Shook, Hardy & Bacon L.L.P.

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LIFE SCIENCES & BIOTECHNOLOGY LEGAL BULLETIN

SCIENCE • TECHNOLOGY
ENGINEERING • ENERGY
PHARMACEUTICAL

CONTENTS

IP NEWS

Unanimous SCOTUS Reverses Determination That Drug Dosage Adjustment Is Patentable

The U.S. Supreme Court has unanimously ruled that methods for determining the optimal dosage of thiopurine drugs used to treat gastrointestinal and non-gastrointestinal autoimmune diseases are not patent-eligible subject matter. Mayo Collaborative Servs. v. Prometheus Labs. Inc., No. 10-1150 (U.S., decided March 20, 2012). So ruling, the Court overturned a Federal Circuit Court of Appeals determination, summarized in Issue 5 of this *Bulletin*.

According to the Court, the patent claims involved "administering," "determining" and "wherein" steps that failed to transform un-patentable natural laws into patent-eligible applications of those laws. As explained by Justice Stephen Breyer, writing for the Court, the process at issue is a diagnostic procedure that helps doctors determine whether they have administered too high or too low a dose of a thiopurine compound, which is metabolized differently by individual patients. Prometheus Laboratories, the patent holder, set forth the specific metabolite levels correlated with likely harm or ineffectiveness, a law of nature according to the Court, because the "relationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harm . . . exist[] in principle apart from any human action. The relation is a consequence of the ways in which thiopurine compounds are metabolized by the body—entirely natural processes."

Unless a process "has additional features that provide practical assurance that the process is more than a drafting effort designed to monopolize the law of nature itself," it cannot be patented, the Court said. Without explaining what those additional features are, the Court found that the steps recited in Prometheus's patent, while "not themselves natural laws," were not "sufficient to transform the nature of the claim." The Court noted that (i) the "administering" step just refers to a pre-existing audience, i.e., doctors who used the drugs to treat patients before anyone asserted the patent claims; (ii) the "determining" step tells the doctor to determine blood metabolite levels "through whatever process the doctor or the laboratory wishes to use,"

methods that were well known in the art; and (iii) the "wherein" clause tells a doctor about relevant natural laws (the correlations between metabolite levels and risks or ineffectiveness), suggesting they should be accounted for when treating a patient.

The Court concluded, "To put the matter more succinctly, the claims inform a relevant audience about certain laws of nature; any additional steps consist of well-understood, routine, conventional activity already engaged in by the scientific community; and those steps, when viewed as a whole, add nothing significant beyond the sum of their parts taken separately. For these reasons we believe that the steps are not sufficient to transform un-patentable natural correlations into patentable applications of those regularities." Throughout the Court's opinion is reference to the tension between impeding innovations by granting a patent on laws of nature, tying them up from future use by others, and promoting innovation by giving a patent holder exclusive rights and thus a financial incentive to make discoveries.

Critics of the ruling, including the Biotechnology Industry Organization, reportedly said that "it introduces new and confusing concepts into the traditional body of patent law." While the medical industry apparently applauded the Court's decision, biotechnology interests expressed concerns about its effect on the thousands of patents that have already been issued for diagnostic tests. A stock analyst predicted that some of these patents will likely be challenged, and that larger companies will be able to weather the challenges, but it could throw "a few start-ups off their moorings." The opinion's impact on personalized medicine is also reportedly raising questions, given that pharmaceutical companies have been turning to those making diagnostic tests to help identify specific patients who will benefit from new drugs. *See The Wall Street Journal*, March 21, 2012.

INVESTOR NEWS

Wellcome Trust Creates £200-Million Fund for UK, EU Biotech Startups

The U.K.-based Wellcome Trust has announced the creation of a £200-million fund to make long-term investments in British and European biotechnology startups. Billed as one of the world's largest philanthropic funders of scientific and medical research, Wellcome Trust will draw the money from its endowment to operate what it is now calling Project Sigma to network with experts "to identify and invest in promising healthcare businesses." "Sigma will enable the Trust to take and retain ownership positions in these companies," Wellcome Trust said. "It will be able to contribute proactively to their development over the long term, for example by bringing together complementary expertise from different companies and scientific fields." *See Wellcome Trust Press Release*, March 20, 2012.

