BIO'S EMERGING COMPANIES

APRIL 1, 2012

FOCUS ON ALLERGY/INFECTIOUS DISEASE/ANTIVIRAL

BIO SERVING AS YOUR WASHINGTON, D.C. OFFICE

A QUARTERLY REVIEW OF ISSUES, REGULATIONS, AND SCIENTIFIC DISCOVERIES IN THE FIELD OF ALLERGY/INFECTIOUS DISEASE/ ANTIVIRAL TREATMENTS AND THERAPIES

INSIDE THIS ISSUE:

SPECIAL POINTS OF INTEREST:

- **TREAT Act and FAST Act introduced to reform FDA (p. 3)**
- **NCATS and CAN funded for FY 2012 (p. 4)**
- **Congress reauthorizes SBIR; passes JOBS Act (p. 6)**

NIAID STUDIES SHOW BENEFITS OF IMMEDIATE ANTI-RETROVIRAL TREATMENT FOR HIV-INFECTED INFANTS

Results from studies presented March 6 at the Conference on Retroviruses & Opportunistic Infections in Seattle demonstrated the importance of identifying & treating HIV-infected infants within the first year of life to prevent harm to the immune system & to enable normal neurological development.

Although immediate ART during infancy benefits HIV-infected babies, the prospect of lifelong treatment raises numerous concerns, including the risk of drug side effects and the potential for resistance to develop to available treatments. The "Children with HIV Early Antiretroviral Therapy" (CHER) trial, funded by NIAID, launched in South Africa in 2005. It tested a novel strategy of giving immediate ART to HIV-infected infants but stopping it after the period of infancy when the risks of consequences from HIV decreases. Treatment was not resumed until there was evidence of health decline. The study initially compared immediate versus delayed treatment, but the delayed treatment arm was stopped in 2007 after a data and safety monitoring board found that infants given ART beginning at an average age of 7 weeks had a significantly lower risk of death within 48 weeks compared with infants in the deferred treatment group. Based on these findings, in 2008 the WHO revised its treatment guidelines to recommend that in HIV-infected children under the age of one, ART be started immediately after HIV diagnosis, regardless of state of health.

Study results presented by Dr. Mark Cotton showed that infants could safely stop ART after 1 to 2 years and continue to fare significantly better than infants in whom the initiation of therapy was delayed until signs of illness or a weakened immune system appeared. Very few infants who received immediate ART had significant disease progression or died after treatment was stopped. Many of the infants who stopped therapy were able to remain off treatment for a long time. In follow up of the 375 study participants, 33% of infants who received 2 years of initial ART and 25% of the infants who received 1 year of initial therapy were still well and able to remain off treatment for roughly 5 years after the study officially ended.

Another presentation highlighted new results from the PREDICT study. This Phase III clinical trial among HIV-infected children in Thailand and Cambodia examined the question of when to begin ART in children who were not diagnosed with HIV during infancy and did not present for treatment until they became sick. The study, which began in 2006 & involved 299 children ages 2-12, compared beginning treatment immediately or delaying treatment until levels of CD4+ T cells fell to a certain threshold. Dr. Jintanat Ananworanich presented findings demonstrating that both study groups experienced comparably low rates of disease progression, while higher rates of drug toxicities & resistance were found in the immediate treatment group. Neurological development problems were frequent & equally prevalent in both groups.

Taken together, both the CHER and PREDICT studies illustrate the importance of identifying and treating HIV-infected infants as soon as possible.

For more information on these studies, please click here.

> ***"Based on these findings, the WHO revised its treatment guidelines to recommend that in HIV-infected children under the age of one, ART be started immediately after HIV diagnosis."***

Bio BIOTECHNOLOGY INDUSTRY ORGANIZATION

NIAID FUNDING ANNOUCEMENTS

PAR-12-109, Targeting Persistent HIV Reservoirs (PaPHIR) (R21/R33) – April 25, 2012

RFA-MH-12-030, Eradication of HIV-1 from CNS Reservoirs: Implications for Therapeutics (R01) – Sept 12, 2012

PA-12-107, Delivering Therapeutics to Residual Active HIV Reservoirs (R01) – June 5, 2012

PA-12-012, HIV Incidence Assays with Improved Specificity (R01) – February 5, 2012

PA-12-106, Mucosal Environment and HIV Prevention (MEHP) (R01) – June 5, 2012

PA-12-105, Functional Glycomics in HIV Vaccine Design (R01) – June 5, 2012

PA-12-104, Enhancing Cellular Immunity in the Female Reproductive Tract (R01) – June 5, 2012

