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Patenting the Gene: The Aftermath

Newcomers Undercut Price of BRCA Test; Myriad Lawsuits Claim Patent Infringement

By Matthew Bin Han Ong

Myriad Genetics, the biotechnology company that in a recent Supreme Court ruling lost exclusive rights to isolated human genes, has filed patent infringement lawsuits against companies that launched competing versions of BRCA tests.

After the high court's ruling June 13, several companies announced plans to accept and analyze samples of BRCA1 and BRCA2, isolated genes associated with breast and ovarian cancer.

Ambry Genetics of Aliso Viejo, Calif., launched BRCA tests at $2,200, undercutting Myriad's $4,040 integrated BRAC*Analysis* test by nearly half. Gene By Gene Ltd. of Houston offered its version of the test at an even lower price: $995.

But by being the first to hit the market, these companies came under Myriad's fire.

Myriad adopted a classic strategy that originates with innovator drug companies: When you lose the principal claim to exclusivity, such as a composition of matter patent, claim infringement of provisions that cover methods of use—the special know-how associated with using your products.

Frequently, pharmaceutical companies use this strategy as a delay tactic which allows them to hang on to monopoly profits for the duration of the legal battle.

The Myriad lawsuits, filed July 9 and 10 in the District Court for the District of Utah, Central Division, are posted on The Cancer Letter website.

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In Brief

Van Etten To Take Over As Director Of UC Irvine Chao Cancer Center

RICHARD VAN ETTEN was appointed director of the **Chao Family Comprehensive Cancer Center at UC Irvine**. He will begin Oct. 1.

Van Etten is the former chief of the Division of Hematology/Oncology at Tufts Medical Center and director of Tufts Cancer Center.

His research focuses on chronic myeloid leukemia and other hematological malignancies. At Tufts, he also directed a research laboratory at the Molecular Oncology Research Institute.

Van Etten will serve as the principal investigator of the Chao cancer center's NCI support grant and will integrate the cancer center's research

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Myriad Claims Infringement Of Methods of Use

(Continued from page 1)

"We think that they are infringing on our intellectual property and our patents, and we'll demonstrate that in court," Myriad spokesman Ron Rogers said to The Cancer Letter. "The vast majority of the patent claims remain valid and enforceable.

"The patent owners are going to demonstrate in these lawsuits that the testing process employed by both Ambry and Gene By Gene infringe ten patents covering synthetic primers, probes and arrays, as well as methods of testing related to BRCA," Rogers said.

The BRCA genes were discovered by Myriad, which said it invested more than $500 million in researching the genes and commercializing testing products (The Cancer Letter, April 19).

Myriad isn't alone in this phase of the legal battle. A group of co-owners of the BRCA patents joined the company's lawsuits.

The other plaintiffs are: the University of Utah; the University of Pennsylvania; the Hospital for Sick Children; and Endorecherche, a Canadian medical research corporation.

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A Classic Patent Dispute

"I think they are basically trying to stave off competition by making Ambry an example, and forcing Ambry to spend a lot of money and hire a bunch of lawyers to accompany their entry into the market," said Robert Cook-Deegan, director of the Center for Genome Ethics, Law and Policy at the Duke University Institute for Genome Sciences and Policy.

Cook-Deegan's guest editorials on the oral arguments in the Myriad Supreme Court Case and the ruling appeared in the April 19 and June 14 issues of The Cancer Letter.

Only two competitors have been sued so far. Others that have announced plans to launch BRCA tests—GeneDx, Pathway Genomics, Quest Diagnostics—appear to be holding back, presumably until the lawsuits blow over.

"I think it's probably, as much as anything, a delaying tactic, and it worked, because Myriad's stocks are back up," Cook-Deegan said.

Myriad's stock traded above $34 per share at the time of the Supreme Court ruling, bottoming out at about $26 June 20, a week after the ruling, and has been rising since. At this writing, it stands at about $31 per share.

