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LIFE SCIENCES & BIOTECHNOLOGY LEGAL BULLETIN

SCIENCE • TECHNOLOGY
ENGINEERING • ENERGY
PHARMACEUTICAL

CONTENTS

IP NEWS

USPTO Adopts Final Rule on Micro Entity Status Under AIA Reduced Patent Fee Provisions

The U.S. Patent and Trademark Office (USPTO) has adopted a **final rule** that implements the micro entity provision of the Leahy-Smith America Invents Act (AIA) by revising "the rules of practice to set out procedures pertaining to claiming micro entity status, paying patent fees as a micro entity, notification of loss of micro entity status, and correction of payments of patent fees paid erroneously in the micro entity amount." Effective March 19, 2013, the rule applies to patent applicants that qualify as small entities with certain restrictions on gross income and numbers of previously filed patents. The reduced fees, which will be addressed in another rulemaking, will be 75 percent less than those required of other patent applicants. *See Federal Register*, December 19, 2012.

INVESTOR NEWS

Ultragenyx Raises $75 Million in Crossover Financing to Advance Rare Disease Therapies

California-based rare disease drug developer Ultragenyx Pharmaceutical Inc. has reportedly raised $75 million from existing and crossover investors in a Series B financing round. According to news sources, Adage Capital Partners, L.P. led the round, and was joined by mutual funds and separate accounts advised by T. Rowe Price Associates, Jennison Associates (on behalf of clients) and other unnamed public market investors. Existing investors TPG Biotech, Fidelity Biosciences, HealthCap, and Pappas Ventures also joined in the expansion round.

"Ultragenyx plans to use the proceeds from the financing primarily to advance development of the company's lead clinical-stage programs, UX001 and UX003, and other undisclosed programs," the company said. "UX001 is a potential substrate replacement therapy for hereditary inclusion body myopathy currently being investigated in a fully enrolled, randomized

placebo-controlled Phase 2 clinical study with results anticipated in 2013. UX003 is a recombinant enzyme replacement therapy intended for the treatment of mucopolysaccharidosis type 7 (MPS 7), which will enter a Phase 1/2 clinical study in MPS 7 patients in 2013."

Ultragenyx Founder and CEO Emil Kakkis said, "We deeply appreciate the support of all our investors, new and existing, and their confidence in our ability to find and efficiently develop compelling new treatments for devastating rare genetic disorders. This financing transaction is critical to expanding our efforts to deliver profound novel therapies that benefit even more rare disease patients." *See Ultragenyx Pharmaceutical Inc. Press Release*, December 20, 2012.

$51-Million Series E Financing to Support Further Clinical Study of Anti-Clotting Therapeutic

New Jersey-based Regado Biosciences, Inc. has reportedly raised $51 million in a Series E financing round led by new investor RusnanoMedinvest, a subsidiary of a state-run Russian investment firm. The financing will be used to support Regado's Phase 3 clinical study of REG1®, an anticoagulant for use in percutaneous coronary intervention (PCI) among acute coronary syndrome patients. According to a company news release, "Reg1's Phase 2b results show trends which may indicate significant pharmacoeconomic benefits, including improved administration convenience, faster onset of action, instantaneous reversal, immediate sheath pull at the end of the PCI procedure, faster patient ambulation, reduced need for closure devices, improved facility and staff efficiency, and better overall outcomes." *See Regado Biosciences, Inc. Press Release*, December 17, 2012.

Molecular Diagnostics Company Raises $28 Million in Series D Round

Crescendo Bioscience® has reportedly secured $28 million in a Series D financing round and intends to use the funds to accelerate commercialization of its Vectra DA®, "a novel test which assesses disease activity in rheumatoid arthritis patients." The San Francisco-based molecular diagnostics company has apparently increased its customer base to some 500 rheumatologists and its test volume to include samples from more than 30,000 patients. According to President and CEO William Hagstrom, "With this new Series D financing and the addition of our new investment partners, Skyline Ventures and Safeguard Scientifics, Inc., we believe that we can build on this progress and generate further momentum in our commercialization and clinical development programs." *See Crescendo Bioscience® News Release*, January 3, 2013.

