

# Focus on Rheumatology, Inflammation, Anesthesia, & Pain

BIO serving as your Washington, D.C. office



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## 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)**

## NIAMS: POST-INJURY RESPONSE COULD BE KEY STEP IN OSETOARTHRITIS DEVELOPMENT

Scientists long considered osteoarthritis (OA) a disease of wear and tear. Use the joints long enough, they reasoned, and they are bound to wear out. But research in recent years has suggested that inflammation plays a role in OA, a disease in which joint cartilage breaks down, leaving bone rubbing against bone. A new study, supported in part by the National Institute of Arthritis and Musculoskeletal and Skin Diseases, helps confirm that role and points to new targets for treatment, and perhaps prevention, of this common joint disease.

The study, conducted in the laboratory of William Robinson, M.D., Ph.D., at Stanford University, found that a pathway called the complement system, which is a major component of the innate immune system, is critical to the development of OA. Through analyses of joint tissue and joint fluid from individuals with OA, they found that expression and activation of complement is abnormally high in people with OA. The innate immune system is designed to protect the body from harmful invaders such as viruses and bacteria. When cartilage is injured, the researchers found, the complement system is activated, leading to inflam-

mation directed against the body's own tissues.

While previous research has shown evidence of complement activation in severe, *long-standing* OA, this study is the first to show the system's activation may play an important role in the *initiation* of osteoarthritis and its early progression, says V. Michael Holers, M.D., head of one of the study groups at the University of Colorado.

To confirm that role, scientists used an animal model of OA – mice that develop a disease characteristic of human OA following injury to the stabilizing ligament of the knee joint. When the scientists genetically engineered those mice to lack part of the complement system, however, they did not develop OA. The same results were seen when the mice were treated with an agent developed by Dr. Holers' lab to inhibit part of the complement system, confirming its role in the development of the disease.

With the insight gained from the study in mice, Dr. Holers says further research is needed to confirm the complement system's role in the development of OA in humans. If these findings hold true in people, though, blocking a

part of the complement system may be an effective treatment for early OA.

Current treatment for OA is primarily limited to relieving symptoms and replacing joints that are too damaged to function well, says Dr. Holers. However, this new research suggests that by giving an agent to block the complement system soon after an injury occurs, doctors may be able to prevent the subsequent occurrence of OA.

Support for this study was also provided by the National Institutes of Health's National Heart, Lung, and Blood Institute, and the National Institute of Neurological Disorders and Stroke, and other organizations.

For more information on this research, please click [here](#).

**"This study is the first to show the [complement] system's activation may play an important role in the initiation of osteoarthritis and its early progression."**



## NEW TECHNOLOGY AVAILABLE FOR LICENSING FROM THE NIH TECHNOLOGY TRANSFER OFFICE

### Antagonists of Hyaluronan Signaling for Treatment of Airway Inflammation & Hyperresponsiveness

Airway inflammation and hyperresponsiveness are hallmarks of airway disease. Investigators at NIEHS identified a new class of compounds that can block hyaluronan signaling and inhibit airway hyperresponsiveness and inflammation. Airway diseases, such as asthma and chronic obstructive airway disease, affect tens of millions of patients worldwide, and are chronic diseases with limited options for treatment. Therefore, a novel class of treatment agents could have significant public health and market impact.

### CD97 Alpha Subunit Antibodies for Treatment of Angiogenesis, Atherosclerosis, and Inflammation

CD97 is a T-cell glycoprotein that is upregulated in activated T-cells and is involved in the onset and maintenance of inflammation and angiogenesis. It is a seven-span transmembrane heterodimer consisting of one variant alpha subunit, which is soluble, and one invariant beta subunit, which is membrane-bound. Upon activation of T-cells, expression of the alpha subunit is dramatically upregulated and it is shed into the extracellular medium. The inventors have demonstrated in *in vitro* and *in vivo* studies that CD97 plays an important role in angiogenesis, inflammation, and atherosclerosis. This technology describes isolated soluble CD97 alpha subunit proteins, selected from three alternatively spliced isoforms, as well as antibodies that bind to these subunits. The technology also describes methods of inhibiting angiogenesis and CD97-associated chronic inflammation.

### Mouse Monoclonal Antibody Targeting Human NOX1, a Target for Cancer and Inflammation

Available for licensing is a mouse monoclonal antibodies targeting human nicotinamide adenine dinucleotide phosphate-oxidase (NAPH) oxidase 1 (NOX1) enzyme. NOX mediates the homeostasis of reactive oxygen species, which play a critical regulatory role in cancer cell signal transduction and tumor cell differentiation. NOX1-generated hydrogen peroxide can trigger an "angiogenic switch" that includes the induction of angiogenic factors that promote tumor cell vascularization. Investigators at NCI found NOX1 is significantly expressed more in colon and gastric cancers compared with adjacent normal bowel and gastric mucosa respectively. To the best of NIH's knowledge, this is the only monoclonal antibody that can be used to detect human NOX1. This antibody detects endogenous levels of the NOX1 protein and could potentially be used in biochemical laboratory studies as well as diagnostic tests that involve the functional significance of NOX1 in human physiology.

To learn more about this technology and to find others available for licensing, please click [here](#).

## FDA ARTHRITIS ADVISORY COMMITTEE MEETINGS

On **May 8, 2012**, the Arthritis Advisory Committee met to discuss supplemental biologics license application 125249, ARCALYST (rilonacept) injection, Regeneron Pharmaceuticals, Inc., for the following proposed indication:

"ARCALYST (rilonacept) is an interleukin-1 blocker indicated for the prevention of gout flares during initiation of uric-acid lowering therapy in adult patients with gout. ARCALYST has not been studied for longer than 16 weeks in this clinical setting."

