IN brief

Merck ditches biogeneric

Merck of Whitehouse Station, New Jersey, has halted development of its lead biogeneric product, MK-2578, a PEGylated erythropoietin-stimulating agent for treating anemia. The decision, announced on May 11, followed a request from regulatory authorities for a cardiovascular outcomes assessment, an expensive and time-consuming process, says Peter Kim, president of Merck Research Laboratories. MK-2578, in phase 2 trials, was Merck's most advanced biosimilar—similar to Amgen's blockbuster Aranesp (darbepoetin alfa). "Other biosimilars counterparts will have to face [similarly] strict regulatory hurdles," says Swetha Shantikumar, research associate at Frost & Sullivan, Chennai, India. The difficulties may dissuade small and medium-sized companies from developing biosimilars, but large companies remain undeterred. Merck itself has two other biogeneric candidates, MK4214 a G-CSF (granulocyte colony stimulating factor) and MK6302 (a recombinant pegylated G-CSF), in development. Moreover, the news boosted share values for Affymax in Palo Alto, California, which is developing a competitor product to treat anemia. And Samsung, of Seoul, South Korea subsequently announced plans to invest about $1.72 billion in biosimilars, hoping to take advantage of biologics patent expiries expected by 2016. Merck's decision does not change the dynamics of the biosimilars market, says Shantikumar. "It is a definite reminder that it is strikingly different from the traditional generics market." *Emma Dorey*

Investors fight Charles River/WuXi merger

In a vote of confidence for China, leading outsourcing company, Charles River Laboratories (CRL) of Wilmington, Massachusetts, plans to spend $1.6 billion to buy Chinese contract research organization WuXi PharmTech of Shanghai. The transaction will create the first global contract research company to offer a fully-integrated drug development service, from molecule creation to early clinical studies. But activist hedge fund Jana Partners, Charles River's largest shareholder, is arguing that the price paid for WuXi is unjustified and intends to stop the merger. Should the deal go ahead, "The new company will be able to provide lower-cost services, though price is probably the least important metric—more significant are quality, know-how and full-service capabilities," says Ross Muken of Deutsche Bank Securities in New York. "There have been quality issues in China in the past, but with support of the Chinese government these have improved." Companies engaging these integrated services will also gain better access to the booming Chinese market. "Carrying out R&D in China will speed up Chinese drug launches and allow companies to optimize therapeutics for Asian people," says Johnny Huang of Frost & Sullivan. Some analysts have suggested that WuXi's animal testing facility will attract companies that no longer want to face Western animal rights campaigners, but Muken does not believe this to be a deciding factor. *Suzanne Elvidge*

vary widely. A recent study from the Catholic University of Leuven in Belgium analyzed European and American patent families pertaining to the diagnosis of 22 different genetic disorders. Their findings revealed that of the 145 gene patents examined, 35 contained a 'blocking claim' that is impossible to circumvent with an alternative diagnostic strategy (*Nat. Biotechnol.* **27**, 903, 2009). "If you read somebody's DNA sequence and gave them information about their sequence related to a disease—that is, if you did whole-genome sequencing—you would be infringing at least one patent in each case for those 15 [medical] conditions," says Robert Cook-Deegan, director of the Duke Institute for Genome Sciences and Policy in Durham, North Carolina.

The recent *ACLU v. Myriad* decision, which rejected Myriad Genetics' claims on isolated sequences for breast cancer risk factors *BRCA1* and *BRCA2* as well as methods for identifying mutations in those genes, has garnered much press in this regard. "It challenges one of the fundamental premises of biotechnology patents, which is that you can just go and patent genes," says Daniel Vorhaus, an attorney at Robinson, Bradshaw & Hinson and editor of the *Genomics Law Report* website. Although the decision stunned many in the patent law world, its impact remains limited to Myriad's patents, and it will almost certainly be appealed, and possibly overturned.

The true 'main event' in diagnostic IP law, some observers believe, is 'association patents'. "Some of the disease-association patents are much more broadly written and problematic for some of these next-generation [sequencing] applications," says Vorhaus. The Supreme Court has yet to rule on so-called association patents, which link a biological state with a medical condition. The only exception is a nonbinding dissent filed in 2006 by Justice Stephen Breyer in *LabCorp v. Metabolite*, where he argued against the validity of a claim for an assay of homocysteine levels as a means for gauging vitamin B deficiency on the grounds that this association was an unpatentable natural phenomenon.

The Supreme Court refused to hear that case, but will soon issue a highly anticipated decision on an equally relevant case, *In re Bilski*. Although this case relates to patentability of business methods, it has clear relevance for clinical diagnostics; the Federal Circuit decision established a test for such patents requiring that any patentable method must employ a "machine or transformation," and although the meaning of this phrase remains ambiguous, it could theoretically prohibit patents based on mere identification or comparison of naturally occurring entities, such as DNA sequences (*Nat. Biotechnol.* **27**, 586–587, 2009).

The *Bilski* decision could also constrain the controversial 5,612,179 patent held by Genetic Technologies in Fitzroy, Australia. This patent, recently upheld by the US Patent and Trademark Office, covers any amplification-based sequencing of intronic DNA sequences, and cases of perceived infringement have been vigorously litigated by the company—most recently against Beckman-Coulter and eight other defendants this past January. "These are method claims and they are quite broad," says Cook-Deegan. "But they would not necessarily be infringed by all forms of full-genome sequencing; single-molecule sequencing almost certainly would not infringe because it entails no amplification step."

The current system is not popular with the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) for the US Department of Health and Human Services. Thee SACGHS has issued a draft report in February (*Nat. Biotechnol.* **28**, 381, 2010) that explicitly defends gene patents, but calls for exemptions against infringement liability for patient care purposes or for research. These recommendations, which have been condemned by the Biotechnology Industry Organization (Washington, DC) as having the potential to "do more harm than good," are unlikely to change patent policy. But they may stir the industry to take the initiative for reform.

Given that most grievances surrounding gene patents are actually condemnations of business practices related to licensing and litigation, reforms may arise from companies hoping to avoid messy, unpopular lawsuits. "I don't think that any company wants to be in the position of losing the PR battle the way Myriad has been for years," says Cook-Deegan. Patent pools or clearinghouses represent one opportunity for compromise, as in a plan recently put forward by Larry Horne, CEO of MPEG-LA, for a 'supermarket' for the simple, nonexclusive licensing of patents related to specific disorders. This could ensure a modicum of profit for patent-holders while expanding IP access, but constructing such a system will not be easy.

An important consideration, however, is that much of the unique power of whole-genome sequencing lies in sophisticated data analysis, and that this is likely to spur previously unforeseen business models and categories of IP in the diagnostic sector. "In the future, when you can do a whole genome within hours in a doctor's office, our service of shipping things around the world won't make sense—we'll have to become a software company," says Knome's Kiirikki. "And because it's digital it's going to grow exponentially and be exciting and it will have speed bumps, but there will be all kinds of things we can't imagine now."

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