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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Nuron Secures $80 Million in Significant Private Investment Deal

Nuron Biotech, Inc., which develops biologics and vaccines for the prevention and treatment of neurodegenerative and infectious diseases, has reportedly announced the closing of an $80-million financing round provided by new investor HealthCare Royalty Partners II, LP (HC Royalty).

According to news sources, the financing consists of a $30-million equity investment by HC Royalty and a $50-million "Synthetic Royalty® agreement" that is tied to future sales of company products, including the vaccine HibTITER® and NU100, a multiple sclerosis treatment. The Pennsylvania-based Nuron plans to use proceeds from the deal to support the commercialization and expansion of Meningitec™, an established commercial vaccine for the prevention of invasive disease caused by *Neisseria meningitidis* serogroup C.

"The successful closing of this transaction provides us the capital needed to execute our Meningitec commercial plan and reach key milestones in advancing our pipeline and in providing new treatment options for patients around the world," said Shankar Musunuri, Nuron Biotech founder and CEO. *See Nuron Biotech, Inc. News Release,* December 20, 2012.

Solstice Biologics Raises Funds for Technology to Enhance RNA Mobility

According to news sources, California-based biotechnology company Solstice Biologics LLC, which focuses on solving the problem of targeting and delivery of nucleic acid therapeutics, has raised $18 million in venture capital funding. The Series A financing round was led by venBio and joined by Aeris Capital AG. The company has also reportedly acquired an exclusive license to University of California, San Diego intellectual property covering technology that enables RNA molecules to cross membranes of multiple cell types, a challenge that has been an obstacle to the delivery of RNA interference (RNAi) and microRNA's therapeutic potential. "Past attempts to solve the RNAi problem have involved large molecules that proved incapable of working in different cell types," said Solstice Biologics Executive Chair and venBio Managing Director Corey Goodman. "Solstice is developing proprietary technology that enables short double-stranded RNAi and microRNA molecules to cross cell membranes." *See StreetInsider.com,* January 4, 2013.

Avaxia Raises $6.4 Million in Series B Financing for IBD Treatment

Lexington, Massachusetts-based Avaxia Biologics, Inc. has raised $6.4 million from a Series B financing round to fund clinical trials for a new drug candidate to treat ulcerative colitis and Crohn's disease, two major inflammatory bowel diseases (IBD) affecting more than 2.5 million people, according to the company.

The new funding will apparently be used to finance a "first-in-human Phase 1b clinical trial of the company's new oral anti-TNF antibody, AVX-470®, for the treatment of ulcerative colitis." Evidently, TNF, tumor necrosis factor, helps regulate immune cells and is often responsible for systemic inflammation associated with several diseases, including IBD. Designed to act locally in the gastrointestinal tract to suppress inflammation, AVX-470® presents a lower risk of immunosuppressive side effects in tandem with the efficacy of existing anti-TNF therapeutics. "AVX-470 is unique in that it is delivered directly to the site of inflammation in the gut," said Avaxia CEO Barbara Fox. "This is the first use of an orally-delivered, locally-acting, gut-targeted anti-body for this indication. We think this has the potential to be a first-line therapy used for the treatment of IBD."

The round was led by existing investor Cherrystone Angels and new investor Golden Seeds Angel Network. Also participating were existing investors Beacon Angels, Boston Harbor Angels, Launchpad Venture Group, Mass Medical Angels, and North Country Angels; new investors the Beta Fund, Granite State Angels, the Keiretsu Forum, and Maine Angels; and individual investors. *See Avaxia Biologics Press Release,* December 18, 2012.