SHB offers expert, efficient and innovative representation to life sciences clients facing complex biotech litigation and intellectual property and regulatory protocols. We know that the successful resolution of biotech-related matters requires a comprehensive strategy developed in partnership with our clients.

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Swiss Biotech to Raise $40 Million to Advance Asthma Clinical Program

Cytos Biotechnology Ltd., a Swiss biotech developing a new class of biopharmaceutical products, has announced that it has signed agreements with international strategic investors to raise up to US$40 million in equity and secured convertible loan notes in two tranches. Led by venBio and a syndicate that includes Abingworth and Aisling Capital, the investment round will be used to advance Cytos's lead product CYT003-QbG10 (CYT003) for patients with allergic asthma. The company will seek shareholder approval for the transaction during its April 2012 annual meeting.

According to Cytos, CYT003 "is a novel allergen-independent immunotherapy with disease-modifying potential that could be used to treat a broad range of different allergies. Cytos will also use the fund to develop additional pipeline programs and to progress its novel Immunodrug™ platform on which CYT003 is based." *See Cytos Biotechnology Press Release*, March 21, 2012.

Grifols Acquires 51 Percent Stake in Araclon Biotech

Grifols, a Spanish plasma-product manufacturer specializing in the hospital-pharmaceutical sector, has announced that it has acquired 51 percent of the equity of Zaragoza-based Araclon Biotech, a company spun off from the University of Zaragoza in 2004 to develop therapies and diagnostics for Alzheimer's disease. The deal will reportedly allow Araclon to continue research and development projects relating to early Alzheimer's detection.

According to Grifols, the company recently launched a second medical trial to evaluate the use of plasma derivatives in Alzheimer's patients. "This new approach involves combining hemapheresis treatment with the administration of albumin and intravenous immunoglobulin, two of the main plasma derivatives, at different intervals and in varying doses," Grifols said, noting that clinical studies in Spain and the United States "suggest a tendency to stabilize the illness in patients receiving treatment." *See PRNewswire*, March 15, 2012.

Aastrom Biosciences Announces Financing Deal to Advance CVD Treatments

Aastrom Biosciences, an Ann Arbor, Michigan-based biotech startup, has announced a $40-million financing deal with large institutional investor Eastern Capital Limited. According to a March 9, 2012, **letter** on the company's Website, the financing represents the largest funding round in the company's history. Aastrom President and CEO Tim Mayleben said the deal comes "through a private placement of redeemable preferred stock, which is convertible into our common stock in five years at $3.25, a substantial premium to our current share price."

The funding will apparently be used to advance a Phase 3 clinical study of ixmyelocel-T as a treatment for patients with critical limb ischemia, a condi-

tion in which blood vessels in the legs become so clogged that doctors are forced to amputate. "We will continue to build on this record of success and seek other high-quality investors and partners as we work to realize the clinical and commercial potential of ixmyelocel-T as a treatment for severe, chronic cardiovascular diseases [CVDs]," Mayleben wrote.

Kala Pharmaceuticals Raises $6.2 Million in Equity Financing; Awarded Two NIH Grants

Kala Pharmaceuticals of Waltham, Massachusetts, has raised an additional $6.2 million in equity financing to complete its $11.2-million seed financing. The new funding round comes from existing venture investors Lux Capital, Polaris Venture Partners, Third Rock Ventures, and Lighthouse Capital Partners. According to Kala, the funds will be used to move its pipeline of products that target diseases affecting mucosal organs, including eyes, respiratory tracts, gastrointestinal tracts, and the female reproductive system, toward human clinical trials. The company has also apparently been awarded two grants from separate divisions of the National Institutes of Health to advance its cystic fibrosis and ocular disease programs.

"We've demonstrated that Kala's formulations of a wide range of therapeutic agents can penetrate and evenly distribute through human mucus secretions, including the exceptionally thick mucus found in cystic fibrosis," said Kala co-founder, Colin Gardner. "Our goal is to develop therapies that lead to improved clinical outcomes for patients by overcoming the challenges posed by mucus barriers." *See Business Wire,* March 14, 2012.

Quotient Biodiagnostics Closes Funding Round for Transfusion Diagnostics

Quotient Biodiagnostics Holdings of Newtown, Pennsylvania, has reportedly closed an $11.2-million funding round led by Glen Partners. Quotient supplies transfusion-diagnostics products to blood banks. "The new funds will be used to fund the growth of the Quotient's U.S. commercial operations, to expand the Group's manufacturing and product development operations in Edinburgh, Scotland, and to accelerate the development of a next-generation automated transfusion diagnostics platform," Galen said. *See Galen Partners Press Release*, March 7, 2012.

