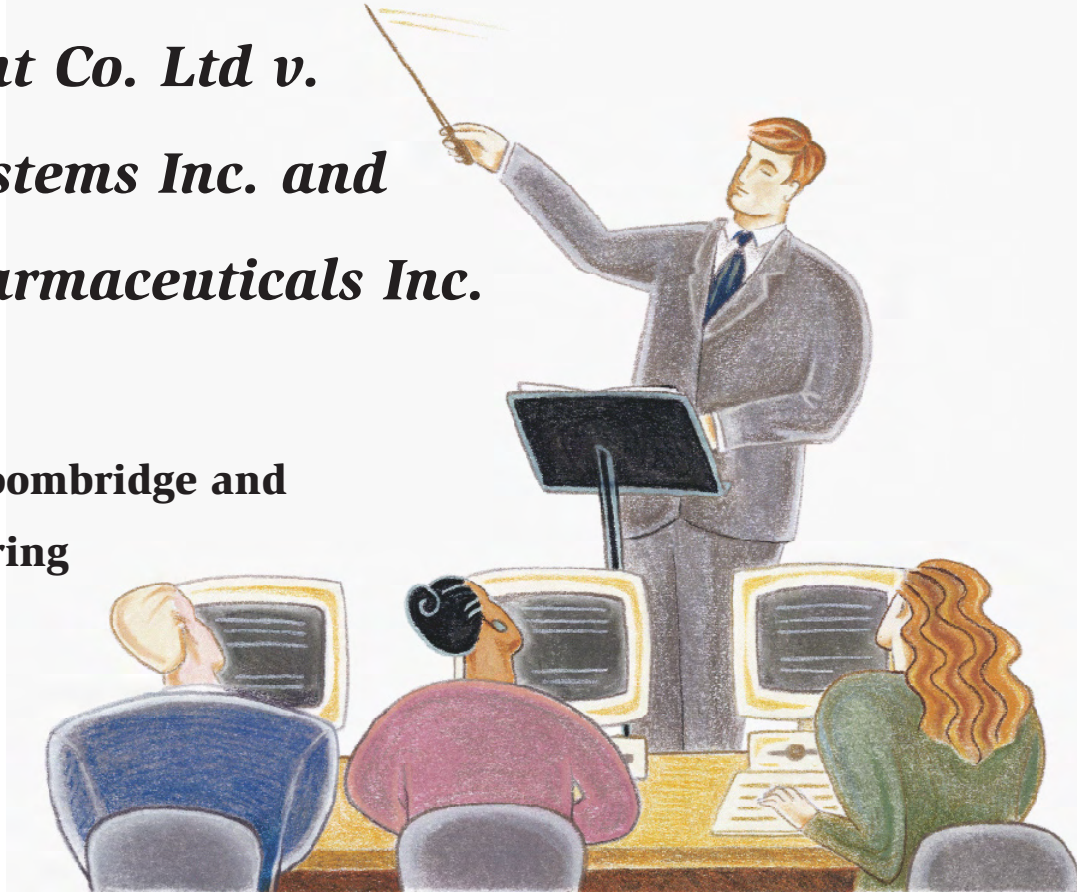
Practical Lessons from a "Made for TV" Patent Litigation: The Trial of *Yeda Research and Development Co. Ltd v. ImClone Systems Inc. and Aventis Pharmaceuticals Inc.*



By Nicholas Groombridge and Brian Paul Gearing

It is often said that success has many fathers but failure is an orphan. This is the story of how a dispute over who was the father of a major scientific breakthrough in the treatment of cancer turned into a five-year patent litigation and the practical lessons learned from the experience. The case is *Yeda Research and Development Co. Ltd. v. ImClone Systems and Aventis Pharmaceuticals Inc.* It was tried in 2006 in the Southern District of New York and is currently on appeal to the U.S. Court of Appeals for the Federal Circuit (which has exclusive appellate jurisdiction in patent actions). The dispute was a magnet for media attention partly because one of the defendants, ImClone Systems Inc., had achieved notoriety as the company at the center of the so-called Martha Stewart scandal several years ago. In addition, many prominent cancer researchers were involved—the testimony included talk of Nobel Prize nominations—and beneath it was a powerful human story of an academic mentor who felt betrayed by his own protégé. In this article, we describe the underlying dispute, how it came to trial, and the lessons we took away from the trial.