Allakos Completes $32-Million Financing Round to Develop Novel Antibodies

Allakos Inc., which develops antibody-based drugs used to treat inflammatory diseases, has reportedly secured a $32-million Series A preferred stock financing. The round was led by Novo Ventures with participation from Alta Partners, RiverVest Venture Partners and the Roche Venture Fund, according to a company news release.

Founder and CEO Christopher Bebbington said, "We very much appreciate the confidence placed in our company by our Series A investors. Our therapeutic antibodies are designed to work through novel mechanisms of action, to have significant safety and efficacy advantages and to have potential in multiple, high-value markets, including large therapeutic areas as well as orphan indications. With these proceeds, we are now well positioned to advance our lead program towards meaningful near-term milestones." The California-based biotechnology company has generated a "preclinical pipeline of novel antibodies targeting cell types implicated in allergic and inflammatory responses, which it intends to advance to clinical proof-of-concept." *See Allakos News Release,* December 17, 2012.

LEGISLATIVE AND REGULATORY DEVELOPMENTS

Obama Signs Patent Law Treaties Implementation Act of 2012

President Barack Obama (D) has signed into law legislation (S. 3486) that implements two patent law treaties: The Geneva Act of The Hague Agreement

Concerning the International Registration of Industrial Designs adopted at Geneva on July 2, 1999, and The Patent Law Treaty. Effective in December 2013, the new law, in part, will allow U.S. citizens and residents to participate in an existing international filing system for industrial design patent applications. Previously, U.S. inventors would be required to file design applications in each individual country in which protection was sought. When fully implemented, the law will allow a single application in one language with one set of filing fees. More than 75 countries participate in the system.

Amendments to Leahy-Smith America Invents Act Awaiting Presidential Action

Among the bills pending before President Barack Obama (D) at the close of the 112th Congress is **H.R. 6621** which would make certain technical corrections to the Leahy-Smith America Invents Act and some improvements pertaining to inter partes review, filing deadlines, the use of patent law fees, and jurisdiction over interference proceedings. If the president does not sign the bill within 10 days of January 3, 2013, excluding Sundays, it will be deemed vetoed.

EU Parliament Approves Unitary Patent Rules

The European Union (EU) Parliament has approved the "**EU patent package**," which establishes a unified patent system in three languages—English, French or German—and a unified patent court. The changes are expected to reduce the cost of an EU patent by 80 percent and will cut costs for small firms. According to the European Commission, when fully implemented, the new system will require applicants to pay approximately €4,725 compared to the average €36,000 needed to acquire protection in each member state today. While patents will be available in each of the three languages and can be filed in any of them, applications made in another language will require an accompanying translation into one of the specified languages. The agreement to create a unified patent court will enter into force January 1, 2014, or after ratification by 13 states, as long as Britain, France and Germany are among them. Spain and Italy have opted out of the patent package for now. *See EU Parliament Press Release*, December 11, 2012.

Researchers Question Accuracy of Generic Drug Safety Labeling

According to Regenstrief Institute researchers, despite U.S. Food and Drug Administration (FDA) requirements that generic medications bear warnings identical to those on brand-name products, more than two-thirds of generic drugs carry safety-warning labels that differ from their brand-name equivalent. Jon Duke, Jeff Friedlin & Xiaochun Li, "Consistency in the safety labeling of bioequivalent medications," *Pharmacoepidemiology and Drug Safety*, December 2012. The labeling discrepancies were relatively minor for most of the generics, but 9 percent showed significant variation. Among the errors

were out-of-date information, missing adverse reactions, incomplete data, and, for one product, information from a completely different drug.

The Indiana-based investigators reviewed 9,105 product labels for more than 1,500 drugs available on an online repository of labeling information maintained by FDA and the National Library of Medicine. Investigator Jon Duke was quoted as saying, "Until this problem is resolved, physicians and patients should rely on brand drug labeling only, even when the patient is getting a generic version of a drug."