PA-12-090, New Technologies for Viral Hepatitis SBIR (R43/R44) – August 5, 2012

PAR-12-087, HIV Vaccine Research and Design (HIVRAD) Program (P01) – June 13, 2012

RFA-AI-12-007, Targeting Inflammation and Immune Activation in HIV Disease (U01) – July 13, 2012

PA-12-037, Research to Advance Vaccine Safety (R01) – June 5, 2012

PA-12-038, Research to Advance Vaccine Safety (R21) – June 16, 2012

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

FDA PULMONARY-ALLERGY DRUGS ADVISORY COMMITTEE MEETING

On February 23, 2012, the FDA Pulmonary-Allergy Drugs Advisory Committee met to discuss NDA 202-450 from Forest Laboratories, Inc. for aclidinium bromide inhalation powder 400 mcg twice daily, proposed for the long-term, maintenance treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema. Aclidinium is a new molecular entity and is categorized as an anticholinergic agent. Due to its duration of action and its specific action on muscarinic receptors, aclidinium belongs to the subclass of long-acting antimuscarinics (LAMA). Aclidinium is supplied as a dry powder inhalation formulation administered by the Almirall inhaler device. To support the 400 mcg BID dose for the proposed indication, Forest conducted a clinical program that included two dose-ranging trials, three pivotal Phase 3 efficacy and safety trials, and three long-term safety trials.

The major issue for discussion at the meeting was whether the totality of the data supports the efficacy and safety of aclidinium 400 mcg BID for the proposed indication. In particular, the size of the safety database and its adequacy to address safety concerns associated with anticholinergic agenda as a drug class was a focus of discussion by the committee.

For more information on this meeting, please click here.

Upcoming FDA Advisory Committee Meetings

April 2-4

Anti-Infective Drugs Advisory Committee

May 10-11

Antiviral Drugs Advisory Committee

October 18

Allergenic Products Advisory Committee

FDA REFORM LEGISLATION

BIO supports two pieces of legislation that would reform and modernize the FDA to speed life-saving treatments and breakthrough medicines to patients living with debilitating diseases. BIO CEO Jim Greenwood issued statements praising both the **TREAT Act** and the **FAST Act**. BIO has also testified on the Hill in support of the proposed reforms.

S. 2113 – Transforming the Regulatory Environment to Accelerate Access to Treatments (TREAT) Act
This bill would ***reform the FDA*** by advancing regulatory science and innovation, elevating FDA and empowering operational excellence, and enabling modernized patient-centric clinical development. Specific proposed reforms include updating FDA's mission statement, enhancing the agency's access to external scientific experts, and ***strengthening the Accelerated Approval pathway***.

Sponsor: Sen. Kay Hagan (NC)
Status: Referred to the Senate HELP Committee

H.R. 4132 – Faster Access to Specialized Treatments (FAST) Act
This bill would reform the Accelerated Approval pathway at the FDA to ***expedite the approval of drugs*** for serious of life-threatening diseases or conditions while maintaining important safety standards.

Sponsors: Rep. Cliff Stearns (FL-6) and Rep. Edolphus Towns (NY-10)
Status: Referred to the House Committee on Energy and Commerce

ALLERGY/INFECTIOUS DISEASE/ANTIVIRAL-FOCUSED LEGISLATION

H.R. 528 – Neglected Infections of Impoverished Americans Act
This bill would require the Secretary of HHS to report to Congress on the epidemiology of, impact of, and appropriate ***funding required to address neglected diseases of poverty***, including neglected parasitic diseases such as Chagas disease, cysticercosis, toxoplasmosis, trichomoniasis, the soil-transmitted helminths, and other related diseases.

Sponsor: Rep. Hank Johnson (GA-4)
Status: Passed House Committee on Energy and Commerce; awaiting action in House

H.R. 1774 – Increasing Access to Voluntary Screening for HIV/AIDS and STIs Act
This bill would require a ***state plan to provide coverage of routine screening services for HIV/AIDS*** and sexually transmitted infections (STIs). It would also require the Director of CDC to track national HIV/AIDS and STI screening trends.

Sponsor: Rep. Alcee Hastings (FL-23)
Status: Referred to the House Committee on Energy and Commerce

S. 2236 – Advancing Breakthrough Therapies for Patients Act
This bill would grant a new FDA designation to certain ***breakthrough drugs*** to expedite development and approval.

