Focus on
Allergy, Infectious Disease, & Antiviral
July 2012
BIO serving as your Washington, D.C. office

INSIDE THIS ISSUE:

SPECIAL POINTS OF INTEREST:

- **Sen. Menendez introduces bill to extend & improve TDP (p. 4)**
- **Congress passes FDASIA (p. 5)**
- **BIO holding JOBS Act & FDASIA webinars (p. 6)**

NIAID SCIENTISTS TO TEST MARAVIROC-BASED DRUG REGIMENS FOR HIV PREVENTION

Scientists are launching the first clinical trial to test whether drug regimens containing maraviroc, a medication currently approved to treat HIV infection, are also safe and tolerable when taken once daily by HIV-uninfected individuals at increased risk for acquiring HIV infection. The eventual goal is to see if the drug regimens can reduce the risk of infection.

The trial involves a strategy known as pre-exposure prophylaxis, or PrEP, in which HIV-uninfected individuals who are at risk for contracting the virus take one or two HIV drugs routinely in an effort to prevent infection. Called Novel Exploration of Therapeutics for PrEP, or NEXT-PrEP, the two-year study is sponsored and funded by NIAID.

"The NEXT-PrEP study will examine whether maraviroc-based PrEP is safe and well-tolerated. It is a necessary first step before we can test the effectiveness of maraviroc-based PrEP, and in the future, potentially expand the selection of drugs that may be used in this emerging HIV prevention strategy," said NIAID Director Anthony S. Fauci, M.D.

Led by principal investigator Roy M. Gulick, M.D., M.P.H., chief of the Division of Infectious Diseases and professor of medicine at Weill Cornell Medical College of Cornell University, the study team will enroll 400 HIV-uninfected men who have sex with men (MSM) ages 18 and older in 12 cities in the United States and Puerto Rico. The volunteers will be assigned at random to take one of the following four PrEP study regimens daily for 48 weeks:

- Maraviroc (300 mg)
- Maraviroc (300 mg) plus emtricitabine (200 mg)
- Maraviroc (300 mg) plus tenofovir disoproxil fumarate (300 mg)
- Emtricitabine (200 mg) plus tenofovir disoproxil fumarate (300 mg)

Placebo pills will be added to the regimens as needed so that neither the participants nor the study team will know who is taking which regimen. The investigators will observe whether the volunteers experience any serious side effects and assess whether they continue taking their PrEP regimens as recommended. If the study drugs appear to compromise a participant's health, he will be directed to stop taking them.

All participants will regularly be tested for HIV infection and receive condoms and counseling on how to reduce their risk of becoming infected with the virus.

The NIH-funded HIV Prevention Trials Network (HPTN), in collaboration with the AIDS Clinical Trials Group (ACTG), is conducting the NEXT-PrEP study, also called HPTN 069/ACTG 5305. Gilead Sciences Inc. of Foster City, Calif., and ViiV Healthcare of Brentford, England, are donating the study drugs.

This trial builds on the results of the NIAID-sponsored iPrEx study, which found in 2010 that the daily PrEP regimen of oral tenofovir plus emtricitabine (brand name Truvada) reduced the risk of HIV infection in MSM by 43.8 percent.

For more information on this research, click here.

"It is a necessary first step before we can… potentially expand the selection of drugs that may be used in this emerging HIV prevention strategy."

NEW TECHNOLOGIES AVAILABLE FOR LICENSING FROM THE NIH TECHNOLOGY TRANSFER OFFICE

Linked Purine Pterin HPPK Inhibitors Useful as Antibacterial Agents

The invention offered for licensing describes and claims novel inhibitors of 6-hydroxymethyl-7,8-dihydropterin pyrophosphokinase (HPPK), a key enzyme in the folate biosynthetic pathway which is essential for microorganisms but absent in mammals. These novel inhibitors are based on linked purine pterin compounds. They can disrupt the folate biosynthesis of bacteria and thus can find utility as potential antimicrobials. Antibiotics based on these lead molecules can be specifically designed and synthesized to serve as broad-spectrum or narrow-spectrum antibiotics. None of the currently established antibiotics target HPPK.

Treatment of Viral Infection by Blocking Interleukin-21

Blocking interleukin (IL-21) may be an effective method to treat or prevent various viral infections. In the course of an immune response to a virus, IL-21, produced primarily by CD4+ T cells, can inhibit or stimulate (regulate), immune cell function (B cells, T cells, natural killer cells, dendritic cells). IL-21 regulation may be either protective or pathological; autoimmune disease pathology has been associated with IL-21 promoted inflammation (in: type 1 diabetes, lupus, and multiple sclerosis). This technology describes methods of blocking IL-21 that may reduce damaging inflammatory responses during certain viral infections. Specifically, the absence of IL-21 during respiratory viral infection such as pneumonia virus infection actually prevents some of the pathogenic effects that may be promoted by IL-21. Methods for controlling IL-21 signaling may be used to treat to prevent many pathological effects of pneumonia viruses, and other viral infections.

