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LIFE SCIENCES & BIOTECHNOLOGY LEGAL BULLETIN

SCIENCE • TECHNOLOGY
ENGINEERING • ENERGY
PHARMACEUTICAL

CONTENTS

IP NEWS

Do DNA Patents Affect Genetic Sequencing and Testing Advances?

University of Missouri-Kansas City School of Law Professor Christopher Holman writes in the most recent issue of *Nature Technology* that while DNA sequencing technology has spawned a myriad of patent-related lawsuits, "aggressive patent acquisition and enforcement practices" show no signs of abating and may not necessarily be hindering the development of next-generation DNA sequencing and analysis technologies.

In his article "Advances in DNA sequencing lead to patent disputes," Holman discusses the early laboratory breakthroughs that led to the current race to develop an individual genome sequencing technology that will cost less than $1,000. He describes in some detail how companies and inventors have kept the courts busy with infringement claims and counterclaims, as well as disputes over who was the first to invent a claimed technology. This has occurred since patents were developed or acquired from the earliest days of sequencing involving dyes and apparatuses through automated sequencing instruments and reagents, then to more recent ion semiconductor sequencing and pyrosequencing technologies.

According to Holman, no human gene patent has ever, to his knowledge, "been asserted in the context of multiplex genetic testing or genome sequencing" because asserted patents appear to be directed not toward genes themselves, "but rather toward methods, apparatuses and reagents used in DNA sequencing and genetic testing." In his view, patents "seem to have had both positive and negative effects on advances in DNA sequencing." While the earliest discoveries were not patented, the crucial protection that patents afford makes the greater investment and risk in the field worthwhile. He concludes, "[F]or better or worse, patents are likely to continue playing an important part in the advance of DNA sequencing technology." *See Nature Biotechnology*, November 2012.

CRS Visiting Scholar Recommends That Congress Clarify Patentable Subject Matter Doctrine

In a Congressional Research Service (CRS) paper titled "*Mayo v. Prometheus:* Implications for Patents, Biotechnology, and Personalized Medicine," visiting

scholar John Thomas considers how the U.S. Supreme Court ruling limiting the patentability of diagnostic methods that simply describe natural phenomena and relations may affect innovation and public health. He provides overviews of the biotechnology industry, the U.S. patent system, the Court's ruling in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, responses to the decision by experts in affected disciplines, and the potential impact on *Myriad Genetics* and the patent eligibility of isolated DNA molecules "that encode sequences identical to human genes."

Observing that *Mayo v. Prometheus* "arguably limited the ability of medical innovators to patent diagnostic methods" and could affect the products of biotech research, Thomas concludes, "As judicial rulings continue to influence the availability of patent protection in the healthcare and biotechnology fields, interested parties may encourage Congress to clarify the doctrine of patentable subject matter through legislative amendments."

USPTO Faces Challenges When Determining Patent Eligibility

According to a news source, the U.S. Patent and Trademark Office (USPTO) has been struggling with how to determine whether an invention is patent-eligible given the lack of clear guidance from the U.S. Supreme Court.

USPTO General Counsel Bernard Knight, speaking at an international intellectual property law symposium on November 9, 2012, reportedly noted that while subject-matter eligibility is the "hottest area" of intellectual property law and is critical for the high-tech and biotech industries, the Supreme Court's failure to provide more than limited statements on the issue combined with deeply divided Federal Circuit rulings have been an obstacle for the office.

"We have 7,000 examiners that have to make patent eligibility decisions every day, and it's very difficult to do that when the only guidance from the Supreme Court is that software is not patent-eligible if it's an abstract idea," Knight said. "That standard was the takeaway from the high court's 2010 *Bilski v. Kappos* decision, which ruled that the so-called machine-or-transformation test used by the Federal Circuit to determine patent eligibility was not the sole test, but only a useful clue." Knight contends that the ruling frustrated the USPTO because not only did it fail to provide guidance about what should be deemed patent-eligible, but it undermined a test that examiners had found useful. "That was a great test for use because we have to make sure we apply the law consistently and that was a pretty easy test for us to apply," he said.

Mayo v. Prometheus did not improve the situation, according to Knight. The court ruled that a diagnostic blood test was not patent-eligible because it involved observing a natural correlation between a drug and metabolite levels in the blood, and USPTO does not agree with the Court's analysis, he said. *See Law360*, November 9, 2012.