Myriad's sales of BRAC*Analysis*, a product that detects mutations in the BRCA genes to determine increased risks for breast and ovarian cancer, added up to $405.5 million in 2012.

Prior to the Supreme Court case, the BRCA patent owners had 24 patents that altogether contained 525 claims, Rogers said.

The high court addressed only nine of those claims, and ruled that five of them were ineligible for patent protection.

"So that left BRCA patent owners with the same number of patents (24), and instead of having 520 patent claims, the BRCA owners had 515 patent claims," Rogers said. "The court also, importantly, ruled that cDNA was patent-eligible.

"On page 17 of the court's opinion, they underscored the importance and applicability of methods of use patents," Rogers said. "And those types of claims weren't at issue in the Supreme Court case."

The suit against Ambry Genetics divides the allegations into three categories: Ambry's preparation of synthetic DNA (cDNA) samples for BRCA1 and BRCA2 sequencing and analysis, sequencing, and large rearrangement analysis of the isolated genes.

"We don't understand it at all," Ambry Senior Vice President of Business Development Ardy Arianpour said to The Cancer Letter. "We will vigorously defend

our position, and we are in full support of the Supreme Court's decision.

"Ambry Genetics does not now, and has never analyzed cDNAs, in any of its diagnostic offerings, including BRCA1 and BRCA2."

Also, the plaintiffs filed a motion for a preliminary injunction to preclude Ambry from "any further sales or offers to sell genetic tests including a BRCA1 or BRCA2 panel pending judgment on the merits."

Source: www.ambrygen.com

Though sued by Myriad, Ambry continues to advertise its BRCA tests.

Legal problems notwithstanding, Ambry continues to advertise its BRCA tests. The company's website features a photo of the Supreme Court with a caption: "Your Genes Are Still Free."

A court in Utah is scheduled to decide on Myriad's motions for an injunction and a preliminary judgment.

The crucial decision will be whether the injunction is granted, and that may depend on the judge's assessment of the likely outcome, whether it is likely that Myriad will prevail. The suit also seeks up to triple the damages for any profits lost if Ambry's alleged infringement is found to be willful.

The case has some unusual characteristics, Cook-Deegan said.

"One is that this follows immediately on two cases about diagnostics that have been unanimously decided against patent-holders by the Supreme Court," Cook-Deegan said. "The other is that many vulnerabilities in these particular patents have never been addressed by either administrative or legal review. Now, perhaps they will be addressed in litigation or negotiation for settlements.

"Myriad's BRCA2 claims are quite vulnerable, because patent documents suggest they were neither first to invent nor file on BRCA2; their claim on short fragments of BRCA1 sequence is extremely vulnerable; and their claims on PCR primers and methods may not have been enabled at the time they filed their patent applications," Cook-Deegan said.

"It could get more interesting if other labs decide to enter the market, and file for declaratory judgments on their home turf, so Myriad is not playing on its home field in Utah federal district court."

Myriad Isn't Suing Academic Labs

On June 15, Emory Genetics Laboratory, a nonprofit academic research unit of Emory University, stood poised to launch BRCA1 and BRCA2 testing. But then the laboratory learned of the suits against Ambry and Gene By Gene.

Emory planned to charge $2,350 for comprehensive BRCA1 and BRCA2 tests. The lab also planned to offer sequencing and deletion/duplication tests, at $2,100 and $750, respectively.

"We had the website all set up and ready to go, but we have put a hold on it now, pending the outcome of the new Ambry lawsuit," EGL Executive Director Madhuri Hegde said to The Cancer Letter. "Given the situation, we have to be careful—the last thing we want is Myriad suing us.

"Ultimately, I think Myriad will lose and this is just delay tactics—they just want to hold onto their advantage a little longer.

"The lawsuit essentially revolves around cDNA, and no clinical lab does cDNA testing, mainly using only genomic DNA.

"I think the labs planning to launch should actually launch quickly, take away the competitive advantage from Myriad, and test their ability to sue multiple labs in the face of the Supreme Court's decision," Hegde said.