The Facts

Yeda Research and Development Co. Ltd. v. ImClone Systems and Aventis Pharmaceuticals Inc. concerned a dispute over who should properly be named as the inventors of U.S. Patent No. 6,217,866 (the '866 patent). The '866 patent stemmed from an original application filed in the U.S. Patent and Trademark Office in 1988. The application was filed on behalf of a group of scientists working for a company then known as Rorer. The series of interactions between the applicants and the Patent Office—what patent lawyers call "patent prosecution"—took a considerable length of time, and the patent did not emerge until 2001. During the intervening 13 years, new corporate entities had become involved: Rorer merged to become Rhone Poulenc Rorer and then merged again to become Aventis Pharmaceuticals. Also, during the course of the patent prosecution, Rorer licensed the application, and any resulting patent, exclusively to ImClone. Thus, when the '866 patent was issued in April 2001, it was effectively controlled by ImClone.

Several months after the patent was issued, it came to the attention of a group of scientists in Israel. These scientists read the patent and were shocked to see that it was based to a great extent on work they had done in the 1980s; indeed, large portions of the text had been copied verbatim from an article they had published in a scientific

publication in 1988. How had their work come to figure in a patent about which they knew nothing? As the Israeli scientists—and later their lawyers—investigated, the facts gradually emerged.

The scientists had conducted their research at a prominent Israeli academic institution, the Weizmann Institute of Science. The plaintiff in the lawsuit, Yeda Research and Development Co. Ltd., is the technology transfer arm of the Weizmann Institute. Often described as "the MIT of Israel," the Weizmann Institute is dedicated entirely to the study of the natural sciences. It has been the birthplace of many breakthrough discoveries and claims among its faculty an impressive number of visionaries in science and technology. One such visionary is Professor Michael Sela, currently a professor of immunology at the institute and formerly its president, who counts among his many accomplishments the discovery behind the highly successful multiple sclerosis drug Copaxone®. But this litigation was about another blockbuster therapy that should have been credited to the work of Sela and two of his colleagues in the mid-1980s—Dr. Esther Aboud-Pirak, a postdoctoral fellow at the time, and Dr. Esther Hurwitz, then a researcher in Professor Sela's laboratory.

In the 1970s, Sela's research lab began to focus on the "magic bullet" approach to fighting cancer. The goal of this approach was to deliver cancer-killing drugs to only the tumor growth and thereby spare damage to surrounding healthy cells and the associated harmful side effects that are a notorious consequence of many forms of chemotherapy. One such approach to fighting cancer involved chemically attaching or "conjugating" a chemotherapeutic drug to a carrier, wherein the carrier is capable of targeting only cancerous cells. Researchers had investigated the use of antibodies as carriers; these are proteins produced by the immune system of humans and other higher animals in response to the introduction into the body of a foreign antigen. One class of carriers they considered were so-called monoclonal antibodies (mAbs), a special type of antibody developed through the Nobel Prize-winning process discovered by Georges Kohler and Cesar Milstein.

In 1986, Sela and his colleagues embarked on a new cancer research project in which they planned to use a naturally occurring hormone, known as epidermal growth factor or EGF, as the carrier that would deliver chemotherapeutic drugs to tumor cells. However, the scientists rapidly discovered this approach would not work because the hormone was both too small and too expensive to be practical. Accordingly, they began looking for an alternative carrier. Why not, they theorized, employ an mAb that would target the same part of the tumor cell as the hormone itself—a structure known as the EGF receptor. The immediate problem, however, was where to obtain such mAbs. The researchers could make the mAbs from scratch; during her research for her Ph.D., Pirak had manufactured mAbs using the Kohler-Milstein approach and was thus familiar with the technique, but the process was laborious and time-consuming, and would surely prevent them from achieving the goal of their research in the time period allotted by the terms of the grant under which they were operating.

