Prompted in part by a successful clinical trial conducted at the National Institutes of Health (NIH), the U.S. Food and Drug Administration (FDA) recently approved the use of anakinra (Kineret) for treating the signs and symptoms of a rare but debilitating disease called neonatal-onset multisystem inflammatory disease (NOMID). The disease strikes within the first weeks of life and, if left untreated, can lead to hearing and vision loss, cognitive impairment and physical disability. Anakinra, originally FDA-approved for the treatment of rheumatoid arthritis, is the first FDA-approved treatment for NOMID.

The approval comes in response to an application from the Swedish Orphan Biovitrum (Sobi), an international company focused on developing treatments for rare diseases, particularly inflammatory and genetic disorders. Sobi filed the application after Dr. Raphaela Goldbach-Mansky of NIH’s National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) and colleagues found in a clinical trial that the drug was able to improve disease symptoms including rash, joint pain and headaches. When study participants took it at sufficiently high doses, it also suppressed the persistent inflammation associated with the disease, and therefore curbed the progression of organ damage.

Data from this study also indicated that young patients who had not yet experienced inflammation-related hearing loss, vision loss or central nervous system damage were able to avoid significant organ damage for up to three years—the time of follow up on the study. Although more data are needed to confirm these findings, the researchers suggested that treatment early in life—before organ damage occurs—may confer maximum benefit.

NOMID affects numerous organs and body systems, including the skin, joints, eyes and central nervous system. It results when an immune system protein called interleukin-1 is overproduced. Prolonged inflammation in multiple organ systems causes irreversible damage and loss of function. Up to 20 percent of untreated children with NOMID do not live to adulthood.

For more information on this article, please click [here](#).
On March 21, 2013, the Psychopharmacologic Drugs Advisory Committee met to discuss the new drug application (NDA) 204442, PROBUPHINE (buprenorphine hydrochloride and ethylene vinyl acetate) subdermal implant, submitted by Titan Pharmaceuticals, Inc., and its safety and efficacy for the proposed indication of maintenance treatment of opioid dependence. Titan Pharmaceuticals provided efficacy data from two placebo-controlled trials, and the submission included safety data from 262 unique patients who were treated with Probuphine, of whom 201 received one course of treatment (24 weeks) and 82 received a second course of treatment (a total of 48 weeks).

For more information on the meeting, including a full webcast, please go here.

On January 23, 2013, NCATS Director Chris Austin, M.D., led his first joint meeting of the NCATS Advisory Council and Cures Acceleration Network (CAN) Review Board. In his director’s report, Austin commented on NCATS initiatives, programs, and policies. He summarized the Center’s accomplishments over the last three months, shared budget and staff updates, and emphasized research advances. For more information or a complete video cast of the meeting, please click here.

On December 11, 2012, NCATS partnered with stakeholders in the regulatory, academic, nonprofit, and private sectors to prioritize policy goals and issues and gain perspective on how policy research and analysis can inform translational research. The purpose of the meeting was to gather thought leaders who could provide advice to NCATS leadership on proactively integrating a policy research and analysis agenda in the Center’s mission. By expanding knowledge of relevant policy issues, NCATS leadership hope to build an agenda that can more productively impact the development of cures and treatments.

Discussion sessions focused on informing regulatory science, navigating intellectual property challenges, streamlining clinical research, and forming effective strategic alliances. For more information on this meeting, please click here.

**NIAMS FUNDING ANNOUNCEMENTS**

**PAR-12-236** Identification and Analysis of Causal Variants: Follow-Up on Genome-Wide Association Studies for Arthritis and Musculoskeletal and Skin Diseases (R01) – November 20, 2013

**PA-12-209** Functions of Skeletal Muscle beyond Contraction (R01) – September 7, 2015

**PA-12-191** Multiplex Assay Development for Arthritis and Musculoskeletal and Skin Diseases (R43/44) – August 5, 2015

**RFA-AR-14-002** Core Centers for Musculoskeletal Biology and Medicine (P30) – July 1, 2013

**RFA-AR-13-001** Skin Diseases Research Core Centers (P30) – September 20, 2013

**NOT-AR-14-003** Notice of Intent to Publish a Funding Opportunity Announcement for Core Centers in Musculoskeletal Biology and Medicine (P30) — July 1, 2013

For more information or to find more funding opportunities, please click here.
**Muramyl Dipeptide as a Therapeutic Agent for Inflammation**

The nucleotide-binding oligomerization domain 2 (NOD2) protein plays a key role in innate immunity as a sensor of muramyl dipeptide (MDP), a breakdown product of bacterial peptidoglycan. Bacterial peptidoglycan promotes the innate immune response through the activation of Toll-like receptor 2 (TLR2), which ultimately provokes inflammation. Activation of NOD2 by MDP negatively regulates the activity of TLR2, and thus reduces inflammation.

The technology includes methods of treating or preventing inflammation associated with an autoimmune disorder, particularly inflammatory bowel disease, via administration of muramyl peptide; also included are methods of reducing symptoms characteristic of inflammation via administration of muramyl peptide.

