Trends-in-Medicine

Quick Takes

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Trends-in-Medicine
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…Highlights from this week's news affecting drugs and devices in development…

SHORT TAKES

- **ALEXZA PHARMACEUTICALS** licensed its Staccato inhaled nicotine device to **Cypress Bioscience**.
- **ATRICURE** plans to settle a $2.8 million class-action lawsuit filed by shareholders who alleged that the company marketed surgical cardiac ablation systems for off-label uses. A judge in Cincinnati scheduled an October 7, 2010, hearing to consider the proposed settlement.
- **AVI BIOPHARMA's AVI-7100** – This potential swine flu treatment had positive results in animal studies, reducing the level of the virus vs. a saline control and vs. Roche's Tamiflu (oseltamivir).
- **BAXTER** bought the exclusive commercial rights to Glassia, a human alpha-1-proteinase inhibitor, for treating emphysema from **Kamada Ltd**. Baxter hopes to introduce the drug in the U.S. market before the end of this year.
- **BOEHRINGER INGELHEIM's Pradaxa (dabigatran)**, a potential alternative to warfarin, will be reviewed by the FDA's Cardiovascular and Renal Drugs Advisory Committee on September 20, 2010, for stroke prevention in atrial fibrillation (SPAF) patients.
- **Centers for Medicare and Medicaid Services (CMS)** widened Medicare coverage of tobacco-related (smoking-cessation) counseling to include up to two tobacco-cessation counseling attempts each year and as many as four individual sessions per attempt. The move is part of the Obama administration's effort to increase preventive measures against tobacco-related diseases.
- **CERUS' Intercept Blood System** – Cerus is buying back from **BioOne Corp.** the Asian marketing rights to this technology for reducing disease transmission during blood and plasma transfusions.
- **CHELSEA THERAPEUTICS' CH-4051 –** The FDA has given permission for a 12-week, 250-patient, Phase II trial to start screening rheumatoid arthritis patients in September 2010.
- **ECHO THERAPEUTICS' Prelude SkinPrep –** The company has finished a clinical trial designed to test the efficacy of this transdermal drug-delivery system in

ablating the skin when used with **Ferndale Pharma Group**'s 4% topical lidocaine. Echo said it will file an application with the FDA in the "near future" for 510(k) clearance.

- **GETINGE –** The FDA issued a warning letter to Getinge regarding issues with vascular graft cleaning procedures at its production plant in Wayne NJ and with a discrepancy related to the 2006 recall of the Hemashield vascular graft. Getinge CEO Johan Malmquist said the warning would not affect the production and marketing of products at the facility and that the company hopes to resolve the issues by the end of 2010.

- **IKARIA's Inomax DS –** The FDA issued a Class I notice to Ikaria after the company's recall of this drug-delivery system, which administers nitric oxide to help patients breathe. The company recalled the product after finding that a component of the device's pressure switch has the potential to tear. Ikaria has started replacing the devices affected by the recall.

- **JOHNSON & JOHNSON/DEPUY ORTHOPAEDICS** is pulling two of its hip implants from the market – the ASR Hip Resurfacing System and the ASR XL Acetabular System – after unpublished data showed that many patients had to undergo procedures to replace the devices. J&J said it will pay for the treatment and monitoring costs related to the recall, including ongoing doctor visits, patient monitoring, and necessary revision surgery, plus the company may have to settle lawsuits for pain and suffering. J&J said there are only 93 ASR systems still implanted worldwide.

- **JOHNSON & JOHNSON/DEPUY's TruMatch Personalized Solutions System** – The FDA sent a warning letter to J&J saying this is an unapproved device. The Agency also accused J&J of marketing another device, the Corail Hip System, for off-label uses. DePuy said the company is "reviewing the letter to understand the FDA's concerns and will respond to their request for information."

- **LIFE TECHNOLOGIES** plans to buy **Ion Torrent**. Life Technologies seems to be most interested in Ion Torrent's Personal Genome Machine, a benchtop instrument which will be launched commercially later this year and which will reportedly be optimal for mid-scale sequencing projects, such as targeted and microbial sequencing.

- **Percutaneous mitral valve repair –** A CRTonline.com poll found that 46% of respondents prefer the percutaneous approach to mitral valve repair, 25% annuloplasty, 12.5% mitral valve replacement, and 16.5% none of these.