Enter Professor Joseph Schlessinger. Widely known as a brilliant scientist and a rising academic star, Schlessinger entered the professorship ranks at the Weizmann Institute after obtaining his Ph.D. in biophysics from the institute in 1974, after working as a postdoctoral fellow at Cornell University from 1974 to 1976, and as a visiting fellow at the National Cancer Institute at the National Institutes of Health in the United States from 1977 to 1978. While Schlessinger was at the Weizmann Institute, his research focused on the basic science behind cell behavior, including the study of the molecular processes that cause normal cells to become cancerous. Although Schlessinger's research was more focused on the basic science, he and Sela were no strangers. On the contrary, Sela had helped Schlessinger rise through the academic ranks, and (at least in Sela's view) their relationship was akin to that of a mentor and his protégé.

In late 1985, Schlessinger accepted a sabbatical position in the United States at a biotechnology company in Maryland called Meloy Laboratories Inc. At that time in the mid-1980s, biotechnology research was all the rage and money was available to fund it. The owners of Meloy wanted to establish a biotech equivalent of Bell Labs, a place where great scientists could perform fundamental research with the underlying assumption that eventually something of commercial value would emerge. This idea was appealing to Schlessinger; he brought several colleagues and former students from the Weizmann Institute with him to Meloy, and they jointly continued his research into the basic cellular mechanisms underlying certain types of cancer. In the course of this research, Schlessinger's group created several mAbs that would bind to the extracellular domain of the epidermal growth factor receptor—exactly the type of mAbs Sela and his colleagues wanted.

During his sabbatical, Schlessinger maintained his laboratory at the Weizmann Institute and periodically returned to Israel. As luck would have it, on a January day in 1987, a chance meeting occurred between Schlessinger and Hurwitz. Schlessinger told Hurwitz that he had "good monoclonal antibodies," and that he could give her a sample if she wanted to test them. Following up on Schlessinger's offer to Hurwitz, Pirak obtained a sample of two mAbs from Schlessinger's Weizmann lab and embarked on a research program directed first to the characterization of the mAbs.

The next year of research would lead Sela and his group to a startling discovery—the in vivo administration of one of the mAbs in a mixture with a chemotherapeutic drug produced a strongly synergistic effect, that is to say both the mAb and the drug inhibited the growth of tumors, but, when used together, the combined effect far exceeded what would be predicted from the performance of the drugs individually. The Weizmann scientists immediately recognized that this synergism could be used as a new way to treat cancer, potentially reducing the harmful side effects of traditional chemotherapy. Unlike prior work performed in Sela's lab, these "mixture" experiments required no conjugation of the mAb to the chemotherapeutic drug. These research results were incorporated partly into a manuscript and the mixture experiments were summarized in a write-

up of experimental results.

Re-enter Schlessinger. In March 1988, soon after Sela and his colleagues had made their discovery, Schlessinger was back in Israel giving a presentation at a seminar at the Weizmann Institute. After his presentation, Pirak invited Schlessinger to attend a meeting with Sela, where they informed Schlessinger of the recent experimental results and discussed the article that was in preparation. Schlessinger was very excited about the results and asked for copies; accordingly, the Weizmann group provided both a copy of the draft article and a write-up of the key experimental data that were sent to Schlessinger separately after he returned to the United States.