Sponsor: Sen. Michael Bennet (CO)
Status: Referred to the Senate HELP Committee

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

H.R. 942 – American Research and Competitiveness Act
This bill would ***extend and make permanent the R&D tax credit***. It would also increase the ASC rate to 20%.

Sponsor: Rep. Kevin Brady (TX-8)
Status: Referred to the House Committee on Ways and Means

NEW TECHNOLOGIES AVAILABLE FOR LICENSING FROM NIH TECHNOLOGY TRANSFER OFFICE

Method of Treating Hepatitis C Virus Infection With a Small Molecule CHK2 Inhibitor

DNA damage sensors such as Checkpoint Kinase 2 (Chk2) are key regulators of the cellular DNA damage response that limits cell-cycle progression in response to DNA damage. It has been reported that these DNA damage sensors also play a key role in Hepatitis C virus (HCV) replication. The subject technology are small molecule CHK2 kinase inhibitors that have been shown to have promising activity against HCV replication. The compounds were discovered by high throughput screening of chemical libraries with more than 150,000 compounds. These novel compounds can potentially be used in combination with other anti-HCV drugs or interferon and represent a novel target for treating HCV. *In vitro* antiviral assay data, as well as preliminary *in vitro* and *in vivo*pharmokinetic data are available upon request.

A New Class of Broad-spectrum Antibiotics: Naturally-occurring Chrysophaetins and Their Analogues

This invention, offered for licensing and commercial development, relates to a new class of naturally occurring antimicrobial compounds called Chrysophaetins, and to their synthetic analogues. Isolated from an alga species, the mechanism of action of these compounds is through the inhibition of bacterial cytoskeletal protein FtsZ, an enzyme necessary for the replication of bacteria. FtsZ is responsible for Z-ring assembly in bacteria, which leads to bacterial cell division. Highly conserved among all bacteria, FtsZ is a very attractive antimicrobial target.

A Novel Treatment for Malarial Infections

The inventions are antimalarial small molecule inhibitors of the plasmodial surface anion channel (PSAC), an essential nutrient acquisition ion channel expressed on human erythrocytes infected with malaria parasites. These inhibitors were discovered by high-throughput screening of chemical libraries and analysis of their ability to kill malaria parasites in culture. Two separate classes of inhibitors were found to work synergistically in combination against PSAC and killed malaria cultures at markedly lower concentrations than separately. These inhibitors have high affinity and specificity for PSAC and have acceptable cytotoxicity profiles. Preliminary *in vivo* testing of these compounds in a mouse malaria model is currently ongoing.

To view full descriptions of these technologies and to find others available for licensing, please click here.

FY 2012 FUNDING FOR NCATS AND CAN

On December 23, 2011, President Obama signed into law the Consolidated Appropriations Act, which appropriated funds for various federal agencies, including the National Institutes of Health (NIH). Included in NIH's $30.690 billion budget authority was an appropriation of $576.5 million for the newly-authorized National Center for Advancing Translational Sciences (NCATS). The goal of the Center is to work in partnership with the public and private sectors to develop innovative ways to overcome obstacles in the translational science pipeline.

NCATS unifies certain existing NIH programs to accomplish these goals, including the Clinical and Translational Science Awards, the Office of Rare Diseases and Research, the Therapeutics for Rare and Neglected Diseases (TRND) program, the Bridging Interventional Development Gaps program, and the NIH Chemical Genomics Center. NCATS will also develop the Cures Acceleration Network (CAN), which was authorized in 2010 and recently appropriated $10 million in new funds to help bridge the "valley of death" between basic and clinical research.

FY 2012 Funding Levels

NIH
$30.690 billion

NCATS
$576.5 million

CAN
$10 million

NIAID
$4.78 billion

HOUSE OF REPRESENTATIVES HEARINGS ON BIOTECHNOLOGY

House Energy and Commerce Committee, Subcommittee on Health
"FDA User Fees 2012: Hearing on Issues Related to Accelerated Approval, Medical Gas, Antibiotic Development and Downstream Pharmaceutical Supply Chain" — March 8, 2012

At this hearing, the Health Subcommittee heard from a variety of industries that are regulated by the FDA and depending on the User Fee Acts being reauthorized. For the biopharmaceutical industry, the committee focused on the FDA Accelerated Approval process. BIO Board Member John Maraganore testified on the importance of the Accelerated Approval pathway and in support of the FAST Act, which would enhance Accelerated Approval at FDA.

