Due to these loosened standards, companies now must walk a fine line in their negotiations with potential infringers.