Focus on
Cardiology, Pulmonology, & Blood

July 2012

BIO serving as your Washington, D.C. office

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- **Congress passes FDASIA (p. 5)**
- **BIO holding JOBS Act & FDASIA webinars (p. 6)**

NHLBI SCIENTISTS: CYSTIC FIBROSIS THERAPY TESTED IN YOUNG CHILDREN

A treatment that benefits adults and older children with cystic fibrosis may not help infants and young children with the disease, a new study reports. The finding could slow the adoption of this therapy in younger children.

Previous studies have found that inhaling a concentrated salt water (hypertonic saline) mist provides some benefits to adults and older children with cystic fibrosis. The mist appears to loosen the thick mucus that builds up in the lungs, which may help reduce recurrent infections known as pulmonary exacerbations. The infections are thought to contribute to the lung damage and respiratory failure associated with cystic fibrosis.

Because of these earlier findings, the use of hypertonic saline in younger children has been rising. The therapy is now used by about 1 in 5 children under 6 years old with cystic fibrosis. But there isn't clear evidence that the therapy is effective for these young children.

To test whether inhaling hypertonic saline helps young children with cystic fibrosis, a research team led by Dr. Margaret Rosenfeld at Seattle Children's Hospital and Dr. Felix Ratjen at the University of Toronto enrolled 321 participants, ages 4 months to 60 months, at 30 cystic fibrosis care centers across the United States and Canada. Twice daily for 48 weeks, the children inhaled either 7% hypertonic saline or a 0.9% saline mist as a control. The study was sponsored by NIH's National Heart, Lung and Blood Institute (NHLBI) and by the Cystic Fibrosis Foundation Therapeutics, Inc.

The scientists reported in the Journal of the American Medical Association on June 6, 2012, that hypertonic saline was well-tolerated and caused few side effects. However, there was no difference between the 2 saline groups in the rate of acute lung problems that required treatment with antibiotics (an average of 2.3 cases per participant per year). The treatment also didn't improve other clinical measurements such as coughing, respiratory rate, height or weight (the disorder can stunt children's growth).

"Even reasonably simple and non-toxic therapies can be burdensome, especially for families of small children with a chronic disease such as cystic fibrosis," says NHLBI Acting Director Dr. Susan Shurin. "This is one more study that illustrates the importance of conducting clinical research in children because medicine is not one size fits all—therapies that benefit adults or even teenagers do not always benefit younger children in the same way."

The researchers note that hypertonic saline treatment might still help younger patients. Early lung damage associated with cystic fibrosis often shows no clinical symptoms. Whether this treatment might slow the progression of airway damage in infants and toddlers, resulting in better lung function later, isn't yet known and will require further study.

For more information on this research, click here.

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NCATS ANNOUNCES INSTITUTIONAL CTSAs

The CTSA program was initiated by the NIH in 2006 to transform the local, regional, and national environment for clinical and translational research. Under NCATS, the goal of the CTSA program remains focused on integrated academic homes for the clinical and translational sciences that increase the quality, safety, efficiency and speed of clinical and translational research, particularly for NIH supported research.

The NCATS CTSA program supports disease- and condition-specific networks funded by other NIH Institutes and Centers, but is disease agnostic in its resources and approach. The NCATS CTSA program will include Institutional CTSA Awards, which are the subject of this FOA, and Consortial Awards and Demonstration Projects which will be the subject of future solicitations.

Institutional CTSAs are made to degree granting institutions or groups of institutions that receive significant funding from the NIH. CTSAs require institutional commitment, the status of a major scientific and administrative entity within and across an applicant and partner institution(s), and a CTSA PD(s)/PI(s) with the authority and influence necessary to successfully create an institutional home for clinical and translational research.

To learn more about the NCATS Institutional CTSA program, click here.

NCATS Institutional CTSAs

Institutional Clinical and Translational Science Award (U54)

RFA-TR-12-006

Letter of Intent Due: **December 10, 2012**

Application Due: **January 8, 2013**

FDA Blood Products Advisory Committee

Upcoming Meetings

July 31-August 1

December 4-5

FDA BLOOD PRODUCTS ADVISORY COMMITTEE MEETING

On June 12, 2012, the FDA Pulmonary-Blood Products Advisory Committee met to hear updates on the research programs of the Laboratory of Emerging Pathogens and the Laboratory of Bacterial and Transmissible Spongiform Encephalopathy Agents, Division of Emerging and Transfusion Transmitted Diseases, Office of Blood Research and Review, Center for Biologics Evaluation and Research, FDA.

The Committee discussed the site visit report of the intramural research programs and made recommendations regarding personnel staffing decisions.

Dr. Carolyn Wilson presented the overview on CBER research. She was followed by Drs. Hira Nakhasi, Sanjai Kumar, and David Asher presenting specific updates on the various research programs.