Rilonacept was approved in the United States on February 27, 2008, for the chronic treatment of the rare genetic disorders of Familial Cold Auto-inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS), also known as Cryopyrin Associated Periodic Syndromes (CAPS), in adults and adolescents 12 years of age and older. The approved dose in adult CAPS patients is 160 mg SC injection once weekly (following a 320 mg SC loading dose).

To support the 80 mg SC dose for the proposed gout

indication, Regeneron conducted a clinical program that included 4 placebo-controlled clinical studies: two pivotal 16-week efficacy and safety studies, and two supportive 16-week safety studies.

On **May 9, 2012**, the Arthritis Advisory Committee met to discuss new drug application (NDA) 203214, tofacitinib tablets, Pfizer Inc., for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs (DMARDs).

Tofacitinib is an inhibitor of the Janus kinase (JAK) family. In kinase assays, tofacitinib inhibits JAK1, JAK2, JAK3 and, to a lesser extent, TyK2. The product is being proposed as immediate-release tablets for oral administration in 5 and 10 mg dosage strengths.

The materials and minutes from both of these meetings are available online, as well as a complete transcript. For more information, please click [here](#).

**NCATS ANNOUNCES INSTITUTIONAL CTSA s**

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 CTSA s are made to degree granting institutions or groups of institutions that receive significant funding from the NIH. CTSA s 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  
CTSA s**

**Institutional  
Clinical and  
Translational  
Science Award  
(U54)**

**RFA-TR-12-006**

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

***Application  
Due:  
January 8,  
2013***

**NIAMS FUNDING ANNOUNCEMENTS**

PAR-12-230, [Identification and Analysis of Causal Variants: Follow-Up on Genome-Wide Association Studies for Arthritis and Musculoskeletal and Skin Diseases](#) (R21) – November 21, 2013

PA-12-191, [Multiplex Assay Development for Arthritis and Musculoskeletal and Skin Diseases](#) (SBIR [R43/R44]) – September 8, 2015

PA-10-006, [Mechanisms, Models, Measurement, & Management in Pain Research](#) (R01) – January 8, 2013

PA-12-018, [Mechanisms Mediating Osteoarthritis in Aging](#) (R21) – January 8, 2015

PAS-12-226, [Advancing Novel Science in Women’s Health Research](#) (R21) – January 8, 2013

PAR-10-204, [NIH Blueprint for Neuroscience Research Competitive Revisions for Studies Focused on Neuropathic Pain or Neural Plasticity to Promote Collaborative Pain Research](#) – September 29, 2012

PA-12-132, [Improving Translational and Basic Research to Control Itch in Humans \(ITCH\)](#) (R21) – May 8, 2015

PAR-10-282, [Pilot and Feasibility Clinical Research Grants in Arthritis and Musculoskeletal and Skin Diseases](#) (R21) – July 2, 2013

For more information or to find more funding opportunities, please click [here](#).

**PATIENT ORGANIZATION EVENTS**

<b>International Assoc. for the Study of Pain</b>	<b>Inflammation Research Association</b>	<b>American Academy of Pain Management</b>	<b>Center to Advance Palliative Care</b>
World Congress on Pain August 27-31, 2012 Milan, Italy	International Conference September 9-13, 2012 Bolton Landing, NY	Annual Clinical Meeting September 20-23, 2012 Phoenix, Arizona	National Seminar November 1-3, 2012 Miami, Florida
Click <a href="#">here</a> for more details. Click <a href="#">here</a> for more details. Click <a href="#">here</a> for more details. Click <a href="#">here</a> 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](mailto:ccrain@bio.org).

## RHEUMATOLOGY / INFLAMMATION / ANESTHESIA / PAIN - FOCUSED LEGISLATION

### **H.R. 2033 – Psoriasis and Psoriatic Arthritis Research, Cure, and Care Act**

This bill would authorize the CDC to undertake **psoriasis and psoriatic arthritis data collection** efforts. It would encourage NIH to develop a Center of Excellence for Collaborative Discovery in Psoriasis & Comorbid Research.

Sponsor: Rep. Jim Gerlach (PA-6)  
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 HHS to develop a system to collect data on acquired bone marrow failure diseases and to establish the **National Acquired Bone Marrow Failure Disease Registry**.

Sponsor: Rep. Doris Matsui (CA-5)  
Status: Referred to the House Committee on Energy and Commerce

### **H.R. 1672 – Scleroderma Research and Awareness Act**

This bill would authorize NIH to expand, intensify, and coordinate activities with respect to scleroderma, with particular emphasis on research focused on the **etiology of scleroderma** and the development of new treatment options.

Sponsor: Rep. Lois Capps (CA-23)  
Status: Referred to the House Committee on Energy and Commerce

### **H.R. 1044 – Medicare Access to Rural Anesthesiology Act**

This bill would provide payment under Medicare Part A on a reasonable cost basis for **anesthesia services** furnished by a physician who is an anesthesiologist in certain rural hospitals.

Sponsor: Rep. Lynn Jenkins (KS-2)  
Status: Referred to the House Committee on Energy and Commerce

### **H.R. 2227 – Medical Gas Safety Act**

This bill would set forth provisions regarding the **regulation of medical gases**, including to establish a certification and approval process for medical gases. It lists designated medical gases, including oxygen, nitrous oxide, and medical air.

Sponsor: Rep. Leonard Lance (NJ-7)  
Status: Referred to the Committee on Energy and Commerce



## 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](http://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](mailto: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](mailto:ccrain@bio.org).