"But we are wary and we want to watch this just a little bit."

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The University of Washington's Department of Laboratory Medicine wasn't thwarted by the lawsuits.

The department launched its BRCA1 and BRCA2 tests June 14, a day after the Supreme Court ruling, and continues to offer the test.

According to a statement, Myriad pledges to not "impede non-commercial, academic research that uses patented technology licensed or owned by us," and will not interfere with "laboratories conducting genetic testing on patients for the purpose of confirming a test result provided by Myriad."

Myriad spokesman Rogers declined to comment on whether the company plans to expand the litigation.

"Myriad isn't suing the University of Washington, firstly, because it would make them more unpopular," said Cook-Deegan. "The second reason is because they would be suing the university that is home to Mary-Claire King, the heroine of the BRCA1 story who most people wish had won the sequencing and cloning race."

It's not useful to speculate about possible outcomes of the suits against Ambry Genetics and Gene By Gene, Myriad spokesman Rogers said.

"These types of cases generally take months, if not years, to resolve themselves," Rogers said. "We'll let the court sort that out, but we are confident that we have a strong case."

The crucial decision will be whether the judge grants an injunction, Cook-Deegan said.

"Most of the claims the patent owners are asserting are for methods that involve amplification steps," Cook-Deegan said. "Their claims on those methods are based on very standard techniques.

"Their argument will be that by cloning and sequencing the BRCA genes, they 'invented' the methods of measuring those genes.

"Most of the primers used in polymerase chain reaction for BRCA gene sequencing lie outside the cDNA sequences.

"Those flanking sequences were not disclosed in the patents, and the claims are 'functional' claims.

"These claims may flunk on enablement and written description (Sec. 112 of Patent Act).

"They probably did not have such sequences in their possession at the time, since they did not get a product onto the market until 1996, after the patent applications were filed.

"Will this matter to a judge?" Cook-Deegan said. "We may see."

Myriad to Keep BRCA Data

Myriad's BRAC*Analysis* is covered by private health insurance plans, Medicare, and about 70 percent of all Medicaid plans, Rogers said. Ambry Genetics, also an approved Medicare provider, offers discounts and has insurance coverage for its BRCA tests.

Ambry plans to cap out-of-pocket health care expenditures based on income levels according to guidelines in the Affordable Care Act, Ambry spokesman Arianpour said.

Patients who have financial difficulties may receive a 25 percent discount, resulting in payments as low as $25 per month.

"We are in network with the majority of the national private insurance plans," Arianpour said.

BRAC*Analysis* made up more than 80 percent of revenue for Myriad last year. However, the value of Myriad's BRAC*Analysis* is measured not only in sales, but also in the databases on BRCA genes and mutations

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that the company has amassed.

"Myriad's laboratory processes, including variant classification and variant databases, are subject to regulatory oversight from either Clinical Laboratory Improvement Amendments or FDA," Rogers said.

"Consistent with these regulations, we are not allowed to distribute our variant databases, as they may only be used to interpret clinical test results for patients tested in our laboratories.

"Myriad will collaborate with laboratories performing non-commercial, academic research projects with IRB approval, by reviewing variants of uncertain significance identified in the study."

Several legal experts said to The Cancer Letter that Myriad has the latitude to place the data in public databases, as long as patients are de-identified. However, the company is under no obligation to do so.

Meanwhile, many scientists say they want access to these data.

Free the Data!, a consortium launched June 13 by policy makers, advocacy organizations, academic centers and industry, seeks to "fill the public information gap caused by the lack of available genetic information for the BRCA1 and BRCA2 genes."

The primary founders of this project include Genetic Alliance, University of California San Francisco, InVitae Corp., and patient advocates.

"There is much known about the human genome but little understanding on how variations in genes can lead to disease," UCSF Chief of Medical Genetics Robert Nussbaum said in a statement.