The meeting included an open public hearing as well as a closed Committee discussion.

The materials and minutes from this meeting are available online, as well as a complete transcript. For more information, please click here.

FDA CARDIOVASCULAR AND RENAL DRUGS ADVISORY COMMITTEE MEETING

On May 23, 2012, the Cardiovascular and Renal Drugs Advisory Committee met to discuss supplemental new drug application (sNDA) 202439/S-002 XARELTO (rivaroxaban), submitted by Janssen Pharmaceuticals, Inc. to reduce the risk of thrombotic cardiovascular events in patients with acute coronary syndrome (ACS) [ST elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI), or unstable angina (UA)] in combination with aspirin alone or with aspirin plus clopidogrel or ticlopidine.

The materials and minutes from this meeting are available online, as well as a complete transcript. For more information, please click here.

FDA Cardiovascular & Renal Drugs Advisory Committee

Upcoming Meeting

September 13-14

NHLBI FUNDING ANNOUNCEMENTS

PAR-12-155, Integrative Omics Data Analysis for Discovery in Lung Diseases (R01) – January 26, 2014

PA-12-143, Toward an Improved Understanding of HDL Function (R01) – September 8, 2012

PA-12-110, Getting from Genes to Function in Lung Disease (R01) – September 8, 2012

PAR-11-307, Discovery of Genetic Basis of Mendelian or Monogenic Heart, Lung, and Blood Disorders (X01) – May 15, 2014

PA-09-249, Directed Stem Cell Differentiation for Cell-Based Therapies for Heart, Lung, and Blood Diseases (SBIR [R43/R44]) – September 8, 2012

RFA-HL-14-005, Comparison of Strategies to Study Pediatric Pulmonary Vascular Disease Outcomes Using Bioinformatics (U01) – February 22, 2013

PA-10-118, New Approaches to Arrhythmia Detection and Treatment (R41/R42) – January 8, 2013

PA-11-053, Studies in Neonatal Hypoglycemia (R01) – May 8, 2014

PA-11-186, Translation of Pluripotent Stem Cell Therapies for Blood Disease (R01) – January 8, 2014

PA-11-121, Ribosomal Disorders and Their Role in Inherited Bone Marrow Failure Syndromes (R01) – May 9, 2014

PA-10-179, Aging Studies in the Pulmonary System (R01) – May 8, 2013

PA-10-117, New Approaches to Arrhythmia Detection and Treatment (SBIR [R41/R42]) – January 8, 2013

PAR-11-204, Early Clinical Trials for Blood Cell Therapies (R01) – January 8, 2013

For more information or to find more funding opportunities, please click here.

NEW TECHNOLOGY AVAILABLE FOR LICENSING FROM THE NIH TECHNOLOGY TRANSFER OFFICE

Sirt3 Knockout (Sirt3$^{tm1.1Cxd}$) Mouse Model for Cardiology and Metabolism Studies

Sirt3 knockout: Sirt3 is a mitochondrial-localized tumor suppressor that maintains mitochondrial integrity and metabolism during stress. Sirt3 is a mitochondrial protein that is a member of the Sirtuin family of NAD-dependent protein deacetylases. Sirt3(-/-) mice are phenotypically normal, but exhibit many proteins whose acetylation is increased. They generate more reactive oxygen species and are more susceptible to mammary tumors than normal mice. Sirt3 is inactivated in a large percentage of human breast and ovarian cancers, suggesting that Sirt3 may be a mitochondria-localized tumor suppressor by maintaining mitochondrial integrity and efficient oxidative metabolism. This technology is in pre-clinical development and has applications for cardiology and metabolism.

To learn more about this technology and to find others available for licensing, please click here.

PATIENT ORGANIZATION EVENTS

International Society of Hypertension	Cardiometabolic Health Congress	American College of Chest Physicians	American Heart Association
24th Scientific Meeting Sept. 29-Oct. 4, 2012 Sydney, Australia	2012 Congress October 10-13, 2012 Boston, Massachusetts	CHEST 2012 October 20-25, 2012 Atlanta, Georgia	Scientific Sessions 2012 November 3-7, 2012 Los Angeles, California
Click here for more details.	Click here for more details.	Click here for more details.	Click here for more details.

CONGRESSIONAL HEARINGS ON BIOTECHNOLOGY

House Financial Services Committee, Subcommittee on Capital Markets
"The 10th Anniversary of the Sarbanes-Oxley Act" — July 26, 2012

At this hearing, the Capital Markets Subcommittee marked the ten-year anniversary of the Sarbanes-Oxley Act (SOX), passed in 2002. Industry representatives testified about the cost burden of SOX, especially the audit required by Section 404(b), and the impact that it can have on innovation and job creation. BIO Board Member Jeff Hatfield, CEO of Vitae Pharmaceuticals, testified about how the lack of product revenue during the biotech development process further increases the cost of the compliance burden.

