July 2012

Focus on Oncology

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)**

SCIENTISTS MAKE BREAKTHROUGH IN BILE DUCT CANCER WITH DISCOVERY OF GENE MUTATIONS

A team of international scientists has made a significant breakthrough in understanding the cause of bile duct cancer. By identifying several new genes frequently mutated in bile duct cancers, researchers are paving the way for better understanding of how bile duct cancers develop.

Bile Duct Cancer, or Cholangiocarcinoma, is a fatal cancer with a poor prognosis. Accounting for 10 to 25% of all primary liver cancers worldwide, bile duct cancer is a prevalent disease in SE Asia.

The research team was led by Bin Tean Teh, Director and Principal Investigator of the NCCS-VARI Translational Cancer Research Laboratory. The team also included Associate Professor Patrick Tan, Associate Professor Steve Rozen (both of Duke-NUS Graduate Medical School of Singapore) and Professor Vajarabhongsa Bhudhisawasdi from Thailand's Khon Kaen University. The breakthrough came after two years of intensive research, which saw scientists from Singapore visiting the villagers in northern Thailand, and Thai researchers coming to Singapore to work in NCCS laboratories.

Dr. Teh said the study will pave the way for a better understanding of the roles that newly identified genes play in the development of bile duct cancer.

"This discovery adds depth to what we currently know about bile duct cancer," said Teh. "More important is that we are now aware of new genes and their effects on bile duct cancer, and we now need to further examine their biological aspects to determine how they bring about the onset of Cholangiocarcinoma."

Using state of the art DNA sequencing, the researchers analysed eight bile duct cancers and normal tissues from Thai patients, and discovered mutations in 187 genes. The team then selected 15 genes that were frequently mutated for further analysis in an additional 46 cases. Many of these genes, such as MLL3, ROBO2 and GNAS, have not been previously implicated in bile duct cancers.

"With this finding we now know much more about the molecular mechanisms of the disease and we can draw up additional measures that can be taken while we identify the most appropriate treatment protocols. We are talking about the potential to save many lives in Thailand," said Professor Vajarabhongsa Bhudhisawasdi, Director of the Liver Fluke and Cholangiocarcinoma Research Center, Khon Kaen University of Thailand.

"This research provides a strong direction for future studies," said Associate Professor Patrick Tan, faculty member of the Cancer and Stem Cell Biology Programme at the Duke-NUS. "Cholangiocarcinoma and Pancreatic Duct Adenocarcinoma appear to share more molecular similarities than earlier studies had indicated, and suggest that there are common biological pathways between the two cancers. By studying these pathways, we can then shed more light on how these tumors develop."

For more information on this research, click here.

"This discovery adds depth to what we currently know about bile duct cancer… More important is that we are now aware of new genes and their effects on bile duct cancer."

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 Oncologic Drugs Advisory Committee

Upcoming Meetings

September 12-13
November 6-7
December 4-5

FDA ONCOLOGIC DRUGS ADVISORY COMMITTEE JUNE MEETING

On June 20, 2012, the Oncologic Drugs Advisory Committee met to discuss New Drug Application (NDA) 203213, with the established name semuloparin sodium injection, application submitted by sanofi-aventis U.S. LLC. The proposed indication (use) for this product is for the prophylaxis of venous thromboembolism (VTE) in patients receiving chemotherapy for locally advanced or metastatic pancreatic or lung cancer or for locally advanced or metastatic solid tumors with a VTE risk score ≥ 3.

The Committee also discussed New Drug Application (NDA) 202714, with the proposed trade name Kyprolis (carfilzomib) for injection, application submitted by Onyx Pharmaceuticals, Inc. The proposed indication (use) for this product is for the treatment of patients with relapsed and refractory (recurring and/or not responsive to other treatments) multiple myeloma who have received at least 2 prior lines of therapy that included a proteasome inhibitor and an immunomodulatory agent.

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

FDA ONCOLOGIC DRUGS ADVISORY COMMITTEE JULY MEETING

On July 24, the Oncologic Drugs Advisory Committee met to discuss the evaluation of radiographic review in randomized clinical trials using progression-free survival (PFS) as a primary endpoint in non-hematologic malignancies. They considered the merits of an independent audit of investigator progression assessment in a pre-specified subgroup of patients instead of an independent review of all progression assessments. The expectation is that an independent audit would streamline the conduct of clinical trials, as well as avoid missing data when no additional protocol specified progression assessments are mandated. Hematologic malignancies are excluded from this discussion because other issues (e.g., blood counts, lymph node exams, and other biomarkers) influence the assessment of PFS.