"We want to create an easy way for patients and physicians to share information with each other, providing the research community with a robust source of data and enabling the rapid improvement of knowledge of clinically relevant genetic mutations which will ultimately accelerate the race for more effective treatments and a cure."

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NCI News

R01 and P01 Grants Will No Longer Support Phase III Clinical Trials

NCI will no longer use R01 and P01 grants to support investigator-initiated phase III clinical trials.

The change, which was announced recently, affects Medical Interventions and Cancer Imaging Modalities.

"NCI has determined that it is no longer appropriate to support investigator-initiated phase III clinical trials for cancer-related medical interventions as well as phase III clinical trials for cancer imaging modalities," a notice on the website of the NIH Office of Extramural Research states. "In general, medical intervention phase III clinical trials require more time (from clinical trial protocol development to enrollment, follow-up, and final analysis) than allowed by a single 5-year funding cycle associated with R01 and P01 awards.

"Spanning a clinical trial over more than one R01 or P01 funding cycle is impractical because the successful renewal of these awards cannot be guaranteed. More appropriate mechanisms for phase III trials of medical interventions and cancer imaging modalities are/will be available through the NCI National Clinical Trials Network (NCTN, which succeeded the NCI Clinical Cooperative Groups Program), the Community Clinical Oncology Program (CCOP) or its eventual successor."

NCI officials said only 15 R01 and P01 grants were used to fund phase III trials, adding up to less than 5 percent of the total number of phase III trials funded by the institute.

Capitol Hill

House Committee Seeks Review Of Indirect Costs of NIH Grantees

The House Committee on Energy and Commerce asked the Government Accountability Office to review the magnitude of indirect costs assessed by NIH grantee institutions.

The request, dated June 24, is signed by Rep. Fred Upton (R-Mich.), committee chairman, and Rep. Tim Murphy (R-Penn.), chairman of the subcommittee on Oversight and Investigations.

The questions that the GAO was asked to address suggest that the committee is weighing an investigation of controls on the institutions' use of indirect costs.

The text of the letter follows:

Dear Mr. Dodaro,

Through its sponsorship of research by institutions

like the National Institutes of Health (NIH), the federal government plays an important role in contributing to American competitiveness and leadership in science. Federal grants are provided for both direct costs (those costs specifically identified with individual research projects) and indirect costs (those that are not directly attributable to a specific project or function, such as costs for administrative staff).

Funding institutions like NIH typically use the indirect cost rates negotiated by either HHS or, Office of Naval Research for which they reimburse indirect costs with grant recipients and they employ varying methods to oversee and validate indirect cost reimbursement.

There has been debate over what portion of indirect costs should be the responsibility of the government and what portion should be the responsibility of the research institution receiving a grant. Moreover, not all funding organizations use the same approach as the federal government.

For example, some nonprofit foundations who also support research exclude indirect costs from allowable reimbursable expenses. GAO's previous work on grants provided by the Department of Defense and the Department of Health and Human Services identified weaknesses in oversight processes that could make the government vulnerable to making improper payments or to waste or abuse.

Given the fiscally constrained environment, ensuring efficient and effective use of federal funding is vital. Thus, we are requesting that GAO review NIH's indirect costs and its processes for overseeing the validity of its indirect cost reimbursements to grant recipients.

Specifically, we would like GAO to address the following:

1. Compare NlH's policies and indirect cost reimbursement rates to other funding institutions, including nonprofit foundations.

2. Assess the dollar value and proportion of NIH's funding that goes to indirect costs and how this has changed over time.

3. Identify the controls NIH uses to validate indirect costs and determine to what extent the design of NIH's controls for validating indirect costs are sufficient to prevent and detect improper payments, waste or abuse.

4. Identify the specific formulas used by NIH for different rates for indirect costs between institutes and describe what subjective and objective measures are used as part of those formulas.

Crime

Entrepreneur Pleads Guilty To Selling Counterfeit Avastin

A Montana pharmaceutical entrepreneur pled guilty to importing and selling misbranded, unapproved, and counterfeit cancer drugs, including a counterfeit version of the cancer drug Avastin.