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NEW BIO BUSINESS VENTURES

Takeda Acquires Access to Envoy's CNS Drug Pipeline and bacTRAP Technology®

Takeda America Holdings, Inc. has reportedly acquired Envoy Therapeutics, Inc. in a deal worth $140 million, including an up-front payment and progress-dependent milestone payments. Envoy has developed technologies to label and extract protein-making components of specific types of cells, deemed particularly useful in treating diseases of the central nervous system (CNS). The deal provides Takeda with Envoy's proprietary bacTRAP technology® and its pre-clinical CNS assets including programs to address Parkinson's disease and cognitive impairment associated with Schizophrenia. According to a Takeda news release, Envoy's bacTRAP technology®, know-how, materials, data, and analytic techniques will enable "the identification of novel targets expressed in disease-relevant cell populations." Most of Envoy's personnel will transfer from Jupiter, Florida, to Takeda's San Diego facility in March 2013. *See Takeda Press Release*, November 6, 2012.

Strategic Partnership Formed to Develop Algae Biofuels

Sapphire Energy will reportedly partner with the Institute for Systems Biology (ISB) to bring systems biology solutions to the development of algae biofuels, an effort that is expected to significantly increase oil yield and improve resistance to crop predators and environmental factors. Sapphire produces algae crude oil, known as Green Crude, a renewable, low-carbon product that can be refined and used as diesel and jet fuel. According to an ISB spokesperson, "Sapphire is dealing with one of the most complicated problems known to humans: how to make fuel from a renewable resource. Together, we have complementary expertise that will allow us to understand, reverse engineer and rationally alter the gene networks for fuel production in algae."

Sapphire Chief Science Officer Alex Aravanis said, "By working with ISB to apply their systems biology approach, we're able to more rapidly identify genes and regulatory pathways that can increase yield and move us toward our goal of making Green Crude a market viable, crude oil alternative." Sapphire has evidently begun operating a 300-acre commercial demonstration farm and bio-refinery in New Mexico in partnership with the U.S. Department of Energy. The facility is expected to produce some 100 barrels of Green Crude per day and will be completed by the end of 2014. The company also operates a 22-acre research and development facility from which a pilot project produced jet fuel for the earliest flights using algae-derived jet fuel. *See Sapphire Energy Press Release*, November 1, 2012.

INVESTOR NEWS

$25 Million Raised to Advance Treatment of Hyperkinetic Movement Disorders

La Jolla, California-based Auspex Pharmaceuticals, Inc. has reportedly raised $25 million in a Series D venture financing round that included investors Panorama Capital, CMEA Capital and Sloan Biotech Fund. The biopharmaceutical company indicated that it will use the funds "to advance the development of its portfolio of drug molecules, particularly the Phase 3 development of its lead molecule, SD-809, expected to begin in the first half of 2013. Auspex has developed SD-809 for the treatment of hyperkinetic movement disorders including Huntington's disease, Tourette syndrome and tardive dyskinesia." It characterizes SD-809 as "a novel inhibitor of the vesicular monoamine transporter 2 (VMAT-2)."

The company uses deuterium in medicinal chemistry to develop products with improved safety, reduced drug-drug interactions and less frequent dosing. Also in the Auspex pipeline are "SD-900, a JAK kinase inhibitor for the treatment of autoimmune diseases, and SD-560, for the treatment of fibrotic diseases." Auspex CEO Lawrence Fritz said, "This new financing round provides resources for the pivotal trial of SD-809 in Huntington's disease and for the acceleration of this compound's development in additional movement disorders." *See Auspex Pharmaceuticals Press Release*, November 8, 2012.

MEI Pharma Secures $27.5 Million in Commitments to Develop Cancer Therapy

According to a news source, San Diego-based oncology company MEI Pharma, Inc. is set to raise $27.5 million from commitments to purchase its stock and warrants in a private placement. Investors include Vivo Ventures, New Leaf Venture Partners, RA Capital Management, and Three Arch Opportunity Fund. The securities purchase agreement involves 55 million shares of common stock and warrants to purchase as many as 38.5 million additional common stock shares. Each unit will be sold for $0.50 and consist of one share of common stock and a warrant to purchase 0.7 of a share of common stock. The warrants will be exercisable at $0.52 per share upon the transaction's closing, which is expected in December 2012; the warrants will expire within five years of issuance.

MEI plans to use the proceeds to advance the clinical development of Pracinostat®, an oral histone deacetylase inhibitor that the company acquired earlier this year and its isoflavone-based drug candidates. The therapy has evidently been tested in more than 150 patients, including those with advanced hematologic malignancies such as myelodysplastic syndrome, acute myeloid leukemia and myelofibrosis. Other drug candidates in the company's pipeline are ME-143 and ME-344 for use in patients with solid refractory tumors. *See PR Newswire*, November 5, 2012.

