

FOCUS ON RHEUMATOLOGY / INFLAMMATION / ANESTHESIA / PAIN
BIO SERVING AS YOUR WASHINGTON, D.C. OFFICE

A QUARTERLY REVIEW OF ISSUES, REGULATIONS, AND SCIENTIFIC DISCOVERIES IN THE FIELD OF RHEUMATOLOGY/INFLAMMATION/ANESTHESIA/PAIN TREATMENTS AND THERAPIES

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- **TREAT Act and FAST Act introduced to reform FDA** (p. 3)
- **Congress reauthorizes SBIR; passes JOBS Act** (p. 6)

NIAMS SCIENTISTS: RA DRUG HALTS ORGAN DAMAGE IN INFLAMMATORY GENETIC DISORDER

A new study shows that Kineret (anakinra), a medication approved for the treatment of rheumatoid arthritis, is effective in stopping the progression of organ damage in people with neonatal-onset multi-system inflammatory disease (NOMID). This rare, debilitating genetic disorder causes persistent inflammation and ongoing tissue damage. The research was performed by scientists at NIAMS.

Kineret, one of a relatively new class of biologics, blocks the activity of interleukin-1 (IL-1), a protein made by cells of the immune system. IL-1 is overproduced in NOMID, leading to damaging inflammation. Previous work by the same NIAMS group showed that blocking IL-1 was effective in relieving symptoms of NOMID. However, this is the first study to show that Kineret works over the long-term and, at higher doses, can also control damage that often results in vision and hearing loss, and brain lesions.

“Inflammation prolonged over many years will eventually cause irreversible damage and loss of function,” said lead author Dr. Raphaela Goldbach-Mansky. “We knew we could effectively block inflammation in the inner ear and in the brain and eyes. The next step

was to find out if we could sufficiently prevent the progression of hearing or vision loss.”

Study participants, who ranged in age from 10 months to 42 years, were treated with daily doses of Kineret based on body weight for at least 36 months and as long as 60 months. Disease activity was monitored with blood tests to measure C-reactive protein, and by daily diaries kept by the patients. The researchers also used sensitive MRI imaging methods to assess inflammation in the inner ear and brain.

Researchers found the initial Kineret doses used were insufficient to control organ inflammation, but by increasing the dose, they were able to do so. By preventing organ inflammation, scientists were able to preserve organ function in most patients. In addition, the scientists found ways to predict who is at greatest risk of hearing and vision loss.

“The few patients in the study who had hearing loss were also the ones who continued to have inflammation in the inner ear,” said the study’s first author Dr.

Cailin H. Sibley. “We also found that people who had thin optic nerves when we assessed their vision were more likely to lose vision than those who had thick optic nerves, simply because they had already lost fibers due to untreated disease and, therefore, started with a huge disadvantage.”

These findings point to the importance of early diagnosis and treatment to keep organ damage from developing. “We are continuing the study with an emphasis on enrolling very young children to prospectively show that we can prevent any organ damage from developing if we start treatment early in life,” Goldbach-Mansky said.

Because IL-1 is needed to fight infections, there has been concern that blocking it with high doses of Kineret might leave the body vulnerable to infections. But overall, the study drug was well tolerated.

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

“These findings point to the importance of early diagnosis and treatment to keep organ damage from developing.”

NIAMS FUNDING ANNOUNCEMENTS

PA-12-132, [Improving Translational and Basic Research to Control Itch in Humans \(ITCH\)](#) (R21) – June 16, 2012

PAR-12-045, [NIAMS Small Grant Program For New Investigators](#) (R03) – July 20, 2012

PA-12-019, [Mechanisms Mediating Osteoarthritis in Aging](#) (R01) – June 5, 2012

PA-10-006, [Mechanisms, Models, Measurement, & Management in Pain Research](#) (R01) – June 5, 2012

PA-09-127, [Multiplex Assay Development for Arthritis and Musculoskeletal and Skin Diseases](#) (SBIR [R43/R44]) – August 5, 2012

PAR-12-032, [Advancing Novel Science in Women's Health Research \(ANSWHR\)](#) (R21) – October 16, 2012

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

FDA ANESTHETIC AND ANALGESIC DRUG PRODUCTS ADVISORY COMMITTEE MEETING

On February 9, the Anesthetic & Analgesic Drug Products Advisory Committee met to discuss the available efficacy and safety data for sNDA 22395/S-013, QUTENZA (capsaicin 8%) Patch, by NeurogesX, Inc., for the proposed indication of management of neuropathic pain related to HIV-associated peripheral neuropathy (HIV-PN).