Paul Bottomley, a distributor who worked within an international network of companies, subsidiaries and suppliers with the goal of selling cheap, imported drugs to be administered by U.S. physicians, was sentenced July 12 to six months house arrest and five years of probation, in addition to a civil forfeiture of $4.45 million.

The companies were involved in shipment of counterfeit Avastin in 2011 and 2012. The drug was traced back to Turkey and was sold across Europe before being shipped to a distribution center in Tennessee.

The counterfeit Avastin contained none of the drug's active ingredient.

Bottomley's guilty plea follows an investigation begun in 2010 by the FDA Office of Criminal Investigations.

"The defendant's conduct in this case was motivated by greed," said Michael Cotter, U.S. attorney for the district of Montana. "Bottomley utilized the grey market and sold potentially dangerous unapproved and misbranded pharmaceuticals at discounted prices to American physicians all for a healthy profit."

The FDA office began to investigate Montana Healthcare Solutions—owned by Bottomley, and founded in 2008—as a source of supply for unapproved cancer drugs in 2010.

According to the Department of Justice documents, Bottomley sold Montana Healthcare Solutions to Canada Drugs, Ltd., in October 2010 for $5 million. Canada Drugs is an Internet pharmacy company based in Winnipeg.

Canada Drugs took over Bottomley's client list, company name and stockpiles on hand, while Bottomley stayed on as an advisor and salesman for Canada Drugs.

Documents from the U.S. Department of Justice state that Bottomley had no involvement in the importation or distribution of the original counterfeit

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Avastin shipment—but he had become aware of the questionable purity and misbranding of medicines distributed by Canada Drugs by January 2012.

In January 2012, FDA received information from the United Kingdom Medicines and Healthcare Products Regulatory Agency regarding a shipment of counterfeit Avastin originating in Turkey.

The MHRA had become aware of a British wholesaler that had shipped 41 packages of Avastin to Volunteer Distribution, a company located in Gainesboro, Tenn., according to Justice Department documents.

Volunteer Distribution was working under contract with a Canada Drugs subsidiary company to receive and ship medicines to American physicians. At the time, Montana Healthcare was selling 400 mg vials of Avastin for $1,995, down from the usual price of around $2,400.

A preliminary investigation by the MHRA found that the Avastin in question, at minimum, included counterfeit labeling—such as not displaying the National Drug Code numbers, and containing non-English use and dosage instructions.

A lab analysis found that the vials contained no active bevacizumab. Volunteer Distribution had already shipped 36 out of 41 packages, according to the Justice Department. The FDA notified and interviewed several physicians and practice managers who purchased medicines from Montana Healthcare.

"All of us who work in enforcement at the FDA have seen this pattern too often—criminal offenders seeking to profit from distributing substandard or ineffective drugs that are ultimately administered to unsuspecting and vulnerable patients," wrote John Roth, director of the FDA Office of Criminal Investigations, in an FDA Voice blog post.

According to Justice Department documents, Bottomley forfeited $1.1 million, a 2011 Aston Martin Vantage V-12 and 10 parcels of property in Montana—which investigators established were the proceeds of the illegal activity. The Aston Martin was sold for $110,000 at a U.S. Marshals auction.

In Brief

Van Etten Named Director Of UC Irvine Cancer Center

(Continued from page 1)

and clinical endeavors.

Van Etten will take over from interim director **Sheldon Greenfield**, executive co-director of the Health Policy Research Institute. The center's previous director, **Frank Meyskens**, was appointed vice dean of the UC Irvine School of Medicine, and assumed the title of director emeritus of the Chao cancer center.

Greenfield has been with UC Irvine since 2003, when he and his wife Sherrie Kaplan, were recruited to co-direct the Health Policy Research Institute.