House Committee on Oversight and Government Reform
"JOBS Act in Action: Overseeing Effective Implementation That Can Grow American Jobs" — June 26, 2012
"JOBS Act in Action, Part II: Overseeing Effective Implementation of the JOBS Act at the SEC" — June 28, 2012

This set of hearings focused on the implementation of the JOBS Act, which was signed into law on April 5. Witnesses and Congressmen spoke about the importance of effective implementation of the JOBS Act in order to maximize the effect its provisions will have on capital formation for growing companies. SEC Chairwoman Mary Schapiro also spoke, and gave the Committee an update on the progress the SEC is making on JOBS Act rule-making. She reported that the SEC would miss its deadline on both the Regulation D rules and the tick size study mandated by the JOBS Act (the deadline for both was July 4). She mentioned that the SEC was more optimistic about the timing of its crowdfunding rules, which are due by the end of the year.

House Committee on Energy and Commerce, Subcommittee on Health
"FDA User Fees 2012: How Innovation Helps Patients and Jobs" — April 18, 2012

At this hearing, the Health Subcommittee heard from witnesses about the importance of reauthorizing PDUFA and the impact that the FDA has on biopharmaceutical innovation and job creation. Dr. Janet Woodcock, Director of CDER at FDA, spoke about the steps FDA has taken to review and approve innovative medicines. Sara Radcliffe, EVP of Health, testified on BIO's behalf, providing the industry perspective on how important a functioning, flexible, and well-funded FDA is to the drug development process.

CAPITAL FORMATION LEGISLATION

H.R. 6161 – Fostering Innovation Act
This bill would amend the filing definitions in **SEC Rule 12b-2** to provide a more accurate picture of growing companies. Under the bill, public companies with a public float below $250 million or revenues below $100 million would be considered non-accelerated filers, providing them with **certain regulatory exemptions**, including from SOX compliance.
Sponsor: Rep. Mike Fitzpatrick (PA-8)
Status: Referred to the House Committee on Financial Services

S. 3232 – to Extend and Improve the Therapeutic Discovery Project
This bill would reauthorize the **Therapeutic Discovery Project** to cover qualifying investments made in 2011 and 2012. The bill would provide an additional $1 billion for the program and make several refinements to ensure that taxpayer dollars go to the most **deserving and innovative companies** and projects.
Sponsor: Sen. Robert Menendez (NJ)
Status: Referred to the Senate Committee on Finance

H.R. 1988 – Qualifying Therapeutic Discovery Project Tax Credit Extension Act
This bill would extend the **Therapeutic Discovery Project** through the year 2017 and fund it at **$1 billion per year**. Qualifying investments in years 2011 through 2015 would qualify for the credit or grant.
Sponsors: Rep. Susan Davis (CA-53) and Rep. Allyson Schwartz (PA-13)
Status: Referred to the House Committee on Energy and Commerce

Important Capital Formation Bills

TDP

S. 3232, Sen. Menendez

H.R. 1988, Reps. Davis & Schwartz

SOX & Rule 12b-2

H.R. 6161, Rep. Fitzpatrick

CONGRESS PASSES PDUFA REAUTHORIZATION & FDA REFORMS

On June 26, 2012, Congress passed the Food and Drug Administration Safety and Innovation Act (FDASIA) and President Obama signed the bill into law on July 16. FDASIA included a reauthorization of the Prescription Drug User Fee Act (PDUFA), along with numerous reforms to the FDA that BIO believes will speed the review and approval of new medicines.

Chief among the reforms are enhancements to the Accelerated Approval process, originally proposed in Sen. Hagan's TREAT Act and Reps. Stearns's and Towns's FAST Act. These changes will expand the applicability of Accelerated Approval and give the FDA the tools it needs to expedite the development of modern, targeted, and personalized therapies for patients suffering from serious and life-threatening diseases while preserving robust standards for safety and effectiveness. The new law also includes provisions to enhance the development and review of innovative new therapies through increased transparency and scientific dialogue, advancements in regulatory science, strengthened post-market review, and increased FDA access to external expertise during the drug review process.

Further, FDASIA includes the permanent reauthorization of the Best Pharmaceuticals for Children Act and the Pediatric Research Equity Act to encourage continued investment in pediatric research and help ensure that new drugs and biologics can be used safely and appropriately in pediatric patients.

For more information about FDASIA, please click here. BIO will be hosting two webinars in September to educate members about the provisions in the new law. If you are interested in attending one of these webinars, please email Charles Crain at ccrain@bio.org.

