Shook, Hardy & Bacon L.L.P.

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LIFE SCIENCES & BIOTECHNOLOGY LEGAL BULLETIN

SCIENCE • TECHNOLOGY
ENGINEERING • ENERGY
PHARMACEUTICAL

CONTENTS

IP NEWS

Inventor Sues U.S. in Challenge to Constitutionality of Patent Reform Law

A man described by the *New York Times* as a "garage inventor" has reportedly filed a lawsuit in a federal court in Florida challenging the validity of the Leahy-Smith America Invents Act on the ground that its change to a "first-to-file" patent system violates the U.S. Constitution's text and original meaning. *MadStad Eng'g, Inc. v. Kappos*, No. 8:2012cv01589 (U.S. Dist. Ct., M.D. Fla., filed July 18, 2012). Plaintiff Mark Stadnyk, who started his company MadStad Engineering in 2006 to commercialize his invention, holds a patent on a motorcycle windshield; he apparently contends that the law will favor large corporations over lone inventors and threatens the nation's position as a global innovator. Among those agreeing with Stadnyk's views is Senator Barbara Boxer (D-Calif.) who apparently stated during debate over the patent reform law, "I strongly disagree with changing the core principle of our patent system—awarding a patent to the true inventor—for the sake of perceived administrative ease." *See The New York Times*, August 26, 2012.

Fractured *Myriad Genetics* Ruling Follows SCOTUS Remand

Ruling that one plaintiff had standing to seek a declaratory judgment as to the patent eligibility of certain genetic discoveries, the Federal Circuit Court of Appeals has once again reversed in part and affirmed in part a lower court's determination that isolated DNA molecules and methods of comparing molecules to determine whether a patient's genes have mutations that could cause breast and ovarian cancer were not patent eligible. ***The Ass'n for Molecular Pathology v. U.S. Patent and Trademark Office (Myriad Genetics, Inc.), No. 1020-1406 (Fed. Cir., decided August 16, 2012)***.

The Federal Circuit's July 2011 ruling, which was reversed by the U.S. Supreme Court for reconsideration in light of *Mayo Collaborative Services v. Prometheus, Inc.*, 132 S. Ct. 1289 (2012), is summarized in Issue 18 of this *Bulletin*.

The court found that nothing in *Mayo* changed its earlier ruling that Myriad's composition claims were all patent eligible because they are products of man, involving skill, knowledge and effort to create. The court also found that nothing in *Mayo* changed its determination that most of Myriad's method claims with the exception of one, were patent-ineligible because they claim "only abstract mental processes." Judge Kimberly Moore again concurred in part to explain that the longer strands of isolated DNA continue to present a "much closer case" on the question of patentability, but would allow them protection for policy reasons. As before, Judge William Bryson, concurring in part and dissenting in part, wrote separately to express his concerns over "whether an individual can obtain patent rights to a human gene."

NEW BIO BUSINESS VENTURES

Biotech Companies Collaborate to Produce New Drug for Strokes

Laureate Biopharmaceutical Services, Inc. has reportedly collaborated with ZZ Biotech, LLC to develop and produce 3K3A-APC, a potential treatment for ischemic stroke. The companies' scientists have apparently successfully overcome certain complexities, such as protease degradation during enzymatic activation and "the undesirable side effect of bleeding" presented by working with challenging proteins. ZZ Biotech has begun a Phase 1 study of the safety and pharmacokinetics of 3K3A-APC in healthy human volunteers.

New Jersey-based Laureate Biopharma focuses on the production of therapeutic proteins and includes in its portfolio of services aseptic filling, cell-line development, analytical and stability testing, as well as regulatory support. Located in Houston, Texas, ZZ Biotech develops "biological treatments for the aging and damaged brain, including those affected by stroke and other neurodegenerative disorders." *See Laureate Biopharmaceutical Press Release*, August 12, 2012.