The arrival of these results at Meloy Laboratories initiated a cascade of events that would eventually lead to litigation. Meloy had been sold, and the new owners, Rorer, wanted to see new drugs emerging from Schlessinger's lab. Immediately upon receiving the experimental results, Schlessinger informed the company's senior management about this scientific breakthrough but gave no credit whatsoever to Sela's group. Rorer then began preparing an Investigational Drug Application, the first step in obtaining the Food and Drug Administration's approval for a new drug. And, naturally, Rorer wanted to safeguard its product with patent protection by filing for a U.S. patent (which was followed by counterpart applications around the world). Rorer filed the initial application in the chain of applications that would lead to the '866 patent—the patent at the center of the litigation—in September 1988, piecing together large portions of the filed specification based upon text and figures literally cut and pasted out of the draft article written by Pirak and based on the original manuscript and write-up of experimental mixture results that Schlessinger received in spring 1988. This original patent application named only Schlessinger and three of his colleagues at Rorer as co-inventors.

Sela and his colleagues were never informed that any of these activities had occurred. Indeed, they had published their article in December 1988, naming Schlessinger and a colleague of his as co-authors because they had provided the mAbs. As a testament to the significance of the work of Sela, Pirak, and Hurwitz, this paper, published in the *Journal of the National Cancer Institute*, signified a watershed event in the field of cancer therapy and sparked the beginning of a new approach to cancer therapy that would be followed by many prominent researchers around the globe.

Fast-forward to the year 2000. By this time, ImClone had taken over responsibility for the patent application. Unfortunately for ImClone, the patent application had run into a snag in the Patent and Trademark Office in the form of a third-party's patent that had come to light and might make it difficult for ImClone to obtain allowance of the pending patent claims. ImClone decided to see if it could eliminate the third-party patent as a concern by proving that it was entitled to an earlier date of invention than that patent. This, of course, would necessitate review of the underlying lab records. After a fruitless search for relevant records from Meloy or Rorer, ImClone's in-house patent counsel sent an e-mail to Sela in January 2000 requesting copies of notebooks from Sela's lab related to the mixture results. A few days later, ImClone's counsel received a response—not from Sela but from Yeda's in-house counsel—saying that, although Yeda was well aware of the scientific research in question, it knew nothing about any patent application. What was he referring to? ImClone's reaction was to provide no response. Several weeks later, Yeda's lawyer followed up with another e-mail again asking what patent application ImClone was talking about. At that juncture, in the words of the District Court, ImClone decided to stonewall Yeda, claiming that the matter had become irrelevant in light of other developments. The '866 patent was ultimately allowed over this third-party patent because of an amendment to the independent claims of the patent. Notably, the issued claims of the '866 patent are directed to the use of an mAb with certain attributes in combination with an anti-neoplastic agent to inhibit tumor growth—that is, the claims are solely based on the work of Sela, Pirak, and Hurwitz.

In April 2001, the '866 patent was finally issued. Shortly thereafter, ImClone entered into an agreement with Bristol Myers Squibb for the development, promotion, distribution, and supply in the United States of Erbitux®—an mAb possessing similar attributes to those of the mAb used by Pirak and Hurwitz in the mixture experiments. To date, under this agreement, ImClone has obtained more than $1.3 billion from Bristol Myers Squibb in royalties and milestone payments.

In early 2002, Yeda discovered the '866 patent and began an investigation as to who the proper inventors were. After discussions with ImClone and Aventis proved unsuccessful as a means of resolving the matter, Yeda filed suit in October 2003 in the Southern District of New York seeking to correct inventorship of the patent under 35 U.S.C. § 256. After a three-week bench trial in summer 2006 before Judge Naomi Reice Buchwald, a 140-page opinion and order was issued finding in favor of Yeda on every issue and removing each of the previously named inventors—that is, Schlessinger and his colleagues—from the patent and also ordering that Sela, Pirak, and Hurwitz be listed as the true inventors.

Practical Lessons Learned

Lesson #1: All trials are credibility contests.

