NCI-SUPPORTED RESEARCH HIGHLIGHTS
ADVANCES IN CERVICAL CANCER SCREENING

Three NCI-supported trials were highlighted at the ASCO Annual Meeting in Chicago on June 2, 2013.

The first trial, examining screening for cervical cancer, demonstrated that visual inspection with acetic acid reduced cervical cancer mortality. The technique used, VIA, relies on direct visualization of the cervix after it is swabbed with vinegar. The trial was conducted in India by local health workers and community residents who were trained to provide VIA to women who needed screening. More than 75,000 women from 10 communities had multiple rounds of VIA. The screened women were compared to over 76,000 women from 10 similar communities where women were informed about cancer risks and the available screening facilities, were given vouchers for free cervical cancer screening at a nearby hospital, but were not offered the outreach system with VIA performed by community health workers. The findings from this study showed that the community screening group had a 31 percent reduction in mortality—meaning that after treatment the disease did not worsen—was 8.2 months for the women who received bevacizumab versus 5.9 months for those who received chemotherapy alone.

To read more about these studies please click here.

The second trial, looking at treatment for cervical cancer, enrolled people with advanced, recurrent, or persistent cervical cancer that was not curable with standard therapy. The patients who had the drug bevacizumab (Avastin) added to their therapy lived 3.7 months longer than patients who did not receive the drug. Bevacizumab blocks the blood supply that feeds a tumor by binding to and inhibiting a growth factor that plays a critical role in tumor blood vessel growth. The clinical trial, GOG240, was sponsored by NCI and conducted by a network of researchers led by the Gynecologic Oncology Group (GOG). In another measure of trial success, progression-free survival—meaning that after treatment the disease did not worsen—was 8.2 months for the women who received bevacizumab versus 5.9 months for those who received chemotherapy alone.

The third trial incorporated bevacizumab, but this time for the treatment of an aggressive brain tumor known as glioblastoma, in newly diagnosed patients. The clinical trial, RTOG 0825, was sponsored by NCI and conducted by a network of researchers led by the Radiation Therapy Oncology Group (RTOG), and enrolled 637 patients. The primary objective of the trial was to determine whether the addition of bevacizumab to temozolomide and radiation improved progression-free and/or overall survival. The drug is given orally and penetrates well into the central nervous system. The results of the trial showed no overall survival benefit for patients who received bevacizumab compared to patients who did not receive the drug (15.7 months vs. 16.1 months, respectively). Patients who received bevacizumab also experienced more side effects compared to those treated with chemoradiation alone.
On May 2, 2013, the Oncologic Drugs Advisory Committee met to discuss the new drug application (NDA) 204408, with the established name tivozanib capsules, submitted by AVEO Pharmaceuticals, Inc. The proposed indication (use) for this product is for the treatment of advanced renal (kidney) cell carcinoma.

During the afternoon session, the committee discussed NDA 201848, a drug/device combination product with the proposed trade name Melblez Kit (Melblez (melphalan) for Injection for use with the Delcath Hepatic Delivery System), submitted by Delcath Systems, Inc. The proposed indication (use) for this product is for the treatment of patients with unresectable ocular melanoma that is metastatic to the liver.

CDER provided a live webcast of the May 2 meeting of the Oncologic Drugs Advisory Committee.

The FDA expects that the trial will be adequately designed and well conducted and that the results will be internally consistent when considering the results from a single randomized trial submitted in support of marketing approval of a new molecular entity.

To find out more information on this meeting, including an agenda and other meeting materials, please click here.

On May 2, 2013, the Medical Imaging Drugs Advisory Committee and Oncologic Drugs Advisory Committee held a joint meeting to discuss the safety and efficacy of currently approved leukocyte growth factors (LGFs) as potential treatments for radiation-induced myelosuppression associated with a radiological/nuclear incident. (Myelosuppression is a reduction of blood cell production, which can be caused by radiation exposure.)

Currently approved LGFs are licensed under biological license applications (BLAs): 103353, NEUPOGEN (filgrastim, Amgen, Inc.), 125031, NEULASTA (pegfilgrastim, Amgen, Inc.), 103362, LEUKINE (sargramostim, Genzyme, Inc.), and 125294, TBO-FILGRASTIM (tbo-filgrastim, Sicor Biotech, UAB). The National Institute of Allergy and Infectious Diseases (NIAID) has submitted efficacy data for filgrastim, based on treatment in an animal model of radiation-induced myelosuppression. Safety and other supportive information are currently described in the labeling for LGFs.

For more information on this meeting, including an agenda and other meeting materials, please click here.
**Non-HLA-A2 Restricted Human T Cell Receptors to Treat Broad Cancer Population**

NIH scientists have developed T cell receptors (TCRs) that recognize melanoma antigen family A3 (MAGE-A3) or MAGE-A12 peptide antigens. The TCRs recognize these antigens in the context of major histocompatibility complex (MHC) class I molecules, HLA-A1 and HLA-Cw7, respectively. Since these TCRs are not HLA-A2 restricted, their therapeutic use would expand the number of treatable cancer patients using MAGE-A3 or A12-specific TCR adoptive immunotherapy.