Non-Profit Joint Venture Formed in Michigan to Support Personalized Medicine

The University of Michigan Health System has reportedly launched a non-profit joint venture with Arizona-based International Genetics Consortium to support genetic research and personalized medicine. Formed under the Michigan Health Corp., a university health system arm that enables outside partnerships, the new entity, known as Paradigm, will offer whole-gene and multi-gene sequencing and molecular diagnostics services to oncologists and oncology groups, pathologists, academic medical centers, and clinical trial groups studying personalized medicine regimens all around the country. Paradigm co-founder Jay Hess said, "We're thrilled to take this important step that allows us to harness the power of genetic information to guide patient therapy and improve outcomes." *See University of Michigan Health System Press Release*, August 16, 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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UK Co. to Collaborate with Research Foundation Focused on Huntington's Disease

London-based Proteome Sciences plc will apparently collaborate with CHDI Foundation, Inc., a non-profit biotech company dedicated to finding therapies that slow the progression of Huntington's disease, on a protein-profiling project. Proteome's PS Biomarker Services™ will be used to deliver potential proteomic markers intended to help "elucidate mechanisms of Huntington's disease pathology," according to Proteome COO Ian Pike. "The link between the Huntington's disease genotype and disease phenotype remains poorly understood and we will apply our Tandem Mass Tag workflows to provide high density protein expression maps in cell lines carrying different CAG-repeat lengths." The analyses will be conducted at Proteome's Frankfurt, Germany, facility. CHDI has offices in California, New Jersey and New York. *See Proteome Sciences Press Release*, August 20, 2012.

INVESTOR NEWS

$23 Million Raised to Develop Antivirals to Treat Hepatitis B and HIV Infections

Novira Therapeutics Inc. has reportedly raised $23 million in a Series A financing round led by three new investors along with existing investors, including BioAdvance, Robin Hood Ventures and Delaware Crossing Investment Group. Based in Radnor, Pennsylvania, Novira will use the capital infusion to further develop its capsid-targeting antivirals for the treatment of chronic hepatitis B and HIV infections. The company has designed its antiviral drugs to disrupt the function of the virus's capsid, a protein required for replication and transmission. By doing so, the drugs prevent further spread of the virus, thus offering treatment options for viral diseases. *See Novira Therapeutics News Release*, August 24, 2012.

Diagnostics Co. Stock Offering Nets $57.8 Million to Further Work on Colorectal Cancer

A Madison, Wisconsin, molecular diagnostics company focusing on colorectal cancer has reportedly completed an underwritten public offering of its common stock, netting about $57.8 million. According to Exact Science Corp., 6.325 million shares were sold at $9.75 per share. The company has developed non-invasive, molecular screening technology and notes that "[s]tool-based DNA technology is included in the colorectal cancer screening guidelines of the American Cancer Society and the U.S. Multi-Society Task Force on Colorectal Cancer." *See Exact Sciences Press Release*, August 13, 2012.

Series C Financing Round Brings $80 Million for Phase 2b Study of Oral Potassium Binder

A clinical-stage California-based pharmaceutical company has announced an $80-million Series C preferred stock financing, which adds to its previous $70-million Series B and $43-million Series A rounds, to fund late-stage development, a new drug application and commercial planning for its patiromer (RLY5016), a high-capacity non-absorbed oral potassium binder. Relypsa, Inc. is developing the binder to treat hyperkalemia, a condition of particular risk for chronic kidney disease patients who are often untreated or undertreated because of the undesirable side effect of increasing serum potassium from treatment with renin-angiotensin-aldosterone-system inhibitors. Prevalent in patients with renal impairment, hypertension, diabetes, and heart failure, hyperkalemia can lead to cardiac arrhythmia and sudden death. Relypsa is also researching additional product candidates through its proprietary polymer platform. *See Relypsa News Release*, August 15, 2012.