HEART/LUNG/BLOOD-FOCUSED LEGISLATION

H.R. 1810 – Tom Lantos Pulmonary Hypertension Research and Education Act
This bill would require the Directors of NIH and NHLBI to continue aggressive work on pulmonary hypertension and also continue research to **find a cure for pulmonary hypertension**.
Sponsor: Rep. Kevin Brady (TX-8)
Status: Referred to the House Committee on Energy and Commerce

H.R. 2505 – Pulmonary Fibrosis Research Enhancement Act
This bill would require the CDC to establish a **National Pulmonary Fibrosis Advisory Board**, develop a system to collect data on pulmonary fibrosis and other interstitial lung diseases, and establish the National Pulmonary Fibrosis Registry.
Sponsor: Rep. Erik Paulsen (MN-3)
Status: Referred to the House Committee on Energy and Commerce

H.R. 1394 – Lung Cancer Mortality Reduction Act
This bill would require the Secretary of HHS to implement a comprehensive program to achieve a **50% reduction in the mortality rate of lung cancer by 2020**. The bill also establishes a Lung Cancer Early Detection Program.
Sponsor: Rep. Donna Christensen (VI)
Status: Referred to the House Committee on Energy and Commerce

H.R. 640 – Bone Marrow Failure Disease Research and Treatment Act
This bill would require the Secretary of HHS to develop a system to collect data on **acquired bone marrow failure** diseases and to award grants to improve diagnostic practices and quality of care for patients with such diseases.
Sponsor: Rep. Doris Matsui (CA-5)
Status: Referred to the House Committee on Energy and Commerce

S. 438 – Heart Disease Education, Analysis, Research, and Treatment for Women Act
This bill would require the Secretary of HHS to report on the quality of **care for women with heart disease**, stroke, and other cardiovascular diseases and to include recommendations for eliminating treatment disparities.
Sponsor: Sen. Debbie Stabenow (MI)
Status: Referred to the Senate Committee on Health, Education, Labor, and Pensions

BIO'S EMERGING COMPANIES

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BIO Meetings and Conferences

BIO India International Conference
September 12-13, 2012
Hyderabad, India

BIO Technology Transfer Symposium
October 8, 2012
San Francisco, California

BIO Investor Forum
October 9-10, 2012
San Francisco, California

BIO China
October 24-25, 2012
Shanghai, China

BIO Europe Fall
November 11-14, 2012
Hamburg, Germany

BIO Asia International Conference
January 29-30, 2013
Tokyo, Japan

For more about BIO events, please visit bio.org.

BIO HOLDING JOBS ACT WEBINARS

This spring, Congress passed the JOBS Act with broad, bipartisan majorities. When President Obama signed the bill into law, it immediately opened up new avenues for capital formation for emerging biotech companies. From changes to the IPO process for small companies to revamped private financing models, the JOBS Act has the potential to stimulate fundraising for important R&D.

Some of the provisions of the JOBS Act took effect upon enactment, while others are awaiting rulemaking by the SEC. Two upcoming webinars sponsored by BIO will provide companies with information on the key facets of the law and offer expert analysis on how to navigate the new rules. Speakers will also give updates on the status of pending regulation and offer a Q&A session with attendees on what to expect in the upcoming months and years and how companies can best take advantage of these new opportunities.

The webinars are scheduled for **Tuesday, September 18 at 2:00 pm (EDT)** and **Wednesday, October 3 at 2:00 pm (EDT)**. The webinars are free for all BIO R&D members and BIO state affiliates. Non-member R&D companies are invited to join for $100. For more information or to register for the webinars, please email Charles Crain at ccrain@bio.org.

BIO HOLDING FDASIA WEBINARS

BIO would like to invite you to participate in our upcoming educational webinar series in September on key provisions contained in the Food and Drug Administration Safety and Innovation Act (FDASIA), which became law on July 9, 2012. These webinars will provide information on the intent and goals of the provisions in FDASIA as well as discuss implementation issues and timelines. The webinars are free for all BIO R&D members and BIO state affiliates. Non-member R&D companies are invited to join for $100.

The first webinar, *PDUFA V: Enhanced Communications and NME Reviews*, will be held on **Thursday, September 13 at 2:00 pm (EDT)**. This webinar will focus on the enhanced communications and NME provisions that were agreed to by industry, stakeholders, and FDA as part of the PDUFA technical agreement.

The second webinar, *New and Enhanced Pathways: Expanded Accelerated Approval and Breakthrough Therapies*, will be held on **Wednesday, September 26 at 2:00 pm (EDT)**. This webinar will focus on two new and enhanced pathways, Enhanced Accelerated Approval and Breakthrough Therapies, that were passed into law as part of FDASIA. For more information or to register for either webinar, please email Charles Crain at ccrain@bio.org.