- **PROLOR BIOTECH'S HGH-CTP** – The company received FDA approval to begin a Phase II study of this longer-acting version of human growth hormone that is being developed as a once-weekly or bimonthly injectable treatment for adults and children who are growth hormone deficient. Prolor said the trial already is underway in Europe, and the company does not plan to add U.S. sites, but an official said FDA clearance will help the company stay "fully in sync with regulatory requirements in key territories."

- **RANBAXY LABORATORIES' arterolane**, an experimental malaria drug, was found to be effective and safe in a Phase II trial. The trial, which was published in the journal ***Clinical Infectious Diseases***, studied 230 people with the deadliest form of malaria in Thailand, India, and Tanzania. Arterolane reportedly "cleared the disease in as many as 72% of patients within 28 days…[and] may provide an alternative to artemisinin-based drugs because it's not derived from plants and can be produced in greater quantities."

- **ROCHE's trastuzumab-DM1 (T-DM1)** – The FDA rejected Roche Holding's request to fast-track this breast cancer drug. The Agency said that, while a Phase II study found that a third of the women with advanced breast cancer had their tumors shrink, the study didn't meet the standard for accelerated approval because it didn't include all available treatments approved for metastatic breast cancer. Roche said that it plans to continue late-stage development of the drug and seek global regulatory clearance in 2012 using additional clinical data.

- **ST. JUDE MEDICAL** is negotiating with the Justice Department to settle claims raised by a former employee related to clinical studies and alleged kickbacks. The company said the trials were "legitimate clinical studies for legitimate clinical purposes." The Justice Department received a 30-day extension to submit its complaint in the case.

- **SANOFI-AVENTIS** made it official: It is trying to buy **Genzyme**. The ***Boston Herald*** reported that Massachusetts biotech firms are watching the current situation, concerned about how the area's economy will be affected if a foreign company buys Genzyme.

- **SHIRE's Pentasa (mesalamine) –** The FDA gave a mixed response to Shire's request for formal guidance on what generic versions of this gastrointestinal drug must prove, denying Shire's request that comparative clinical endpoint studies be used. However, other aspects of Shire's citizen's petition were granted. As a result, Pentasa could face generic competition.

- **SHIRE's VPRIV (velaglucerase alfa)** – European regulators granted marketing approval for this treatment for Type 1 Gaucher disease. It was approved by the FDA in February 2010.

- **Stem cells –** The FDA asked a federal court to issue an injunction stopping **Regenerative Sciences** from offering its Regenexx, an adult stem cell transplant that uses injected autologous mesenchymal stem cells, to treat joint injuries and bone damage. The FDA hasn't approved any stem cell therapeutics yet.

NEWS IN BRIEF

BIODEL's VIAject (insulin) – FDA warning letter may delay approval

Biodel said that FDA review and approval of VIAject, an experimental diabetes drug, may be withheld as a result of a warning letter from the FDA to Albany Molecular, which owns the facility which manufactured vials for the drug. The FDA warned of possible violations at the facility, which Albany Molecular bought as part of its purchase of privately held pre-filled syringe maker Hyaluron in June 2010. Biodel said that it is working with another manufacturer, Wockhardt Ltd., on producing finished VIAject product and does not expect the warning letter to have any long-term impact on its commercialization plans for the drug. VIAject is a formulation of regular human insulin that is designed to be absorbed into the blood faster than currently marketed, rapid-acting insulin products.

Doctors are too quick to prescribe drugs – that's what consumers think

Doctors are too eager to prescribe drugs in place of effective non-pharmaceutical disease-management options, according to 50% of respondents in a ***Consumer Reports*** prescription drug poll of 1,154 adults who take prescription drugs. In the poll, 69% of respondents said drugmakers have too much influence on doctors' prescribing decisions, 87% said prescription drug safety is a priority for them, 79% said drug interactions are a concern, and 78% said they care about drug side effects.

Embryonic stem cell ruling – judge's ban shocks NIH and doctors

National Institutes of Health (NIH) director Dr. Francis Collins said that he was "stunned" by the preliminary injunction granted by a federal judge who ruled that NIH funding of stem cell research violates a federal law. The Department of Justice said that it will appeal the judge's ruling.