Duke also suggested that a centralized drug side-effect listing, maintained independently of individual labels, could be referenced on drug labels, "rather than attempting to maintain all the information within a single document. Clinicians could refer to this resource for the most up-to-date safety information regardless of generic manufacturer." The research was apparently prompted by a U.S. Supreme Court ruling allowing generic drug makers to escape inadequate warning claim liability because "the warning labels of a brand-name drug and its generic copy must always be the same."

LITIGATION

SCOTUS Refuses to Hear Challenge to Government Stem Cell Research Funding

The U.S. Supreme Court (SCOTUS) has rejected a request that it review a D.C. Circuit Court of Appeals ruling dismissing a challenge to government funding of embryonic stem cell research. ***Sherley v. Sebelius*, No. 12-454 (U.S., certioriari denied January 7, 2013)**. Additional details about the lower court's ruling appear in **Issue 41** of this *Bulletin*. The researchers who sought to stop the funding had asked the Court to find error in the D.C. Circuit Court's determination that the National Institutes of Health was not required to specifically respond to comments asking the government to cease funding all stem-cell research and that a preliminary-injunction ruling is binding law of the case.

Validity of AIA's Retroactive Elimination of *Qui Tam* Provision Upheld in False Marking Suit

The Federal Circuit Court of Appeals has determined that Congress's retroactive elimination of a provision allowing private parties to prosecute false-marking claims as *qui tam* relators did not violate the Due Process Clause of the U.S. Constitution. ***Brooks v. Dunlop Mfg. Inc.*, No. 2012-1164 (Fed. Cir., decided December 13, 2012)**.

Recognizing a "surge of vexatious litigation [posing] a risk of grossly disproportionate penalties for false marking," Congress included in the Leahy-Smith America Invents Act (AIA) a provision allowing only the United States or a person suffering competitive injury to bring a cause of action against

someone who affixes to a product a mark that falsely asserts that the item is patented. Previously, the law allowed any person to sue for the statutory penalty. The new AIA provision is expressly applicable "to all cases, without exception, that are pending on, or commenced on or after, the date of the enactment of this Act."

The false-marking plaintiff here brought his lawsuit in September 2010 against a company that allegedly marked a guitar string winder with the number of a patent that was expired and invalidated. The case was stayed pending resolution of a case raising an issue similar to one raised by the defendant, and, in the interim, Congress enacted the AIA. The defendant thereafter sought to dismiss the case, arguing that the plaintiff no longer had standing "because he can no longer recover a statutory penalty and has not alleged any right to damages for competitive injury." The plaintiff raised Takings Clause and Due Process challenges to the new law, both of which the district court rejected.

On appeal, the only issue remaining was whether the Due Process Clause prevents Congress from applying the AIA's amendments to pending *qui tam* actions. The plaintiff contended that the retroactive elimination of his right to sue was arbitrary and capricious and constituted an unlawful repudiation of a binding contract between him and the United States. The court disagreed finding that (i) Congress had legitimate concerns with respect to the cost and constitutionality of pending *qui tam* actions, and (ii) nothing in the *qui tam* provision, as it existed before amendment, created private contractual or vested rights.

Federal Court Denies HHS Motion to Seal Documents in Medical-Device Whistleblower Dispute

A federal court in the District of Columbia has denied the government's request to seal an exhibit in Freedom of Information Act litigation over records in a dispute involving claims by current and former employees of the Department of Health and Human Services (HHS) that the agency spied on them because they were suspected of leaking confidential material about the agency's medical-device review process. *Nat'l Whistleblower Ctr. v. HHS*, No. 10-2120 (JEB) (U.S. Dist. Ct., D.D.C., decided January 3, 2013). Additional information about the spying allegations appears in **Issue 39** of this *Bulletin*.

According to the court, HHS requested "that the exhibit be sealed so the public cannot access confidential commercial information concerning unapproved and uncleared medical devices." The court determined that the agency failed to "overcome the strong presumption in favor of public access to judicial proceedings." In this regard, the court agreed with the plaintiffs that (i) "there is a significant public interest in HHS's allegedly improper approval of medical devices and surveillance of its employees," (ii) the public previously had access to the material for a substantial period of time, and (iii) HHS failed to demonstrate "a property or privacy interest sufficient to override the presumption."