Orphan Drug Co. Raises $15 Million from Second Series A Round to Address Sialic Acid Deficiency

According to a news source, Ultragenyx Pharmaceutical Inc. recently raised $15.1 million from an apparent second closing of a $45-million Series A round announced in 2011. The California company is expected to use the funds to start a phase 2 study of UX-001, a sialic acid replacement therapy for the treatment of hereditary inclusion body myopathy, a rare progressive neuromuscular disease associated with a sialic acid deficiency that apparently causes muscles to waste away. The company is also developing an enzyme replacement therapy for another rare genetic metabolic disorder, Sly syndrome. UX-003 received an orphan drug designation in February 2012. While orphan drugs treat conditions and diseases with fewer than 200,000 patients, there has reportedly been a renewed interest in them by both startups and major pharmaceutical companies. *See MedCity News*, August 14, 2012.

$9.2 Million in Equity Reported to SEC by Stem-Cell Treatment Corp.

In a regulatory filing with the U.S. Securities and Exchange Commission (SEC), Fate Therapeutics, Inc. has reported that it raised $9.2 million in equity. The San Diego, California-based company is developing stem-cell modulators that guide the "fate" of non-embryonic stem cells as they mature thus enhancing their "homing" and proliferation for cancer patients undergoing stem-cell transplants. The company is developing other pipeline products for use in patients with cardiovascular disease, type 1 diabetes and muscle-wasting disorders. *See North County Times*, August 23, 2012.

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BUSINESS CLIMATE

Venture Capital Investments Increase in Q2 2012, but Life Science Sector Declines

While PricewaterhouseCoopers MoneyTree™ report for the second quarter (Q2) of 2012 shows a double-digit increase in venture capital investment activity over the first quarter of the year, investments in life sciences declined. In Q2 2012, $7 billion was invested overall in 898 deals, a 17-percent increase in dollars invested and 11-percent increase in the number of deals compared to Q1 2012. In the life sciences, investments apparently declined for the fourth consecutive quarter—biotechnology led the way with "the lowest quarterly total for the industry since the first quarter of 2003." Overall investments in biotechnology and medical devices reportedly fell 9 percent in dollars and 6 percent in deals, a 29-percent decrease from the same time period in 2011. Still, the medical devices and equipment sector received its third-highest investment amount in Q2 with $700 million for 84 deals, an 11-percent increase in deals over Q1. *See pwc.com*, July 20, 2012; *MedCityNews*, August 15, 2012.

Revenue Stream for Orphan Drugs Could Outshine Non-Orphan Drug Sector

According to a recent *Thomson Reuters* report, "The Economic Power of Orphan Drugs," the pharmaceutical sector is beginning to change its view of the returns that can be realized by developing and commercializing drugs to treat rare diseases, i.e., those that affect up to 200,000 patients. Apparently, the revenue potential of drugs that can address unmet needs in these populations is greater than previously thought given "the high cost of therapy and attractive developmental drivers, such as government incentives, smaller and shorter clinical trials, extended exclusivity and high rates of regulatory success" vis-à-vis non-orphan drug peers.

The report's conclusions are based on sales data and the impressive increase in orphan drug sales (25.8 percent) between 2001 and 2010 compared to just 20.1 percent for a comparable control group of non-orphan drugs. The report concludes, "[u]ltimately, the analysis validates the significance of targeting rare disease in the global pharmaceutical market. This attention will not only potentially affect the lives of millions worldwide who suffer from rare diseases, it will also propel the evolution of precision medicine."

LEGISLATIVE AND REGULATORY DEVELOPMENTS

Efforts Continue to Include 12-Year Biologics Exclusivity in Trans-Pacific Pact

With the 14th round of Trans-Pacific Partnership (TTP) talks scheduled for September 6-15, 2012, in Virginia, a number of lawmakers have expressed their support to the Obama administration for the inclusion of a provision

protecting the 12 years of reference product exclusivity provided under U.S. law for biological medical products. Twelve years of protection would align the pact with the Biologics Price Competition and Innovation Act of 2009, although the administration's 2013 budget proposal apparently seeks to reduce that period to seven years.