The American Association for Cancer Research (AACR) reiterated its support for the responsible conduct of human embryonic stem cell research that, until the judge's ruling, had been funded by NIH, and expressed concern that the injunction is a setback for scientific discovery. Dr. Margaret Foti, AACR chief executive officer, warned, "This decision will slow the important research that has the potential to save lives from cancer and will significantly affect the ability of the United States to be a leader in this cutting-edge field of science." AACR president Elizabeth Blackburn, PhD, a Nobel laureate, said, "It is disconcerting that the scientists who were given the opportunity to pursue important research questions through the investigation of stem cells, not their creation, have now been stopped in their tracks."

Fingerstick devices – increase the risk of transmitting blood borne pathogens

The FDA and the Centers for Disease Control and Prevention (CDC) noted a progressive increase in reports of blood borne infection transmission – primarily hepatitis B – over the past 10-15 years due to shared use of reusable fingerstick (blood lancing) devices and point-of-care (POC) blood testing devices (e.g., blood glucose meters, PT/INR anticoagulation meters, cholesterol testing devices, etc.). The FDA warned that fingerstick devices should never be used for more than one person, and POC blood testing devices should be used only on one patient and not shared.

GENZYME's Cerezyme (imiglucerase) and Fabrazyme (agalsidase beta) – availability increasing

Genzyme is increasing the availability of Cerezyme for Gaucher's disease and Fabrazyme for Fabry disease to patients who have experienced shortages because of production problems at its Allston MA plant that makes both medications. Cerezyme users will be able to receive normal, twice-a-month doses beginning in September 2010, while Fabrazyme users will get one dose in September and one in October. Genzyme also will add Cerezyme users from a waiting list beginning in September, according to the ***Wall Street Journal***, which noted that the plant shut down for a time last year and has been the subject of regulatory rulings.

Hypertension medications – may *boost* blood pressure in some patients

Study results published in the ***American Journal of Hypertension*** found that popular prescription medications taken to control hypertension may actually boost blood pressure in a statistically significant percentage of patients. In a study of 945 patients, researchers found, "Overall, 7.7% of the patients had a clinically significant increase in blood pressure of 10 mmHg or more," with the highest percentage of the responses –16% – occurring in patients with low renin levels who were given a beta blocker or an ACE inhibitor.

Methicillin-resistant Staphylococcus aureus (MRSA) – frog skin cure?

The U.K.'s ***Telegraph*** reported that a research team found a way to modify chemicals in frog skin so that it can be used for its germ-fighting capabilities in antibiotics to combat bacteria, such as MRSA. Frog skin has been known as a germ fighter, but it can be poisonous to humans. Now, scientists are screening skin secretions from more than 6,000 species of frogs for antibiotic activity, with the Foothill Yellow-legged Frog showing promise in the treatment of MRSA. The findings were presented at the American Chemical Society conference in Boston.

NOVARTIS's Gleevec (imatinib) – NICE limits stomach cancer use

The U.K.'s National Institute for Clinical Excellence (NICE) said it will not recommend Gleevec as a follow-up treatment for stomach cancer patients who have had a gastrointestinal stromal tumor (GIST) removed and are at risk of the cancer recurring, citing cost/benefit considerations. NICE chief executive Andrew Dillon said, "At around £19,500 (about $30,000) per patient per year, this is an expensive drug, and we need to be more confident about how well it works and what its side effects are before we consider recommending it for use in the National Health Service." NICE does recommend the drug for patients with chronic myeloid leukemia (CML) and for patients whose gastrointestinal stromal tumors cannot be removed by surgery.

SANOFI-AVENTIS's Multaq (dronedarone) – approved by NICE for AFib

The U.K.'s NICE approved Multaq for atrial fibrillation. Draft guidance from the institute said that the drug was more expensive and not as effective as existing treatments, but 176 cardiologists and 25 members of parliament and peers wrote to NICE to push for its approval. NICE recommended that Multaq be used after treatment on other drugs, usually beta-blockers, have failed.

FDA NEWS

FDA may prosecute executives at companies issuing numerous recalls

CNNmoney.com reported that the people familiar with the FDA's thinking believe the Agency is serious about identifying and potentially prosecuting executives at companies which have issued a number of recalls due to manufacturing violations.

FDA's Drug Safety Oversight Board

The FDA's Drug Safety Oversight Board is discussing "much broader drug safety issues," including deaths among children with attention deficit hyperactivity disorder (AD/HD) taking stimulants, the abuse and misuse of opioids, fire risks linked to alcohol-based skin preparations, and the potential cancer risk of CT radiation, according to a Center for Drug Evaluation and Research media update.