All trials ultimately boil down to a credibility contest, where the prevailing party is usually the side that puts on the most credible witnesses. A bench trial is no exception. Indeed, Judge Buchwald stated in her opinion:

Although many of the underlying facts in this case are not disputed, the Court was nonetheless compelled to make many findings of fact that hinge in large part on credibility findings. Having carefully considered all of the testimony and evidence, we have concluded that the plaintiff's witnesses were, as a whole, far more credible than the defendant's witnesses.[1]

A particularly salient example of the court's finding that one of the defendants' witnesses was not credible occurred when the court considered Schlessinger's testimony regard-

ing his offer of "good monoclonal antibodies" to Hurwitz. According to Schlessinger, the word "good" was intended to cover all the attributes of those antibodies that eventually were described in the '866 patent. The court stated: "We find Schlessinger's account of this conversation not credible for several reasons."[2] The court then went on to list no fewer than eight different reasons why it did not find Schlessinger's account believable. No such similar statements appear in the opinion with respect to Yeda's witnesses.

Another important take-away here is that, in preparing witnesses for trial, it is always of paramount importance for them to tell their story in their own way. Instead of trying to shoehorn the facts into the framework of the best legal theory, the theory should fit the facts. Perhaps it goes without saying, but it should be much easier for a witness to appear credible to the judge or a jury when he or she is simply telling the truth. Additionally, it is always better to have witnesses keep to the subject matter they can cover. It is important not to push the limits of the witness' capacity. And it is always better to concede a point and maintain credibility before a judge or jury, rather than to risk having the reverse occur.

Lesson #2: A bench trial is still a trial.

It is important not to lose sight of the fact that many of the same factors driving a jury trial are present in a bench trial. Just as in a jury trial, of paramount importance is the theme of your case. You should always strive to tell a compelling story to the decision-maker—be it a judge or a jury. In this case, the "made for TV" facts lent themselves to a compelling theme: no one should take credit for someone else's work, no matter how tempting it may seem. This is the rarer case, however; the facts of a case are seldom so rich. Regardless, good lawyers should develop the skill needed to craft a compelling theme from any set of facts with which they happen to be presented.

Remember that, at the end of the day, the decision-maker wants to render justice. Themes should be developed from the decision-maker's perspective, which is "Don't tell me why you should win, tell me why I should want you to win."

Lesson #3: Exploit the best technology to present your case.

The Elmo overhead projector should now be a relic of the past (or, at least, it should only be used as a backup when more sophisticated current technology fails). There are a number of excellent software packages available, such as TrialDirector®, which are much more effective in getting those key points across to the judge or jury.

Two particular areas where the use of new technology had great effectiveness during the trial were in cross-examining witnesses about documents and impeaching witnesses with deposition clips. For example, Schlessinger was cross-examined regarding the start of his sabbatical leave in March 1986 and on his employment at Meloy Laboratories. As it turns out, Schlessinger officially accepted his employment at Meloy in September 1985—that is, before he requested and began his sabbatical from the Weizmann Institute. On cross-examination, this period of Schlessinger's moonlighting—as demonstrated by a differential time line, with the overlapping employment times in bright yellow, and projected on a floor-to-ceiling screen—was highly effective. The time line that was projected not only helped to elicit testimony (Schlessinger admitted that he had been moonlighting) but also dramatically brought home the point that he had different and inconsistent obligations to two separate employers.

Another relic of the past should be live read-ins to the record of impeaching deposition testimony. Instead, as was done in this case, depositions should be videotaped and appropriate software should be used at trial to play the impeaching testimony live in court. There is nothing comparable to playing a live clip of a witness on a huge screen, showing the witness saying exactly the opposite of what he or she just said on the stand. Just make sure the clip does indeed contradict the testimony!

An additional effective use of technology that is particularly helpful for cases involving complicated science or other technical subject matter, such as was the case here, is technology tutorials with a voice-over from your expert. This method can save a fair amount of live court time and may be more effective in explaining complicated subject matter (for example, the DVD can be played again if needed, and so forth).

Lesson #4: Consider procedural mechanisms to streamline the trial.

In order to use court time efficiently, Judge Buchwald requested that the parties submit all direct testimony in the form of written witness statements. The plan that was instituted was that each day before a particular witness would be called to testify, the witness' direct testimony would be given to the other side and submitted to the court. The next day, the witness would be cross-examined in open court in light of the written direct testimony.