Investors Provide $28.05 Million for CVD Drug Development

A biopharmaceutical company headquartered in Chapel Hill, North Carolina, has reportedly raised $28.05 million in an equity financing round involving investors Aurora Funds and New Enterprise Associates. Cardioxyl Pharmaceuticals, Inc. announced the funding round in a Securities and Exchange Commission filing. The company will evidently use the funds to advance its lead therapeutic, CXL-1020, through clinical development. The compound has reportedly been designed to treat acute decompensated heart failure, a condition responsible for more hospitalizations among adults 65 and older than any other. The condition, said to affect some 5 million people, can apparently cause reduced cardiac function and result in fluid accumulation in the lungs and extreme shortness of breath. CXL-1020, which the company describes as "a novel, proprietary nitroxyl donor," aims to improve heart muscle contractions and also widen blood vessels to increase blood flow without increasing heart rate. *See MedCity News*, November 7, 2012.

Equity Financing Provides Financing for Cardiac Inflammation Test

Specialty clinical laboratory Cleveland HeartLab Inc. has completed a $14.7-million financing round. While Mutual Capital Partners, Cleveland, led the round, existing shareholders Excel Venture Management and Cleveland Clinic also participated. The Cleveland-based laboratory, which also describes itself as a cardiovascular disease management company, has developed tests that practitioners use to manage and prevent heart disease. The company's research and development lab reportedly develops next-generation cardiovascular disease biomarkers. According to company President and CEO Jake Orville, "This financing will support the development and commercialization of our pipeline of new biomarkers, making our approach even stronger and enabling us to continue our leadership in cardiovascular and chronic disease management. Together, the work supported by this round will allow us to develop even greater breadth and depth in our test offerings and will strengthen our ability to reach and retain key customers." *See Cleveland HeartLab News Release*, October 22, 2012.

Advaxis Announces Equity Financing to Support Cancer Therapy Trials

A clinical-stage biotechnology company in Princeton, New Jersey, has secured commitments of $10 million in equity financing and an additional $1.4 million from the assumption of convertible notes owned by third parties and the purchase of convertible notes by private and institutional investors. Advaxis, Inc. will reportedly use the funds to continue developing the next generation of immunotherapies for cancer and infectious diseases caused by the human papillomavirus. The company recently reported positive preliminary data from a Phase 2 trial of ADXS-HPV in patients with recurrent/refractory cervical cancer in India.

According to a news source, ADXS-HPV was selected as the Best Therapeutic Vaccine at the 5th Annual Vaccine Industry Excellence Awards by the industry and the journal *Expert Reviews of Vaccines*. The company's "immunotherapies are based on a novel platform using live, attenuated bacteria that are bio-engineered to secrete antigen/adjuvant fusion protein(s) designed to redirect the powerful immune response all human beings have to the bacterium to the cancer itself." Advaxis is also apparently evaluating ADXS-HPV for head and neck cancers. *See Advaxis Press Release*, October 31, 2012.

Series B Funding Round Brings $12 Million to Expand Clinical Diagnostics Products

Advanced Cell Dynamics, Inc. (ACD) has reportedly completed a $12-million Series B equity financing round that will support the commercial expansion of the company's RNAscope®-based products and services. The Hayward, California-based company will also use the proceeds to accelerate RNAscope's entry into the clinical diagnostics market. ACD apparently offers its products and services globally to scientists in a range of areas, including basic research and companion diagnostics for personalized medicine. According to the company, the technology "is the first automated multiplex in situ hybridization platform capable of detecting and quantifying RNA biomarkers in situ at single-molecule sensitivity." ACD develops cell- and tissue-based diagnostic tests for personalized medicine. *See Advanced Cell Diagnostics, Inc. Press Release*, November 1, 2012.

Biotech Investors Turn to LinkedIn to Make Connections

If you are in the biotech and pharma industries and are not using LinkedIn, you may be missing something. That is **according** to Luke Timmerman, *Xconomy* national biotech editor, who writes recently, "While many in the tech press mock LinkedIn as an oh-so-boring compiler of mere resumes, it has become the indispensable online hub for networking in life sciences—an industry where relationships make the world go round."