FDA investigating unnamed University of Miami cancer study

The University of Miami is not adding new patients to any of its cancer-research trials while the FDA and the university investigate a problematic trial, according to the ***Miami Herald***. The university is not saying which study is being investigated, but the FDA reportedly sent a warning letter to University of Miami researcher Dr. Sean Scully, an orthopedic oncologist and surgeon who is researching a device to repair hip joints. The university said that the investigation and the letter are not related.

FDA/NIH study links MLV-related viruses and CFS

Researchers from the FDA, NIH, and Harvard Medical School said that they found MLV-related viruses in 86.5% of blood samples taken from 37 chronic fatigue syndrome (CFS) patients. While the finding indicates that the virus could be linked to CFS, it cannot yet be proven whether the virus is the cause of the condition, the researchers said. Advocates for CFS patients hope the study will lead to the identification of the cause of the disease as well as the development of treatments.

Upcoming FDA Advisory Committees and Other Regulatory Meetings of Interest

(*items in red are new since last week*)

Date	Topic	Committee/Event
September 2010		
September 7	**Forest/Cerexa's ceftaroline fosamil injection** for infection	FDA's Anti-Infective Drugs Advisory Committee
September 14	**Reauthorization of the medical device user fee program**	FDA public meeting
September 15	**Abbott's Meridia** (sibutramine), a diet drug	FDA's Endocrinologic and Metabolic Drugs Advisory Committee
September 15	**Laboratory-developed test** (LDT) regulations	FDA extension for comments ends
September 16	**Alkermes' Vivitrol** (naltrexone ER) for opioid dependence	FDA's Psychopharmacologic Drugs Advisory Committee
September 16	**Arena Pharmaceuticals/Eisai's Lorqess** (lorcaserin), a diet drug	FDA's Endocrinologic and Metabolic Drugs Advisory Committee
September 16	**AstraZeneca's Brilinta** (ticagrelor), an anticoagulant	PDUFA date
September 17	**Generic drug user fee program**	FDA public meeting
September 20	**Boehringer Ingelheim's Pradaxa** (dabigatran), an anticoagulant	FDA's Cardiovascular and Renal Drugs Advisory Committee
September 22	Meeting on the challenges in developing medical devices, biotech drugs, and other treatments for **neglected tropical diseases**	Public hearing
September 23-24	Meeting on scientific issues in clinical development of aerosolized **antimicrobials for cystic fibrosis**	FDA public workshop
September 24	**Hologic's Selenia Dimensions** digital mammography tomosynthesis system	FDA's Radiological Devices Advisory Committee
September 30	Meeting on clinical trials for the development of **pediatric cardiovascular devices**	FDA public workshop
October 2010		
October TBA	**Allergan's Botox** (onabotulinumtoxinA) for chronic migraine	PDUFA date
October 15	**Boehringer Ingelheim's Pradaxa** (dabigatran), an anticoagulant	PDUFA date
October 22	**Arena Pharmaceuticals/Eisai's lorcaserin**, a diet drug	PDUFA date
October 22	**Lilly/Amylin's Bydureon** (exenatide long-acting) for Type 2 diabetes	PDUFA date
October 24	**Warner Chilcott's Actonel delayed-release** (risedronate) for osteoporosis	PDUFA date
October 28	**Vivus's Qnexa** (phentermine + topiramate), a diet drug	PDUFA date
November 2010		
November 18	**Amgen's denosumab** for cancer patients	PDUFA date
November 18	**Mela Sciences' MelaFind** for melanoma detection	FDA's General and Plastic Surgery Devices Advisory Committee
December 2010		
December 7	**Orexigen Therapeutics' Contrave** (naltrexone + bupropion), a diet drug	FDA's Endocrinologic and Metabolic Drugs Advisory Committee
December 9	**Human Genome Sciences/GSK's Benlysta** (belimumab) for lupus	PDUFA date
December 25	**Bristol-Myers Squibb's ipilimumab** for advanced melanoma	PDUFA date
Other future meetings		
January 31, 2011	**Orexigen Therapeutics' Contrave** (naltrexone + bupropion), a diet drug	PDUFA date
Date TBA, 2011	Review of **accelerated drug approval process**	FDA's Oncologic Drug Products Advisory Committee (ODAC)
Summer 2011	Report on **FDA 510(k) reform**	Institute of Medicine

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