The latest comments appear in an August 6, letter to President Barack Obama (D), from Senator Claire McCaskill (D-Mo.) who said, "Providing 12 years of exclusivity for biologics in the United States and abroad safeguards an important foundation for a vibrant U.S. biopharmaceutical industry and workforce." Data exclusivity, said to preserve innovation incentives, is the period of time between the Food and Drug Administration's approval of a reference product and the point at which an abbreviated filing for a biosimilar relying on the innovator's data on safety and efficacy can receive final approval.

Union Cabinet Approves Indian Agriculture Ministry's Plan to Establish Ag Biotech Institute

The Union Council of Ministers of India (Union Cabinet) has reportedly approved the Agriculture Ministry's proposal to establish an Indian Institute of Agricultural Biotechnology at Ranchi at a cost of Rs 287.50 crore (US$51.6 million). The institute will include schools focusing on genomics, bioinformatics, genetic engineering, nano biotechnology, diagnostics, basic and social sciences, and commercialization. Among other matters, the institute will be charged with conducting research to develop crops for traits that will increase yield or increase tolerance to biotic and abiotic stresses, awarding post-graduate doctoral and post-doctoral degrees and developing curricula and course materials for India's agricultural universities. By 2020, India will apparently need 284 million tonnes of foodgrain, 160 million tonnes of vegetables, 97 million tonnes of fruit, and 69 million tonnes of oilseeds, amounts substantially higher than current demand. *See The Hindu Business Line*, August 24, 2012.

LITIGATION

D.C. Circuit Turns Aside Challenge to Federal Funding of Stem-Cell Research

The D.C. Circuit Court of Appeals has upheld National Institutes of Health (NIH) guidelines on federal funding of stem-cell research, finding that the agency properly interpreted the Dickey-Wicker amendment, attached as a rider to a number of federal appropriations bills, when it distinguished between research using but not creating stem cells from human embryos and allowed funding for the former but not the latter. ***Sherley v. Sebelius*, No. 11-5241 (D.C. Cir., decided August 24, 2012)**. Accordingly, the court affirmed the district court's grant of the federal government's motion for summary judgment.

The court decided that its previous ruling, which remanded the matter to the district court, constituted the law of the case, and thus it would not revisit two of the challengers' issues. Those issues were that (i) the NIH guidelines violate the Dickey-Wicker ban on federal funding of "research in which a human embryo or embryos are destroyed," and (ii) the guidelines violate the amendment's ban on "research in which a human embryo or embryos are . . . knowingly subjected to risk of injury or death" because federally funded embryonic stem cell (ESC) research increases the demand for more ESC lines, "which in turn incentivizes the destruction of more embryos to create those lines." The court's previous ruling applied *Chevron's* deferential standard to NIH's statutory interpretation in rejecting the challengers' request for preliminary injunction.

The court also determined that NIH was not required under the Administrative Procedure Act to specifically respond to comments asking the government to cease funding all stem-cell research. The guidelines had been developed under President Barack Obama's (D) executive order restoring funding to certain stem-cell research, and because the order's "entire thrust was aimed at *expanding* support of stem-cell research, it was not arbitrary and capricious for NIH to disregard comments that instead called for termination of all ESC research."

Two of the three judges on the D.C. Circuit panel wrote separately to concur in the result only. Both believed that the court should not have deferred to NIH under a *Chevron* analysis during the first appeal. Judge Karen LeCraft Henderson agreed that the court was nevertheless bound by the law of the case, but noted that if the court had not deferred to NIH's interpretation, it would have invalidated the guidelines in the first instance "as contrary to the Amendment's plain and unambiguous text." Judge Janet Rogers Brown opined that *de novo* review would not change the outcome of the prior decision that affirmed NIH's interpretation, but distanced herself from the majority's failure to impose "any clear limits on an agency's ability to ignore comments that contravene the executive's policy goals."

Third Circuit Refuses to Stay Effect of Anti-Competitive Ruling in Pay-for-Delay Case

The Third Circuit Court of Appeals has denied a request that it stay the mandate of its July 2012 ruling that "any payment from a patent holder to a generic patent challenger who agrees to delay entry into the market [must be treated by a factfinder] as *prima facie* evidence of an unreasonable restraint of trade." *In re K-Dur Antitrust Litig.*, Nos. 10-2077, -2078, -2079, 04571 (3d Cir., order entered August 14, 2012). Additional details about the ruling appear in Issue 39 of this *Bulletin*. The order was "without prejudice to the applicant's right to file a timely petition for writ of certiorari" to the U.S. Supreme Court.