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NEWS BYTES

The U.S. Patent and Trademark Office (USPTO) **schedules** an Additive Manufacturing Partnership Meeting on January 23, 2013, at its Alexandria, Virginia, campus. Additive manufacturing, or "3D printing," refers to a group of new technologies that create objects from 3D computer models, usually by joining thin materials, layer upon layer. Among the many fields in which it is used are the dental and medical industries. The meeting will enable USPTO to expand its relationship with individual users as well as serve as a forum for users to share ideas, experiences and insights into this emerging field.

The U.S. Patent and Trademark Office (USPTO) **announces** a Medical Device Technology Partnership Meeting on January 29, 2013, at its Alexandria, Virginia, campus. Intended to bring medical device and biotechnology stakeholders together to share ideas, experiences and insights on best practices and provide a forum for how USPTO can improve and expand its relationship with medical device technology stakeholders, the meeting is sponsored by Technology Centers 3700 and 1600. Also on the agenda will be discussions about the Leahy-Smith America Invents Act, the Cooperative Patent Classification system and section 101 subject-matter eligibility.

The U.S. Patent and Trademark Office (USPTO) and the European Patent Office (EPO) **launch** the Cooperative Patent Classification (CPC) system, a global classification system for patent documents. According to USPTO, "CPC is the product of a joint partnership between the USPTO and the EPO to develop a common, internationally compatible classification system for technical documents used in the patent granting process that incorporates the best classification practices from both offices." USPTO and more than 45 patent offices—a user community including more than 20,000 patent examiners—will use the system and, by sharing the same classifications, will help to establish the CPC as an international standard. USPTO and EPO have worked jointly for two years to develop the system, which includes approximately 250,000 classification symbols based on the International Patent Classification system. Examiners and patent users around the world will be able to access the same classified patent document collections when conducting their searches.

The Food and Drug Administration (FDA) **announces** a public workshop titled "Accessible Standardized Medical Device Labeling," to be held April 29-30, 2013, in Silver Spring, Maryland. The workshop aims "to discuss the growing need for medical device labeling to be delivered in a clear, concise, and readily accessible format so that patients, caregivers, and healthcare providers may access and utilize device labeling as efficiently and effectively as possible." The workshop will also "engage stakeholders in active discussion with FDA and . . . encourage public comments regarding standard content and format for medical device labeling and the use of a repository containing medical device labeling." It will include public-comment and topic-focused sessions.

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The Food and Drug Administration (FDA) issues draft **guidance** titled "Enrichment Strategies for Clinical Trials to Support Approval of Human Drugs and Biological Products." The guidance will provide recommendations to industry "on enrichment strategies that can be used in clinical trials intended to support effectiveness and safety claims in new drug applications (NDAs) and biologics license applications (BLAs)." According to FDA, "the guidance defines and discusses three enrichment strategies: Decreasing heterogeneity, predictive enrichment, and prognostic enrichment. The guidance also discusses general clinical trial design considerations, provides examples of potential clinical trial designs, and discusses regulatory considerations when using enrichment strategies in clinical trials." Comments are requested by February 15, 2013.

UPCOMING CONFERENCES AND SEMINARS

Shook, Hardy & Bacon Life Sciences & Biotechnology Partner **Rob McCully** will serve as a panel moderator during AdvaMed's "2013 Latin America Medical Device Industry Compliance Conference," scheduled for January 17-18, 2013, in Miami, Florida. SHB is a co-sponsor of the **conference**, described as "the most comprehensive medical technology meeting for device industry executives, specialty device industry lawyers, compliance professionals, international policy-makers, and other industry stakeholders focused on Latin American compliance issues." McCully's panel will address "Managing Third Party Distributors in Key Latin American Markets."

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