Greenfield and Kaplan started a master of science program in evidence based medicine and comparative effectiveness research at UC Irvine School of Medicine

He is a founding member and president of the Society of General Internal Medicine and is currently

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senior co-editor of the Journal of Comparative Effectiveness Research.

ANN GEIGER was named chief of the Health Services and Economics Branch in the Applied Research Program within NCI's **Division of Cancer Control and Population Sciences**.

Geiger brings expertise in cancer survivorship, age-related treatment disparities, assessment of patient capacity to withstand treatment, and the translation and dissemination of appropriate follow-up care and behaviors into clinical practice.

Geiger is an associate editor of the Journal of the National Cancer Institute. Before her NCI appointment, Geiger was an associate professor of public health sciences at Wake Forest University School of Medicine.

She has held several leadership roles in the HMO Cancer Research Network, a HSEB initiative, and she has served as site principal investigator for CRN studies in domains including infrastructure, recurrence predictors, survivorship, determinants of late-stage cancer, efficacy of early screening and prophylactic mastectomy in women with a family or personal history of breast cancer, and organizational barriers to HMO participation in cancer clinical trials.

HSEB's mission is to study demographic, social, economic, and health system factors as they relate to preventive, screening, diagnostic, and treatment services for cancer and to develop and improve the methods and techniques of economics and health services research related to cancer.

JOSEPH FAY was named executive director of **ThinkCure!**, a community-based nonprofit that raises funds to accelerate collaborative research at City of Hope and Children's Hospital Los Angeles.

Fay was the executive director of the Children's Brain Tumor Foundation in New York. He has worked for over twenty years in the non-profit sector and held leadership positions in marketing and fundraising at the national offices of the American Red Cross, American Lung Association, and Reading Is Fundamental.

Fay has chaired the American Marketing Association's Non-Profit Marketing Conference and taught non-profit marketing at Georgetown University.

He graduated from Boston College and received an MBA from Columbia University, and he served as an officer in the U.S. Navy after college.

FDA News

FDA Approves Gliotrif Tablets In Non-Small Cell Lung Cancer

FDA approved Gilotrif (afatinib) tablets as a first-line treatment for patients with metastatic non-small cell lung cancer whose tumors have epidermal growth factor receptor exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test.

The safety and efficacy of afatinib have not been established in patients whose tumors have other EGFR mutations.

Among patients diagnosed with NSCLC, it is estimated that between 10 and 15 percent of Caucasians and approximately 40 percent of Asians have EGFR mutations. Two of the EGFR mutations for which Gilotrif is indicated occur in 90 percent of these cases.

The drug, which was discovered and developed by Boehringer Ingelheim Pharmaceuticals is the first FDA-approved oncology product from the company.

BI collaborated with QIAGEN on the development of a companion diagnostic for Gilotrif. QIAGEN's therascreen EGFR RGQ PCR Kit for detection of EGFR exon 19 deletions or exon 21 (L858R) substitution mutations was reviewed and approved by the FDA in parallel to Gilotrif, and will be used to identify patients who may be eligible for treatment.

The approval of afatinib was based on the demonstration of improved progression-free survival in an international, open-label, randomized trial.

This trial enrolled 345 patients with metastatic NSCLC whose tumors tested positive for EGFR mutations. Patients were randomized to receive afatinib 40 mg orally once daily (n=230) or pemetrexed/cisplatin (n=115).

Randomization was stratified according to EGFR mutation status—exon 19 deletion vs. exon 21 (L858R) vs. 'other'—and by race: Asian vs. non-Asian. The major efficacy outcome was progression-free survival as assessed by an independent review committee.

Of 345 patients enrolled, 65 percent were female, the median age was 61 years, 26 percent were Caucasian, and 72 percent were Asian.

The majority of patients had a tumor sample with an EGFR mutation categorized as either exon 19 deletion (49 percent) or exon 21 (L858R) substitution (40 percent), while the remaining 11 percent had 'other' mutations.