All three parties were initially reluctant to handle direct testimony in this manner—perhaps because deep down all trial lawyers believe they can bring out a witness' testimony better than anyone else—but this procedural mechanism worked very well to streamline the trial and to focus the court's attention. By having an opportunity to study the direct testimony, the court was better prepared and indeed was able to ask virtually all the witnesses highly relevant questions of its own. A subsidiary lesson may be that, when the court suggests a new way of handling some aspect of the trial, be willing to embrace the suggestion rather than merely accepting it as unavoidable.

Lesson #5: Try to make the court's job easier to perform.

A simple but not trivial point is that even the little things count when making it easier for the court to do its job. A perfect example from the trial was the decision to provide the court with different colored binders of witnesses' statements and cross-examination materials to make clear which binder came from which party. At the outset, all

three parties were using black binders and the first few witnesses often had difficulty identifying which binder they were being asked to review. We began to color-code the binders and the problem never recurred. Remember, anything you can do to help the court perform its job will inure to your benefit.

Lesson #6: Maintain good relations with opposing counsel.

Perhaps this goes without mentioning, but it will usually be to your benefit to maintain good relationships with your adversaries. For example, in this litigation, all discovery disputes were resolved informally between the parties without requiring court's involvement. In the spirit of helping the court to perform its role, the congeniality of counsel will be appreciated.

In this particular case, one of the provisions of the Local Rules of the Southern District of New York was very helpful in avoiding discovery motion practice. The Local Rules contain a mechanism that prevents the precipitous filing of motions by requiring that a party contemplating a motion first submit a letter to the court requesting a pre-motion conference. This method worked well and allowed the parties to resolve a number of issues that otherwise would likely have required extensive (and expensive) briefing.

Lesson #7: Manage your time effectively.

The most important lesson of all: Time management will always be key to the presentation of your case. Unfortunately, most lawyers tend to be terrible at time management. It is vital to learn to make a realistic estimate of how long that killer cross-examination will really take and to be able to stick to one's predetermined allocations of time so as not to run out of time when there are witnesses who still must be examined. This is an area in which almost all trial lawyers could improve. We can only hope that, with discipline and practice, we will collectively be able to do so. **TFL**

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Endnotes

[1]*Yeda Research and Dev. Co. v. ImClone Sys. Inc.*, 443 F. Supp. 2d 570, 578 (S.D.N.Y. 2006).

[2]*Id.* at 594—595 n.43.

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financial sacrifice. It is not that large inventors are not negatively affected—it is that the proportional impact on small inventors is much greater.

Also, at present, if the Patent and Trademark Office rejects an application, the idea behind the application still has a chance to remain a trade secret. Publication prior to the granting or rejection of a small inventor's patent not only exposes the inventor to early infringement but also erases any prospect of maintaining the idea as a trade secret. Again, this is especially harmful for inventors with few patents or products and little money available for litigation.

As originally introduced, the patent reform bill had proposed eliminating provisions in current law that permit applicants to delay publication. During the debate on this legislation, I offered an amendment, which was adopted, that will allow applicants to delay publication until the later of three months after a second action by the Patent and Trademark Office or 18 months after the filing date. This amendment is a good compromise that protects American inventors.

There is no reason that the small inventor community must be tread upon by patent reform legislation. In fact, the little guys come up with some of the biggest and most important ideas, and their constructive participation in advancing patent reform would be most useful in crafting legislation designed to foster innovation. Patent reform must protect the future of the inventor in his or her garage, and the entire patent community should concern itself with preserving these roots of innovation. Throughout this debate, some small inventors have dropped their objections while others have maintained a vitriolic rancor. What will benefit the final legislative product the most, and thereby benefit small inventors the most, is for those within that community to find a middle ground—something like the sky isn't falling, for the most part. **TFL**

Darrell Issa is a member of the U.S. House of Representatives and represents the 49th District of California. Rep. Issa serves on the House Judiciary Committee, the House Oversight and Government Reform Committee, and the House Permanent Select Committee on Intelligence.