HIV-PN is one of the most common neurological complications associated with HIV, with a prevalence of 0.7 to 39.7 per 100 person-years. Pain associated with this complication has been reported in 40% of HIV-PN patients and symptoms can be a major cause of morbidity in HIV-infected patients. At present there are no FDA-approved drug products for the treatment of pain associated with HIV-PN.

QUTENZA was approved by the FDA on 16 November 2009 for the management of neuropathic pain associated with post herpetic neuralgia (PHN). On 6 September 2011, NeurogesX submitted a supplemental NDA to the Agency seeking approval to market Qutenza for the management of neuropathic pain associated with HIV-PN.

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

**Upcoming FDA
Arthritis
Advisory
Committee
Meeting**

May 8-9, 2012

FDA ARTHRITIS ADVISORY COMMITTEE MEETING

On March 12, the Arthritis Advisory Committee met to discuss the Anti-NGF drug class that is currently under development and the safety issues possibly related to these drugs. These drugs are being developed for the treatment of a variety of chronic painful conditions. The committee was asked to determine whether reports of joint destruction represent a safety signal related to the Anti-NGF class of drugs, and whether the risk benefit balance for these drugs favors continued development of

the drugs as analgesics.

There are three sponsors that have conducted clinical trials with anti-NGF agents. These drugs are all monoclonal antibodies directed against nerve growth factor, and are being developed for the treatment of a variety of chronic painful conditions.

For more information on this meeting, 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

NIAMS
\$534 million

NEW TECHNOLOGIES AVAILABLE FOR LICENSING FROM NIH TECHNOLOGY TRANSFER OFFICE

Potential Use of anti-IgE in the Treatment of Lupus Nephritis

The inventors have used a *Lyn* ^{-/-} mouse model that develops an autoimmune disease exhibiting some features of human SLE. Using this model the inventors identified basophils & self-reactive IgEs as important components in development of autoantibody-mediated kidney disease. The inventors found that depletion of basophils or the absence of IgE causes a considerable reduction in autoantibody production and preserves kidney function in the *Lyn* ^{-/-} mice. The inventors’ work demonstrates that IgE immune complexes can activate basophils and that removal of self-reactive IgEs that form functional circulating immune complexes prevents kidney disease. Further, the inventors have shown that basophils are contributors to the production of the self-reactive antibodies that cause lupus-like nephritis in the *Lyn* ^{-/-} mice.

A Highly Potent Human sRAGE Protein for Treating Vascular Disease, Injury, or Inflammation

The administration of sRAGE has been used to treat atherosclerosis and arterial restenosis in animal models. The inventors established a way to produce human sRAGE with more than 1000-fold greater potency than current methods. Production of full length human sRAGE in cultured mammalian cells enables addition of mammalian post-translational modifications that dramatically enhance potency.

To view full descriptions of these technologies and to find others available for licensing, please click [here](#).

PATIENT ORGANIZATION EVENTS

<p>American Pain Society</p> <p>Annual Scientific Meeting May 17-19, 2012 Honolulu, Hawaii</p> <p>Click here for more details.</p>	<p>Cambridge Healthtech Institute</p> <p>Targeting Pain with Novel Therapeutics June 6-7, 2012 Philadelphia, Pennsylvania</p> <p>Click here for more details.</p>	<p>Arthritis Foundation</p> <p>Juvenile Arthritis Conference July 19-22, 2012 Indianapolis, Indiana</p> <p>Click here for more details.</p>	<p>American College of Rheumatology</p> <p>Annual Scientific Meeting November 9-14, 2012 Washington, D.C.</p> <p>Click here for more details.</p>
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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.

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

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. 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

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](#).