Their normal function is not well defined, but in cancer cells they block the functions of tumor suppressor proteins to mediate tumor growth and spreading. The MAGE-A proteins are some of the most widely expressed cancer testis antigens expressed on human tumors. Other than non-MHC expressing germ cells of the testis, normal cells do not express these antigens, which make them ideal targets for cancer immunotherapies anticipated to generate less toxic side effects than conventional cancer treatments. These TCRs deliver a robust immune response against MAGE-A3 or A12 expressing cells and could prove to be a powerful approach for selectively attacking tumors without generating toxicity against healthy cells.

**Diagnostic Assays for the Detection of Thyroid Cancer**

NIH scientists have developed two novel methods for distinguishing malignant from benign thyroid biopsy samples. Midkine and pleiotrophin, both low molecular weight growth factors, are over-expressed in many cancerous tissues. NIH researchers have developed ELISA assays to quantify the amount of midkine and pleiotrophin present in thyroid tissue samples. Levels of both growth factors are substantially higher in fine needle aspirates from thyroid cancers than from benign thyroid nodules. Application of this technique for the identification of thyroid cancer represents a first-in-class diagnostic for this disease. To determine whether nodules are malignant, current practice involves obtaining a needle biopsy which is inspected microscopically. Therefore, there is a need for methods such as the present invention to improve diagnostic accuracy.

To learn more about this technology and to find others available for licensing, please click [here](#).
BIO recently announced it has joined the Coalition of Small Business Innovators (CSBI) as a founding member. CSBI is a national, non-partisan coalition of organizations dedicated to stimulating sustained, private investment in small, highly innovative companies focused on the development of new technologies.

The Coalition’s mission is to advocate and support policies that will lower the corporate tax rate and spur private investment in pre-revenue intensive businesses. The Coalition is advocating for the following tax proposals:

- Stimulating private capital for research by relaxing the passive activity loss rules in Section 469 for small research-intensive companies;
- Removing financing restrictions in Section 382 to allow small companies to retain their net operating losses generated by R&D expenditures; and
- Improving capital gains treatment for small research-intensive companies by changing the gross assets test in order for these companies to qualify for Section 1202.

The Coalition supports a U.S. tax code that recognizes innovation as a crucial part of the 21st century American economy and believes that, by itself, a lower corporate tax rate will not support growth and innovation in America’s small businesses, many of which are pre-revenue. The Coalition advocates for policymakers to both lower the corporate rate and to specifically promote innovative pre-revenue research-intensive businesses through incentives which spur private investment, encouraging other companies, individuals, and funds to invest in small companies and support their research.

Recently, the Coalition submitted a statement to the Ways & Means Subcommittee on Select Revenue Measures in response to a May 15 hearing that discussed small businesses and pass-throughs in tax reform. To read this testimony, please click here.

The Coalition will continue educating policymakers about the importance of pre-revenue innovators as Congress considers tax legislation.

To read BIO’s press release announcing its membership in CSBI, please click here.

For more information on the Coalition of Small Business Innovators, please visit smallbusinessinnovators.org. The Coalition also has Facebook and Twitter accounts.

### Members of the Coalition of Small Business Innovators

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<td>Association of Clinical Research Organizations (ACRO)</td>
<td>National Council for Advanced Manufacturing (NACFAM)</td>
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<td>Advanced Medical Technology Association (AdvaMed)</td>
<td>NanoBusiness Commercialization Association (NanoBCA)</td>
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<td>Biotechnology Industry Organization (BIO)</td>
<td>National Association of State Energy Officials (NASEO)</td>
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<td>Water Innovations Alliance (WIA)</td>
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LEGISLATION THAT IMPACTS MARKET STRUCTURE REFORM

The challenges that emerging biotech companies face on the public market are myriad, including costly regulatory burdens, stagnant liquidity, low trading volume, and a lack of market transparency. The JOBS Act has helped companies ease the IPO process and take the first steps toward accessing the vital funds available on the public market, but, once public, they will likely face liquidity and pricing issues that can be detrimental to their public float and cash flow. To that end, BIO has been working to develop and support targeted market structure reforms that will decrease the cost of capital and increase liquidity for innovative emerging biotechnology companies. It is critical that these market structure reforms address small company liquidity, price discovery, and regulatory barriers in order to realize the full potential of the JOBS Act and increase capital availability for growing innovators. The following bills have been introduced and are supported by BIO.

**Fostering Innovation Act — Sponsored by Rep. Michael Fitzpatrick (R-PA)**
The Fostering Innovation Act will amend the filing status classifications in SEC Rule 12b-2 to allow companies with a public float below $250 million or revenues below $100 million to qualify as non-accelerated filers. This change will reduce their regulatory burden (especially by exempting them from compliance with SOX Section 404(b)) and, for growing biotech innovators, allow them to spend valuable innovation capital on breakthrough research.