While it might pale by comparison member wise to Facebook—187 million members versus 1 billion—Timmerman says, "LinkedIn is the singular site for finding people in biotech, whether they are biologists, chemists, toxicologists, admin assistants, business development people, finance pros, or CEOs." A search he conducted recently produced more than 513,000 people in the LinkedIn database who self-identify as members of the "biotechnology" or "pharmaceutical" industry.

Timmerman notes that some areas on the LinkedIn site are far from perfect, complaining that one of the most irritating aspects about the site is that "even though it has achieved critical mass, many C-suite executives and venture capitalists still resist signing up. For example, when I searched on the 40 names of '**young and proven**' biotech venture capitalists listed in this column two weeks ago, only 24 of the 40 (60 percent) showed up in the LinkedIn database."

"I find it baffling that so many senior people in the industry still resist taking advantage of this resource, and [you] have to wonder if they have some better idea on how to network. There's no getting around the importance of networking. Biotech is a geographically far-flung industry, with hundreds of companies and vendors, who all need to work together in trusting relationships to keep the whole enterprise afloat."

Meanwhile, Timmerman has opined in a more recent column that biotech financing is on the upswing and involves "[a] whole new class of investment banking firms [that have] stepped up to compete for the business of helping biotech companies raise money." According to his optimistic analysis of this year's class of 12 biotech company IPOs, 21 different firms participated, including some the more recognizable underwriters, such as JP Morgan, Bank of America/Merrill Lynch and Lazard Capital Markets. *See Xconomy*, November 5 and 12, 2012.

BUSINESS CLIMATE

Biotech Jobs Relatively Stable in 2012 Q3

According to *Nature Biotechnology* Senior Editor Michael Francisco, the number of advertised biotech and pharma sector jobs in the third quarter (Q3) of 2012 remained stable from Q2. While some firms experienced hiring slowdowns, others have significantly expanded. Among the biotech companies advertising the most openings on Monster.com, LinkedIn.com and Naturejobs.com were Genzyme, Celgene, Illumina, and Life Technologies. Among the firms downsizing in Q3 were Actelion and Dendreon. *See Nature Biotechnology*, November 2012.

Fiscal Cliff Causing Unease in Biotech Sector

According to Jeanne Haggerty, director of federal relations for the Washington-based Biotechnology Industry Organization, the "looming" fiscal cliff is a real concern and if "a lame-duck session of Congress doesn't act to avoid the cliff, it could cost the state of Michigan 31,000 jobs, drastically slow approval for new drugs and medical devices, and eliminate billions in research grants." Haggerty delivered her remarks in a session titled "Federal Policy Update: What Now for Pharma?" on November 8, 2012, at the eighth annual MichBio Expo.

Apparently, Haggerty doubts that the lame-duck session and the Obama administration will be able to come to a permanent agreement before the January 2, 2013, deadline and thinks that a temporary agreement will be reached that will delay the economy falling off the cliff until spring. "What they will likely do is punt it until the end of March. They'll agree on a sequestration bridge," she said. "That will give time for new members of Congress to come in."

According to a news source, the law that was passed calling for sequestration if an agreement could not be reached on tax policy and budget cuts also called for funding to the National Institutes of Health (NIH) and the U.S. Food and Drug Administration (FDA) to be cut by 8.2 percent each.

Haggerty said that the NIH cuts would total about $2.5 billion and eliminate 2,100 research grants, including 300 through the National Cancer Institute. These cuts would hit Michigan particularly hard. Its three major research universities, the University of Michigan, Michigan State University and Wayne State University, and many of its researchers rely on NIH grants to fund their work and lab help. She also estimated that FDA would lose $320 million, resulting in 1,000 layoffs at the agency, already a target of criticism by researchers and executives at biotech startups for its slow pace in approving new drugs or devices. *See crainsdetroit.com*, November 8, 2012.

LEGISLATIVE AND REGULATORY DEVELOPMENTS

FDA Warns Competing Drug Makers over Unsubstantiated Superiority Claims

The U.S. Food and Drug Administration (FDA) has sent warning letters to competing drug manufacturers for allegedly promoting their neonatal respiratory distress syndrome treatments using "unsubstantiated superiority claims" that also "omit and minimize important risk information, and present unsubstantiated claims for the drug product."

According to FDA, the studies cited in the promotional materials, including Webpages and video, do not support the product claims thus making the products misbranded in violation of the Federal Food, Drug, and Cosmetic Act. FDA's Office of Prescription Drug Promotion requests that the companies immediately cease disseminating these promotional materials and respond by November 15, 2012, "stating whether you intend to comply with this request" and explain their plans for discontinuing the use of violative materials.