A statistically significant prolongation of PFS determined by the IRC was demonstrated for patients

assigned to the afatinib treatment arm [HR 0.58 (95% CI: 0.43, 0.78); $p < 0.001$, stratified log-rank test].

The median PFS was 11.1 months in the afatinib arm and 6.9 months in the chemotherapy arm. Objective response rates were 50.4 and 19.1 percent in the afatinib and chemotherapy arms, respectively. No statistically significant difference in overall survival between the two arms was demonstrated.

In patients whose tumors have exon 19 deletions or exon 21 (L858R) substitution mutations, the median PFS was 13.6 months in the afatinib arm and 6.9 months in the chemotherapy arm.

The most frequent adverse reactions from afatinib were diarrhea, rash/dermatitis acneiform, stomatitis, paronychia, dry skin, decreased appetite and pruritus.

Serious adverse reactions were reported in 29 percent of patients treated with afatinib. The most frequent serious adverse reactions were diarrhea, vomiting; and dyspnea, fatigue, and hypokalemia. Fatal adverse reactions in afatinib-treated patients included pulmonary toxicity/interstitial lung disease-like adverse reactions, sepsis, and pneumonia.

Full prescribing information is available at the FDA website.

The company must now seek for second-line marketing authorization, said an analyst with research and consulting firm GlobalData.

Brooke Baker, who covers oncology and hematology, said the drug has significant challenges in the NSCLC market. "There are concerns regarding Gilotrif's toxicity among some in the NSCLC space, and indeed Gilotrif's FDA prescribing information carries a warning against severe diarrhea," Baker said.

"We believe these safety concerns, combined with a lack of head-to-head data against entrenched anti-EGFR therapies such as Tarceva, could limit Gilotrif's uptake in the U.S. NSCLC market starting from 2013."

Following entry into the U.S. market, BI expects to launch Gilotrif in the E.U. and Japan later this year. However, once launched in these markets, Gilotrif will have to contend with established drugs, Iressa and Tarceva.

"Based on expected positive results from the LUX-Lung 5 phase III trial investigating Gilotrif as a second-line therapy in NSCLC patients failing other first-line treatments, the second-line setting could present a great opportunity for BI's drug to gain patient and market share," Baker said.

"Iressa and Tarceva both face patent expiration by the end of the decade, and Gilotrif is well positioned to become the leading branded EGFR-targeted therapy after that occurs; but until that time, we believe that BI will need to push hard for second-line marketing authorization in the U.S. and E.U. in order to fully realize Gilotrif's sales potential."

FDA granted clearance to a new version of the xTAG CYP2D6 kit developed by Luminex Corporation.

Cytochrome P450 2D6 (CYP2D6) is a clinically important gene that encodes a phase one drug metabolizing enzyme. CYP2D6 metabolizes greater than 25 percent of the drugs in use today including cardiovascular drugs, antipsychotics, antidepressants, pain medications, b-blockers, antiemetics, antiarrhythmics and anticancer drugs.

Variations in the CYP2D6 gene can result in distinct drug metabolizing phenotypes leading to suboptimal drug responses, such as drug toxicity, adverse drug reactions, or inadequate therapeutic effects.

The IVD assay is run on the Luminex 100/200 instrument. This new version of the kit optimizes performance on the *17 allele and features an updated software algorithm that detects all 17 genotypes that the assay is cleared for, including deletion and duplication genotypes.

The European Medicines Agency granted orphan drug designation for Zybrestat (fosbretabulin tromethamine) for the treatment of ovarian cancer. A disease is defined as rare in the EU if it affects fewer than five in 10,000 people.

A phase II trial of Zybrestat and Avastin (bevacizumab) is being conducted by the Gynecologic Oncology Group, in collaboration with Genentech, the manufacturer of Avastin. A total of 107 patients with advanced, platinum-sensitive and resistant ovarian cancer have been enrolled in this trial at over 80 clinical sites in the U.S. Data is expected to be available in early 2014. Zybrestat is sponsored by OXiGENE Inc.

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