Novel Reduced Toxicity Tropolone Derivative Compounds That Have Anti-Viral Activity Through Inhibiting RNase H Activity

Several novel tropolone derivatives have been identified that inhibit HIV-1 RNase H function and have potential for anti-viral activity due to reduced cellular toxicity. Inhibiting RNase H function is a potential treatment for many viral infections, since RNase H function is essential for viral replication for many pathogenic retroviruses such as HIV-1 and HIV-2. Although many hydroxytropolone compounds are potent RNase H inhibitors biding at the enzymatic active site, they are limited as therapeutic candidates by their toxicity in mammalian cells. The toxicity thought to be a result of inhibition of multiple essential mammalian metalloenzymes. We reasoned that the potential beneficial application of tropolone RNase H inhibition might be of therapeutic use if the toxic effects in mammalian cell were eliminated. By selectively adding steric bulk to add new drug-enzyme contacts for the RNase H active site, a number of novel compounds, that have initially demonstrated reduced cytotoxicity, have been produced. Importantly, these novel compounds appear to retain antiviral activity essential for use as therapeutics.

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

FDA ANTI-INFECTIVE DRUGS ADVISORY COMMITTEE

On April 3, the Committee met to discuss the development of an animal model of pneumonic plague in African Green monkeys and provide advice concerning the relevance of the animal model to pneumonic plague in humans resulting from exposure to Yersinia pestis in a bioterrorism event.

On April 4, the Committee discussed the data provided to support the safety and efficacy of levofloxacin for the treatment of pneumonic plague in humans. Janssen Pharmaceuticals submitted efficacy supplements for Levaquin tablets, injection, and oral solution (NDA 20-634, NDA 20-635, & NDA 21-721) for treatment of pneumonic plague. Efficacy data is based on treatment in an animal model of plague.

For more information on this meeting, click here.

FDA ANTIVIRAL DRUGS ADVISORY COMMITTEE

On May 10, the Committee met to discuss an efficacy supplement for new drug application (NDA) 21-752, TRUVADA (emtricitabine/tenofovir disoproxil fumarate) Tablet, submitted by Gilead. The supplemental application proposes an indication for PrEP to reduce the risk of sexually acquired HIV-1 infection.

On May 11, the Committee discussed NDA 203-100, for a fixed dose combination tablet of elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate, submitted by Gilead Sciences, Inc. The application proposes an indication for the treatment of HIV-1 infection in adults who are antiretroviral naïve or have no known substitutions associated with resistance to the individual components.

For more information on this meeting, click here.

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**

NIAID FUNDING ANNOUNCEMENTS

PAR-12-174, Multidisciplinary Studies of HIV/AIDS and Aging (R21) – April 8, 2015

PA-12-090, New Technologies for Viral Hepatitis SBIR (R43/R44) – January 8, 2015

PA-11-014, HIV Infection of the Central Nervous System (R01) – January 8, 2014

RFA-AI-12-028, Understanding the Function of Uncharacterized Genes in Infectious Disease Pathogens (U19) – November 14, 2012

PAR-12-036, Investigations on Primary Immunodeficiency Disease (R01) – January 8, 2015

PAR-12-109, Targeting Persistent HIV Reservoirs (R21/R33) – April 26, 2014

RFA-MH-13-030, Eradication of HIV-1 from CNS Reservoirs: Implications for Therapeutics (R01) – September 13, 2012

PA-12-012, HIV Incidence Assays with Improved Specificity (R01) – January 8, 2015

PA-12-106, Mucosal Environment and HIV Prevention (MEHP) (R01) – January 8, 2015

PA-12-105, Functional Glycomics in HIV Vaccine Design (R01) – January 8, 2015

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

PATIENT ORGANIZATION EVENTS

HepChange, Janssen Pharmaceuticals	Global HIV Vaccine Enterprise	Elsevier Conferences
Viral Hepatitis Congress September 7-9, 2012 Frankfurt, Germany	AIDS Vaccine 2012 September 9-12, 2012 Boston, Massachusetts	2nd Antivirals Congress November 11-13, 2012 Cambridge, Massachusetts
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.

ALLERGY/INFECTIOUS DISEASE/ANTIVIRAL 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.CON.RES.123 – Recognizing the potential for virtual elimination of pediatric HIV and AIDS and keeping HIV positive mothers alive

This resolution recognizes the importance of U.S. leadership in the **fight to eliminate pediatric HIV** by preventing mother-to-child transmission of HIV. It also expresses support for providing women with HIV counseling and testing services and calls for **greater access to more efficacious antiretroviral drug regimes** for women and children living with HIV and as a prophylaxis to stop mother-to-child transmission.

Sponsor: Rep. Trent Frank (AZ-2)
Status: Referred to the House Committee on Energy and Commerce

H.R. 4470 – Routine HIV Screening Coverage Act

This bill would require group health plans and health insurance issuers offering group of individual health insurance coverage to **provide coverage for routine HIV screening** in the same manner as other routine preventive health services.

Sponsor: Rep. Maxine Waters (CA-35)
Status: Referred to the House Committee on Energy and Commerce

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

BIO'S EMERGING COMPANIES

1201 Maryland Avenue SW, Suite 900
Washington, DC 20024
Phone: (202) 962-9200
Email: cesham@bio.org

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.