**Novel Methods for Reducing Inflammation and Treating Diseases such as Parkinson’s and Alzheimer’s Disease**

Activated microglia mediate inflammation in the CNS by secreting various cytokines and free radicals that could damage neurons. Brains from patients with Parkinson disease show microglia reaction, and previous studies by this laboratory show microglia activation leads to inflammation mediated dopaminergic degeneration. Thus identification of drugs that reduce microglia activation could prevent or reverse neuronal degeneration in Parkinson’s Disease, Alzheimer’s Disease, ischemia and other degenerative CNS disorders.

Considerable research has shown the ability of various peptides to attenuate microglia activation and prevent neuronal degeneration in vitro with a bi-modal dose response curve. These peptides demonstrate maximum effects at femto-molar and micro-molar concentrations. These inventors have now discovered small-peptide and non-peptide molecules that also inhibit microglia and prevent neuronal degeneration with the same bi-modal dose response curve. The non-peptide compounds have also been shown to prevent dopamine neuronal degeneration in animal models. The present invention provides compositions and methods for inhibiting inflammatory mechanisms and treating inflammation-related condition by administering ultra-low (femto-molar) doses of at least one compound of the invention. These compounds include morphinans, opioid peptides, and the tripeptide GGF.

**Pain Control by Selective Local Ablation of Nociceptive Neurons**

The vanilloid receptor (VR) is a cation channel predominantly expressed on the peripheral processes and perikarya of nociceptive primary afferent neurons. Previous studies have shown that activation of the peripheral receptors by agonists such as capsaicin from hot peppers, or the much more potent resiniferatoxin, produces acute pain sensation which may be followed by desensitization. These inventors discovered that administration of VR agonists in the vicinity of neuronal cell bodies expressing the VR receptor can actually destroy those cells. To control pain and inflammatory disorders, the present invention provides methods and kits for the selective ablation of pain sensing neurons. For example, the intraganglionic administration of a VR agonist selectively ablates primary afferent nociceptive neurons without impairing other sensory modalities. This invention will greatly enhance the ability to control pain, inflammation and other conditions mediated by nociceptive neurons while sparing mental function and other sensations.

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

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### PATIENT ORGANIZATION EVENTS

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<tr>
<th>American Academy of Pain Medicine</th>
<th>American College of Rheumatology</th>
<th>Inflammation Research Association</th>
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<tr>
<td>29th Annual Meeting&lt;br&gt;April 10-12, 2013&lt;br&gt;Philadelphia, PA</td>
<td>2013 State of the Art Clinical Symposium&lt;br&gt;April 20-21, 2013&lt;br&gt;Chicago, Illinois</td>
<td>11th World Congress on Inflammation&lt;br&gt;September 21-25, 2013&lt;br&gt;Natal, Brazil</td>
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Click [here](#) for more details.
PANDEMIC AND ALL-HAZARDS PREPAREDNESS (PAHPA) REAUTHORIZATION ACT UPDATES

On March 14, 2013, President Obama signed into law the Pandemic and All-Hazards Preparedness (PAHPA) Reauthorization Act, which reauthorizes the Project BioShield and Special Reserve Fund provisions of PAHPA. The legislation also requires the FDA to develop a formal process for regulatory management plans through which companies can obtain scientific feedback on the development and regulatory review of eligible medical countermeasures (MCMs). In addition, it expanded MCMs to include noninfectious agents, opening the door for biotech companies pursuing products that could be used in national emergencies.

Congress established Project BioShield in 2004 and provided it with 10 years of guaranteed funding. PAHPA was first passed in 2006, and it granted further authority to facilitate BioShield implementation. This legislation established the Biomedical Advanced Research and Development Authority (BARDA) within HHS to coordinate and fund the acceleration of MCM advanced research and development. Since that time, the government has strategically invested in a diverse set of products to treat, diagnose, or prevent a range of pathogens and toxins identified as significant national threats. BARDA awards grants and contracts to develop and purchase medical countermeasures (MCMs), and Project BioShield provides incentives for companies to develop those countermeasures.

The reauthorization of PAHPA demonstrates our nation’s commitment to prioritizing health preparedness and response when confronted by national security issues.

For more information on this legislation, please click here.

FINANCIAL SERVICES LEGISLATION UPDATES

On February 14, Representative Patrick McHenry (R-NC) introduced H.R. 701, a bill to speed the implementation of Regulation A, a key provision in the Jumpstart Our Business Startups (JOBS) Act that will increase access to capital for growing companies, such as biotech innovators.

BIO supports expeditious and effective implementation of the JOBS Act and efforts to incentivize and encourage capital formation for emerging biotech companies.

Before the JOBS Act was enacted, Regulation A allowed companies to conduct direct public offerings of up to $5 million; the JOBS Act increased the offering limit to $50 million. Once these changes are implemented, Regulation A will spur fundraising for emerging biotech companies, for which a $50 million capital influx could support groundbreaking research and stimulate job creation.