Primus Green Energy Raises $12 Million for Demonstration Plant

Biofuel company Primus Green Energy Inc. has completed a third round of funding by raising $12 million from IC Green Energy Ltd., the renewable energy arm of Israel Corp. Ltd. Primus has apparently received $40 million from IC Green Energy since 2007 and developed a proprietary process to produce gasoline and other fuels from biomass or natural gas; it plans to use the funding for an "integrated, single-loop" demonstration plant under

construction at the company's pilot plant in Hillsborough, New Jersey. The company plans to break ground in early 2013 on its first commercial plant. "Now that our technology is in place, we look forward to partnering with additional strategic investors to bring our biomass/natural gas-to-gasoline process to market," said Primus Chair Yom-Tov Samia. *See PRNewswire*, March 14, 2012.

BUSINESS CLIMATE

WSJ Says Venture Capital Tougher to Find for Biotech Companies

Noting that venture capitalists invested just $3.92 billion in biotech companies in 2011, down from the $6.17 billion watermark in 2007, and that shares in biotechs that went public last year averaged nearly 30 percent less than their anticipated midpoint offering price, a recent *Wall Street Journal* article warns biotechs, "The gravy days are over." Some venture capitalists have reportedly ceased funding risky biotech startups altogether; those that have stayed in are reportedly finding that they can no longer cash out through IPOs, but have to invest even more by buying shares. The article suggests that the challenging economic environment and pharmaceutical companies' demand for deals tying proof of success to funding are among the factors to blame for the financing slowdown. Biotechs that have not closed their doors have apparently responded by adopting belt-tightening measures, contracting out certain tasks and searching for funds overseas or from private foundations. *See The Wall Street Journal*, March 16, 2012.

In-House Counsel Survey Suggests Biotech Mass Torts Will Increase

Thousands of in-house counsel, surveyed over 11 years by BTI Consulting Group, are reportedly predicting that more class action attorneys with technological know-how will be needed in coming years because of an anticipated increase in chemical and biotech mass tort litigation. In its new report, titled "BTI's Strategic Review and Outlook for the U.S. Legal Services Industry," the Wellesley, Massachusetts-based firm notes that class actions due to negligence and accidental exposure to chemicals or personal injury from drug use are already on the rise.

The expected mass tort litigation will likely be based in part on misleading product labeling, off-label drug use and marketing, and negligent testing, according to the report. The cases could also arise from improved chemical-detection methods as well as regulations that ban or limit chemicals once considered safe. BTI clients are also apparently looking at increasing globalization as a source of liability exposure.

BTI President Michael Rynowecer told a news source that corporate clients believe intellectual property (IP) may be a significant factor in these cases, placing large law firms with established IP and class action practices at an advantage given their technological expertise. "Especially in the biotech area, you're going to have to look at what technology caused the unintended outcomes or circumstances, where it came from, what was the chain of command, and could it have come from another substance," he was quoted as saying. *See Product Liability Law 360*, March 23, 2012.

LEGISLATIVE AND REGULATORY DEVELOPMENTS

FDA Considers Expanding the Definition of OTC Drugs

Seeking input from consumers, pharmacists, health care providers, regulators, and insurers, the Food and Drug Administration (FDA) is considering expanding the definition of nonprescription drugs. The agency recently held hearings on whether some of these drugs, including those for cholesterol, blood pressure, asthma, and birth control, should be made available over-the-counter (OTC).

To ensure safety, FDA said special conditions would apply to some OTC drugs. For example, people seeking these products may have to first talk with a pharmacist, undergo a diagnostic test or visit a physician to obtain an initial prescription but not to obtain refills. "FDA is also considering whether some drugs could be a prescription drug and a nonprescription drug with conditions of safe use," the agency said.

"OTC drugs have had great success in providing consumers with excellent self-care options, but our concept of self-care is limited to conditions that can be self-diagnosed and self-treated based on the information in the drug facts box, combined with common knowledge," said Center for Drug Evaluation and Research Director Janet Woodcock. "What we are asking is, should there be more flexibility in the concept of nonprescription drugs? Can we broaden the assistance a consumer gets and increase the types of medicines that might be available over-the-counter?" *See FDA Press Release*, March 23, 2012.