House Appropriations Committee, Subcommittee on Labor, HHS, Education, & Related Agencies
"Budget Hearing – Department of Health and Human Services – NIH" — March 20, 2012

This hearing focused on the newly-established National Center for Advancing Translational Sciences (NCATS) at NIH. NIH Director Collins and NCATS Acting Director Insel testified on the process of getting NCATS up and running and the expectations they have for the Center. Industry representatives, including BIO Board Member Scott Koenig, testified on the importance of NCATS and the key role it will play in advancing translational research.

House Committee on Science, Space, and Technology, Subcommittee on Technology and Innovation
"Fostering the U.S. Competitive Edge" — March 27, 2012

The Technology and Innovation Subcommittee held this hearing to better understand how federal policies and regulations affect competition, innovation, and job growth. BIO Board Chairman Ron Cohen testified on several steps that Congress has already taken to spur innovation, including SBIR, TDP, and patent reform. He also spoke in favor of reforms to the Accelerated Approval pathway at FDA.

SENATE HEARINGS ON BIOTECHNOLOGY

Senate Committee on Banking, Housing, and Urban Affairs
"Spurring Job Growth Through Capital Formation While Protecting Investors, Part II" — March 6, 2012

The Senate Banking Committee held this hearing to discuss several proposals on how to ease capital formation for emerging companies. The bills under consideration included an on-ramp to the public market for emerging growth companies and reforms to SEC Regulation A, SEC Regulation D, and the SEC private shareholder limit. OncoMed Pharmaceuticals CFO Will Waddill testified on how these policies would affect growing biotech companies and stimulate innovation and job growth. The legislation that BIO supported at the hearing was later combined into one bill and passed as the JOBS Act.

Senate Committee on Health, Education, Labor, and Pensions
"Strengthening FDA and the Medical Products Industry for the Benefit of Patients" — March 29, 2012

The Senate HELP Committee held this hearing to discuss the upcoming reauthorization of PDUFA and how FDA and its regulated industries can speed treatments and therapies to patients. Sara Radcliffe, Executive Vice President of Health, testified on behalf of BIO; she was joined by other industry representatives as well as Janet Woodcock (CDER) and Jeffrey Shuren (CDRH) from the FDA.

BIO'S EMERGING COMPANIES

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BIO Meetings and Conferences

BIO International Convention
June 18-21, 2012
Boston, Massachusetts

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

Livestock Biotech Summit
September 19-21, 2012
Kansas City, Missouri

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

PRESIDENT OBAMA SIGNS SBIR REAUTHORIZATION

On December 31, 2011, President Obama signed into law the **National Defense Authorization Act**, which reauthorized the SBIR program through 2017. Included in the reauthorization was an end to the eligibility ban on venture-backed companies. Now, venture-backed companies will be able to compete for 25% of SBIR funds at NIH, NSF, and the Department of Energy and 15% of funds at all other agencies. Additionally, research agencies with SBIR programs will increase the set aside from 2.5% to 3.2% by 2017. BIO is in the process of reaching out to SBA, which will propose rules on affiliation in the upcoming months.

CONGRESS PASSES THE JOBS ACT

In late March, Congress passed the **Jumpstart Our Business Startups (JOBS) Act** to ease capital formation for growing startup companies. The legislation includes an "on-ramp" to the public market for "emerging growth companies," which will give them a five-year transition period before having to comply with certain regulatory burdens, including Sarbanes-Oxley (SOX) Section 404(b). The bill will also allow companies to conduct direct public offerings of up to $50 million under SEC Regulation A, eliminate the ban on general solicitation in Rule 506 of SEC Regulation D, and raise the shareholder limit that requires private companies to register with the SEC. The JOBS Act passed both houses of Congress with broad bipartisan support and President Obama has indicated that he will sign it into law.

BIO ADVOCATES FOR TDP EXTENSION AND EXPANSION

BIO has been advocating Congress for an extension and expansion of the Therapeutic Discovery Project (TDP) tax credit program. The TDP was enacted in 2010 and awarded $1 billion in tax credits and grants to breakthrough biotechnology companies with fewer than 250 employees. To support extension and expansion of this important program, BIO produced three video vignettes which give policymakers a view of what TDP has done for biotech companies already. The videos highlight companies that received awards through the program and emphasize the positive effect that the funding had on job creation, the development of treatments, and U.S. competitiveness. To view these videos, please click **here**, **here**, and **here**.

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