The company targets, ONY Pharmaceuticals and Cornerstone Therapeutics, reportedly have a history of "behaving badly." In 2011, ONY evidently sued Cornerstone, its foreign parent, a scientific journal, and the authors of a study appearing in the journal, claiming they "cherry-picked" and "manipulated" data in a way that unfairly disparaged ONY's product. The study apparently claimed that Cornerstone's drug significantly reduced the risk of death when compared with ONY's product. According to ONY, Cornerstone's parent sponsored the study, three of the four authors served as the parent's consultants and the fourth worked as a contractor for the parent. Two of the four authors purportedly served on the journal's editorial board.

A federal court reportedly disagreed with ONY, ruling that the courtroom was not the appropriate forum for this dispute. Because the study disclosed the criteria used to reach its conclusions and the intended readers are a "highly

specialized group" with "a well-developed understanding of the issues facing biomedical research," the court determined that the scientific debate must be resolved in the scientific community. *See Pharmalot*, November 8, 2012.

EC Approves First Gene Therapy Medicine in Western World

The European Commission (EC) has given **final approval** to uniQure's gene therapy Glybera® for the treatment of lipoprotein lipase deficiency (LPLD) patients with recurring acute pancreatitis. This reportedly marks the first approval in the Western world of a gene therapy. It follows the 2003 approval in China of Gendicine, a head and neck cancer therapy developed by Shenzhen SiBiono GeneTech Co. Ltd.

University of Amsterdam Professor John Kastelein reportedly said that the therapy will dramatically affect LPLD patients whose pancreatitis attacks often cause early onset diabetes and cardiovascular complications. "Glybera's approval means LPLD patients, for the first time, have a medical treatment option for a very complex and severe disease," he said. "By helping to normalize the metabolism of fat, Glybera prevents inflammation of the pancreas thereby averting the associated pain and suffering and, if administered early enough, the associated co-morbidities."

uniQure CEO Jörn Aldag said, "The final approval of Glybera from the EC marks a major step forward in making gene therapies available not only for LPLD but also for a large number of rare diseases with a very high unmet medical need. The EC's approval is an important validation of our innovative product platform and offers strong support for our other advanced development programs, which focus on acute intermittent porphyria, Sanfilippo B, hemophilia B and Parkinson's disease." *See uniQure Press Release*, November 2, 2012.

LITIGATION

Myriad Genetics Calls on SCOTUS to Reject Petition from Ruling Finding DNA Molecules Patent-Eligible

According to Myriad Genetics, Inc., the U.S. Supreme Court should not grant review in *Association for Molecular Pathology v. Myriad Genetics, Inc.* Details about the Federal Circuit Court of Appeals decision on remand from the lawsuit's previous sojourn before the U.S. Supreme Court appear in **Issue 41** of this *Bulletin*. The American Civil Liberties Union (ACLU) has requested that the Court review the Federal Circuit's decision.

Myriad contends that the ACLU has mischaracterized the issues and that the Federal Circuit relied on settled principles in deciding that certain isolated genetic material is patent eligible. According to its brief in opposition, the U.S. Patent and Trademark Office (PTO) "long ago determined that claims to 'isolated' molecules of DNA reflect human-made, patent-eligible inventions.

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Thus, over the last 30 years it has issued thousands of patents directed to isolated DNA molecules—indeed, the challenged patents themselves began issuing 15 years ago. And the PTO has issued over 40,000 patents drawn to DNA-related subject matter." Myriad also cites PTO's guidelines on patenting DNA molecules to emphasize consistent industry practices based on those guidelines and on which "the investing and inventing communities have relied … to develop significant advancements in human, agricultural, and industrial products."

According to Myriad, "This case is unworthy of certiorari because it concerns the application of settled law to particular facts. … The court's decision is also consistent with the policy goal of the Patent Act, the considered judgment of the PTO, and longstanding practice. Further, the issues presented are unique and fact-bound, and in order to even reach the § 101 issues, the Court would have to take up antecedent jurisdictional questions and preempt percolation in the Federal Circuit, the appellate court statutorily vested with unifying and clarifying U.S. patent law."

NEWS BYTES

The U.S. Food and Drug Administration issues draft guidance for industry and agency staff titled "Highly Multiplexed Microbiological/Medical Countermeasure in Vitro Nucleic Acid Based Diagnostic Devices." The draft includes recommendations for studies to establish the analytical and clinical performance of these devices. Comments are requested by February 7, 2013. ■

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