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

NCI FUNDING ANNOUNCEMENTS

PA-12-135, Translational Research at the Aging/Cancer Interface (R21) – May 8, 2015

PA-12-220, Biomarkers for Early Detection of Hematopoietic Malignancies (R21) – September 8, 2015

PA-12-213, Identifying Non-coding RNA Targets for Early Detection of Cancer (R01) – September 8, 2015

PA-12-082, Biomechanisms of Peripheral Nerve Damage by Anti-Cancer Therapy (R21) – May 5, 2012

PA-11-159, Biomarkers of Infection-Associated Cancers (R01) – May 8, 2014

PA-11-073, Mitochondria in Cancer Epidemiology, Detection, Diagnosis and Prognosis (R21) – January 8, 2014

PAR-12-140, Role of the Microflora in the Etiology of Gastro-Intestinal Cancer (R01) – March 5, 2014

PAR-12-039, Small Grants Program for Cancer Epidemiology (R03) – November 19, 2014

PAR-11-152, The Role of Microbial Metabolites in Cancer Prevention and Etiology (U01) – November 16, 2012

PA-11-297, Pilot studies in Pancreatic Cancer (R21) – January 8, 2015

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

NEW TECHNOLOGIES AVAILABLE FOR LICENSING FROM THE NIH TECHNOLOGY TRANSFER OFFICE

Individualized Cancer Therapy that Suppresses Tumor Progression and Metastasis Through Decreased Expression of TGF-beta Receptor II in Bone Marrow Derived Cells
Scientists at the NIH have developed a method of suppressing tumor progression and metastasis by targeting a pathway. This novel treatment method is an individualized therapy that first screens patients to determine if they are a candidate for the treatment, and then utilizes their own altered bone marrow to inhibit tumor progression. Tumor inhibition is achieved through decreased expression of TGF-beta receptor II (TGFbeta r2) in bone marrow derived myeloid cells.

Rapid Isolation of Central Memory T Cells for Adoptive Immunotherapy
This technology is a new technique to rapidly isolate tumor-reactive central memory T cells in a highly enriched, non-invasive manner from the peripheral blood of cancer patients for cancer adoptive cell immunotherapy. Cells are drawn from a patient's blood, divided into subsets, and contacted with the tumor antigen of interest to identify T cells whose T cell receptor (TCR) recognizes the tumor antigen.

Software for Modeling Tumor Delivery and Penetration of Antibody-Toxin Anti-Cancer Conjugates
Available for licensing is software for modeling permeability and concentration of intravenously administered antibody anti-cancer agent conjugates in solid tumor. The models can be used to determine optimal dosing regimen of a therapeutic in a particular cancer type. Thirty factors that affect delivery rates and efficiencies are analyzed as variables in generating the models.

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

PATIENT ORGANIZATION EVENTS

Association of Community Cancer Centers	American Society for Radiation Oncology	American Association for Cancer Research
National Oncology Conference October 3-6, 2012 San Antonio, Texas	54th Annual Meeting October 28-31, 2012 Boston, Massachusetts	AACR Cancer Health Disparities October 27-30, 2012 San Diego, California
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.

ONCOLOGY-FOCUSED LEGISLATION

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

H.R. 733 – Pancreatic Cancer Research and Education Act
This bill would require the Secretary of HHS to establish and implement a **Pancreatic Cancer Initiative** to assist in coordinating activities to address the high mortality rate associated with pancreatic cancer.
Sponsor: Rep. Anna G. Eshoo (CA-14)
Status: Referred to the House Committee on Energy and Commerce

H.R. 912 – Colorectal Cancer Prevention, Early Detection, and Treatment Act
This bill would allow the Secretary of HHS to make grants to states to carry out programs to increase quality **colorectal cancer screening**. It would gives priority to low-income individuals who lack adequate coverage.
Sponsor: Rep. Kay Granger (TX-12)
Status: Referred to the House Committee on Energy and Commerce

H.R. 1970 – National Childhood Brain Tumor Prevention Network Act
This bill would require a National Childhood Brain Tumor Prevention Network to provide grants and coordinate research with respect to the causes of and **risk factors associated with childhood brain tumors**.
Sponsor: Rep Barbara Lee (CA-9)
Status: Referred to the House Committee on Energy and Commerce

H.R. 111 – Breast Cancer Patient Protection Act
This bill would require health plans that provide medical and surgical benefits also provides inpatient (and in the case of a lumpectomy, outpatient) coverage and radiation therapy are for **breast cancer treatment**.
Sponsor: Rep. Rosa DeLauro (CT-3)
Status: Referred to the House Committee on Education and the Workforce

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.