LITIGATION

U.S. Supreme Court Remands *Myriad Genetics* to Federal Circuit

As anticipated, the U.S. Supreme Court has granted the petition for *certiorari* filed in a case involving to what extent genetic discoveries can be patented, and then vacated the Federal Circuit Court of Appeals judgment and remanded the matter for reconsideration in light of *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, No. 10-1150 (U.S., decided March 20,

2012). *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, No. 11-725 (U.S., petition for cert. granted, March 26, 2012). The Court's decision in *Mayo Collaborative Services* is summarized elsewhere in this *Bulletin*.

Myriad Genetics previously divided the Federal Circuit, with the majority ruling that while most of Myriad's challenged method claims were patent-ineligible because they involved just one step of "comparing" or "analyzing" two gene sequences, one method claim, which involved "growing," "determining" and "comparing" steps, claimed patentable subject matter. Additional information about the vacated ruling appears in Issue 18 of this *Bulletin*. The dissenting jurist contended that the process of isolating genetic material from a human DNA molecule does not make the isolated genetic material a patentable invention.

NEWS BYTES

The Food and Drug Administration (FDA) issues a final rule, effective March 20, 2013, except for the amendment adding 21 C.F.R. § 211.122(g)(4), which takes effect April 19, 2012, amending the packaging and labeling-control provisions of its current good manufacturing practice regulations for human and veterinary drug products. According to FDA, the changes are intended to protect consumers from labeling errors while allowing manufacturers to use a broader range of error prevention and labeling-control techniques.

The Food and Drug Administration (FDA) makes available additional draft and revised draft product-specific bioequivalence (BE) recommendations. FDA notes that the recommendations "provide product-specific guidance on the design of BE studies to support abbreviated new drug applications." Comments are requested by May 21, 2012.

The Food and Drug Administration (FDA) reopens the comment period on a proposed rule "to establish standards that would be considered in determining whether the major statement in direct-to-consumer (DTC) television and radio advertisements relating to the side effects and contraindications of an advertised prescription drug intended for use by humans is presented in a clear, conspicuous, and neutral manner." Comments are requested by April 9, 2012.

UPCOMING CONFERENCES AND SEMINARS

Shook, Hardy & Bacon Government Enforcement & Compliance Partner Carol Poindexter will serve as moderator of a panel discussion during AdvaMed's "2012 International Medical Device Industry Compliance Conference," scheduled for May 9-11, 2012, in Stockholm, Sweden. Poindexter's panel involves product distributors who will be discussing the latest compliance issues. Shook, Hardy & Bacon is a conference co-sponsor.

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Shook, Hardy & Bacon Pharmaceutical & Medical Device Litigation Practice Partners Scott Sayler and David Brooks will participate in DRI's Drug and Medical Device Seminar slated for May 10-11, 2012, in New Orleans, Louisiana. Co-sponsored by SHB, the event will feature "trial skills demonstrations, panel discussions of judges overseeing coordinated pharmaceutical proceedings, and litigation insights from leading defenders of drug and device cases." Brooks will present a session titled "When a Good Medical Device Fails: Successfully Defending Medical Device Suits When Causation Is Not in Doubt," which will address the substantive and strategic consideration of defending these cases. Sayler will also deliver remarks as chair of DRI's Drug and Medical Device Committee.

The American Conference Institute's "3rd Advanced Forum on Biosimilars" will be held May 22-23, 2012, in New York City. Industry leaders will address the legal, regulatory and commercial aspects of "follow-on biologics," and a keynote address on implementing the biosimilar pathway will be presented by a Food and Drug Administration official.

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Shook, Hardy & Bacon attorneys are experienced at assisting biotech and life sciences clients with a variety of legal matters such as U.S. and foreign patent procurement; licensing and technology transfer; venture capital and private financing arrangements; joint venture agreements; patent portfolio management; biomedical research and development; risk assessment and management; records and information management issues and regulations; and employment matters, including confidentiality and non-compete agreements. The firm also counsels industry participants on compliance issues, ranging from recalls and antitrust matters to facility inspections, subject to FDA, SEC, FTC, and USDA regulation.

SHB is widely recognized as a premier litigation firm in the United States and abroad. For more than a century, the firm has defended clients in some of the most challenging national and international product liability and mass tort litigations.