**Tick Size Flexibility Act — Sponsored by Reps. Sean Duffy (R-WI) and John Carney (D-DE)**
The Tick Size Flexibility Act institutes a pilot program that will allow small issuers to choose a larger tick size (either $0.05 or $0.10) in order to spur trading activity in their stock. Companies that meet the revenue test of the emerging growth company definition in the JOBS Act will be eligible for the pilot program – an important marker for growing biotechs that do not have product revenue to fund their vital research. Allowing an increased tick size will grant flexibility to growing companies and increase the liquidity and capital availability necessary for emerging biotechs to be successful on the public market.

**H.R. 1952, the Spread Pricing Liquidity Act — Sponsored by Rep. David Schweikert (R-AZ)**
The switch to the standard tick size of a penny was enacted in order to boost trading in large company stocks, but many smaller issuers have experienced the opposite effect. The Spread Pricing Liquidity Act will grant tick size flexibility to growing companies and increase the liquidity and capital availability necessary for emerging biotech companies to be successful on the public market.

**H.R. 1564, the Audit Integrity and Job Protection Act — Sponsored by Reps. Robert Hurt (R-VA) and Gregory Meeks (D-NY)**
Forcing small businesses to periodically rotate their audit firm, as favored by the PCAOB, would place an undue burden on emerging biotech companies, who have no product revenue to pay for expensive audit fees and other regulatory costs. The Audit Integrity and Job Protection Act will prevent PCAOB from adopting such an onerous regulatory burden.

**H.R. 701, to speed Regulation A rulemaking at the SEC — Sponsored by Rep. Patrick McHenry (R-NC)**
Passed the House by a vote of 416-6
Once implemented, the changes to Regulation A mandated by the JOBS Act will spur fundraising for emerging biotech companies, for whom a $50 million capital influx could support groundbreaking research and stimulate job creation. However, delays at the SEC have blunted the potential impact of the mandated reform. H.R. 701 will give the SEC a deadline to complete rulemaking on Regulation A.

ONCOLOGY-FOCUSED LEGISLATION

**H.R. 1417 — Cancer Patient Protection Act of 2013**
This bill would direct the Secretary of Health and Human Services (HHS) to make any payments under Medicare Part B that may be required to reimburse for reductions in payments made under the sequestration order for drugs and biological furnished on or after April 1, 2013, and before enactment of this Act
Sponsor: Rep. Renee Ellmers (NC-2)
Status: Referred to the House Subcommittee on Health

**H.R. 1320 — SCREEN Act of 2013**
This bill would amend title XVIII (Medicare) of the Social Security Act to waive cost-sharing for colorectal cancer screening tests.
Sponsor: Rep. Richard Neal (MA-1)
Status: Referred to the House Subcommittee on Health
BIO announces new FDA survey

BIO recently launched a survey to examine interactions between the biotechnology industry and the U.S. Food and Drug Administration (FDA) during drug development. More specifically, this survey will help BIO capture information about sponsors' interactions with FDA during the various stages drug development prior to submitting an NDA/BLA.

This survey was designed to gain insight from the biomedical community that BIO can utilize to more effectively engage with FDA during the next round of PDUFA technical discussions on topics relevant to drug development. Specifically, this initial survey is designed to assist in the implementation of the Prescription Drug User Fee Act (PDUFA V) program on Enhancing Communication during drug development. Each company's feedback will be used to better understand and measure FDA's existing communication practices and to help identify best practices for communicating with sponsors, which will further inform BIO's advocacy relating to the development of future FDA standard operating procedures and guidance for industry and staff. We are also seeking volunteers to participate in a more detailed survey that will enable us to examine interactions associated with drug development during specific phases of development, specific pathways, and disease areas. Participants of this initial survey will be provided an opportunity to sign up for the more detailed survey initiative.

To take this survey, please click here.

SBIR and STTR Omnibus Grant solicitations

NIH recently reissued its SBIR Omnibus Grant Solicitation announcement. With this re-issuance, small business concerns that are majority-owned by multiple venture capital operating companies (VCOCs), hedge funds, and/or private equity firms are now eligible to apply the NIH SBIR program and compete for up to 25% of NIH's SBIR set-aside. Implementation of this VCOC provision is available to applicants to the NIH SBIR program through this Omnibus FOA and any other NIH SBIR Funding Opportunity Announcement issued after January 28, 2013. For more information or to read the full announcement, please click here.

NASDAQ withdraws internal audit function

In early 2013, Nasdaq proposed a rule change that would have required all its listed companies to maintain an internal audit function. BIO provided comment to the SEC strongly opposing the proposal. BIO’s comment letter noted that the rule change would impose a significant and unnecessary cost burden on growing biotechs. After the comment period closed, the SEC extended its decision window given the negative feedback. Nasdaq later pulled the proposal entirely in the face of overwhelming opposition. To read BIO’s comment letter opposing the rule, please click here.