Federal Circuit Addresses Personal Jurisdiction in Patent Infringement Litigation

Finding that the U.S. Supreme Court "has yet to reach a consensus on the proper articulation of the stream-of-commerce theory" of personal jurisdiction to assess whether a court has jurisdiction over a non-resident defendant in a patent infringement suit, the Federal Circuit Court of Appeals has applied its own theory, which assesses the pleadings and evidence under "any articulation of the stream-of-commerce theory," and has determined that a district court in Wyoming properly dismissed two patent infringement lawsuits for lack of jurisdiction. ***AFTG-TG, LLC v. Nuvoton Tech. Corp.*, Nos. 2011-1306 and -1307 (Fed. Cir., decided August 24, 2012)**. In this case, the defendants either sold their products to various companies that in turn sold them to consumers in Wyoming or made "drop shipments" to Wyoming addresses at the instruction of third-party resellers that were also not Wyoming residents. The district court concluded, and the Federal Circuit agreed, that the complaints failed to alleged sufficient facts to demonstrate minimum contacts with Wyoming.

Chief Judge Randall Rader concurred in the result but wrote separately to contend that Justice Stephen Breyer's holding, the narrowest of the plurality opinions in *McIntyre Machinery, Ltd. v. Nicastro*, 131 S. Ct. 2780 (2011), provides a more solid approach than a simple recitation of the stream-of-commerce concept. That approach requires "something more" of a defendant than simply placing a product into the stream of commerce and acknowledges the defendant's intent and awareness. Judge Rader contended that the majority's reliance on a 1994 Federal Circuit ruling "is now shaky precedent to the extent that it runs counter to the *McIntyre* decision."

NEWS BYTES

The U.S. Patent and Trademark Office (USPTO) **schedules** a September 6, 2012, roundtable "to obtain public input from organizations and individuals on issues relating to the USPTO's proposed implementation of the first-inventor-to-file provisions of the [America Invents Act]."

The Food and Drug Administration (FDA) **advises** applicants no longer seeking approval of their pending original abbreviated new drug applications (ANDAs) "to withdraw them as soon as possible to avoid paying a fee." The one-time fee, authorized under the Generic Drug User Fee Amendments of 2012, "will apply to any original ANDA that is pending (neither withdrawn nor tentatively approved) at FDA on October 1, 2012." The fee could amount to $25,000 per application depending on the number of ANDAs pending and not withdrawn by that date.

The Food and Drug Administration (FDA) **requests** public comments by October 26, 2012, about draft guidance for industry on self-identification of generic drug facilities, sites and organizations. The guidance aims to assist

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industry as it prepares to meet identification information requirements under the Generic Drug User Fee Amendments of 2012 and "explains who is required to self-identify, what information must be requested, how the information should be submitted to FDA, and what the penalty is for failure to self-identify."

The Food and Drug Administration (FDA) also **requests** public comments by October 26, 2012, about draft guidance for industry on generic drug user fee amendments of 2012. "This guidance is intended to provide answers to common questions from the generic drug industry and other interested parties involved in the development and/or testing of generic drug products regarding the requirements and commitments of the [Generic Drug User Fee Amendments of 2012]." According to FDA, new user fees will be determined after generic drug facilities, sites and organizations complete the self-identification process.

The Food and Drug Administration (FDA) **schedules** a September 21, 2012, public meeting "to discuss implementation of the Generic Drug User Fee Amendments of 2012" (GDUFA). While comments should be submitted before the meeting, the deadline for submission is October 12. Those wishing to attend and/or present at the meeting must notify FDA by September 14. The public will have the opportunity to discuss views on the guidance and other materials FDA has issued pertaining to its implementation of the GDUFA.

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