Eight of the eleven biotech IPOs since the JOBS Act was signed into law were undertaken by emerging growth companies using the IPO On-Ramp. Other provisions of the JOBS Act, including a new crowdfunding pathway and reforms to SEC Regulations A and D, are still awaiting rulemaking at the SEC.

The JOBS Act provided implementation deadlines for Regulation D (July 4, 2012) and crowdfunding (December 31, 2012). Rep. McHenry’s legislation would add an implementation deadline of October 31, 2013 for the Regulation A reforms. Companies cannot take advantage of these capital formation provisions until the SEC Acts.

R&D TAX CREDIT EXTENSION

On January 1, 2013, Congress passed fiscal cliff legislation which included a year-end tax extenders package that extended the R&D credit through the end of 2013. BIO strongly supports the provisions of this credit and has continued to work to make the credit permanent. To read BIO’s press release, click here.
BIO ENGAGES WITH FEDERAL AGENCIES

BIO Comments on Final SBIR Rule
On December 31, 2011, President Obama signed into law a bill reauthorizing 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.

When BIO began its advocacy to reform the SBIR program, it had two primary goals: 1) Allow majority venture-backed companies to once again be able to participate in the SBIR program; and 2) Reform the affiliation rules so that SBIR applicants are not affiliated with their investors’ portfolio companies simply on the basis of shared investors and not on any actual mutual control or shared businesses practices.

The SBA published a proposed rule on changes to ownership and affiliation eligibility rules pursuant to the reauthorization and also released a policy directive to agencies participating in the SBIR program. BIO submitted comments to SBA regarding the policy directive, which can be read here.

On December 27, 2012, SBA published a final rule for determining ownership, affiliation, and size standards. SBA adopted many of BIO’s recommendations on exception for portfolio companies, calculation of stock ownership, identify of interest, and newly organized concerns.

The final rule was effective January 28, 2013, and can be viewed here.

BIO Comments on Nasdaq Internal Audit Function Proposal
On March 4, Nasdaq filed a proposed rule change with the SEC that would require listed companies to have an internal audit function. The stated goal of the rule is to ensure that listed companies have a mechanism in place to assess their system of internal controls. BIO submitted comments asking the SEC to disapprove the proposed rule, as this requirement would be extremely costly and duplicative with SOX 404(a) and 404(b) for growing biotech companies.

To read BIO’s comment letter, please click here.

RHEUMATOLOGY / INFLAMMATION / ANESTHESIA / PAIN-FOCUSED LEGISLATION

H.R. 1366—To direct the Commissioner of Food and Drugs to modify the approval of any drug containing controlled-release oxycodone hydrochloride to limit such approval for the use to relieve severe-only instead of moderate-to-severe pain, and for other purposes
- Status: Referred to the House Committee on Energy and Commerce

H.R. 1339—To amend the Public Health Service Act to increase the number of permanent faculty in palliative care at accredited allopathic and osteopathic medical schools, nursing schools, and other programs, to promote education in palliative care and hospice, and to support the development of faculty careers in academic palliative medicine
- Sponsor: Rep. Eliot Engel (NY016)
- Status: Referred to the House Committee on Energy and Commerce

This bill would direct the Secretary of Health and Human Services, in conjunction with the Director of the Centers for Disease Control and Prevention, to develop and disseminate to school administrators, et al, public education and resources that increase education of cardiomyopathy among school administrators and families.
- Sponsor: Rep. Frank Pallone (NJ-6)
- Status: Referred to the House Subcommittee Committee on Health

On February 20, 2013, The Michael J. Fox Foundation for Parkinson’s Research (MJFF) launched a series of new funding programs. All programs are open to both academic and industry researchers and the Foundation estimates allocating $55 million in 2013 to research programs.

MJFF seeks projects promoting drug development for Parkinson’s disease around exciting therapeutic pathways and targets, including but not limited to programs on alpha-synuclein and LRRK2. Access to MJFF’s growing inventory of pre-clinical and clinical tissues and resources to address promising Parkinson’s ideas will also be made available.

More information and application instructions can be found at https://www.michaeljfox.org/research/apply-for-grant. For questions about how MJFF works with industry, please contact Tracey Mumford, Senior Associate Director of Research Partnerships at tmumford@michaeljfox.org.

To receive email updates about MJFF research programs and other news, write to research@michaeljfox.org.


Beginning March 1, a series of automatic spending cuts known as sequestration took effect. Of the $1.2 trillion slated to take effect over the next 10 years, $85 billion is scheduled for this year. Across the board cuts for 2013 include the calculated equivalent of a 5.8% cut from the NIH budget and an 8.2% reduction from the FDA budget.

On March 21, the House gave final approval to a continuing funding resolution that outlines spending through the end of the fiscal year, September 30. It ensures that government agencies will stay open after the current funding measure expired on March 27. A broader battle over taxes and spending for the year is still a central topic in Washington and will continue throughout the year.