



## **Roche Licenses First-in-Class Treatments for Chronic Pain to Afferent Pharmaceuticals; Afferent Secures \$23 Million in Series A Financing**

*- Pappas, Third Rock, Domain and New Leaf Launch New Company Centered on Novel Pain Management Technology; Afferent to Initiate Clinical Trials in First Half of 2010 -*

**Basel, Switzerland and Palo Alto, Calif., 16 December 2009** – Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today it has licensed its P2X3<sup>1</sup> receptor program aimed at developing first-in-class treatments for chronic pain to Afferent Pharmaceuticals. Afferent was co-founded by Anthony Ford, Ph.D., Pappas Ventures, and Third Rock Ventures, and is focused on developing compounds that treat chronic pain by targeting a novel biological pathway. In conjunction with this announcement, Afferent successfully closed a \$23 million Series A financing, which was led by Third Rock Ventures and Pappas Ventures, and included Domain Associates and New Leaf Venture Partners. Proceeds from the financing will be used to accelerate the development of P2X3 receptor targeted pain therapies.

More than 270 million people worldwide suffer from chronic pain. While product reformulations or combinations of established molecules have led to new product introductions, there has been little recent success in identifying novel mechanisms for successfully managing and treating pain. Existing therapeutic approaches such as opioids, antiepileptic drugs and non-steroidal anti-inflammatory drugs, including COX-2 inhibitors, have documented drawbacks in inadequately addressing patient needs and presenting safety, efficacy, tolerability and addiction concerns.

“A major drawback of existing pain medications is their lack of specificity for pain pathways,” commented Dr. Ford, who will serve as chief scientific officer of Afferent. “Afferent is poised to lead the way with an entirely novel, targeted mechanism for treating chronic pain. Research shows that P2X3-containing receptors are highly specific to nerve fibers that transmit the sensations of pain and discomfort in response to inflammation or injury, particularly in chronic conditions. P2X3 antagonism represents a breakthrough and potentially transformative approach to treating chronic pain associated with conditions such as osteoarthritis, back pain, visceral pain and neuropathy. Our preclinical and clinical data on this program suggest a very compelling first-in-class, orally delivered product, and we look forward to initiating clinical trials to test the safety and efficacy of the lead product candidate, AF-219, in several indications early in 2010.”

Dr. Ford is a former vice president of research at Roche who initiated and drove the P2X3 program for the last decade, including collaboration with Professor Geoffrey Burnstock of University College London, a leading expert in the P2X3 receptor area. Dr. Ford brings more than 20 years of research and development experience at Roche and Syntex to Afferent. Liam

Ratcliffe, M.D., Ph.D., Afferent Board member and venture partner, New Leaf Venture Partners, will work closely with Dr. Ford and play a key role in advising the company on clinical development strategies. Dr. Ratcliffe is the former senior vice president and development head for Pfizer Neuroscience and brings over 15 years of drug development experience in pain and related indications to the company. Afferent's Board of Directors is chaired by Kevin Starr, partner, Third Rock Ventures, and also includes Arthur M. Pappas, managing partner, Pappas Ventures, Dr. Ratcliffe, and Jesse I. Treu, partner, Domain Associates.

“Understanding how pain is processed at each stage in the peripheral and central nervous system is key to developing safe and effective therapies for the treatment of pain,” commented Dr. Ratcliffe. “We now understand that P2X3 is an important receptor in a variety of pain conditions and provides an opportunity to block pain at its source. We believe Afferent is well positioned to be the leader in P2X3 targeted drugs and fully exploit this opportunity.”

Afferent has exclusively licensed the P2X3 program from Roche. Dan Zabrowski, global head of partnering, Roche commented, “We consider the P2X3 pathway to be an innovative and promising area worthy of further clinical development. Investing this program, related assets and intellectual property in Afferent provides the ideal focused vehicle to ensure this opportunity can be maximized for the potential benefit of the millions of patients suffering from chronic pain. We are very pleased to be collaborating with Dr. Ford and this leading life sciences syndicate to launch Afferent and advance the P2X3 program.”

### **Blocking Pain at its Source**

Treating pain by targeting P2X3 heralds an exciting new approach to pain management, and this program marks the first in a new class of drugs poised to meet the significant unmet needs in pain management. P2X3 receptor subunits are expressed specifically in so-called C-fiber afferent neurons in multiple organ systems including joints and hollow organs suggesting a high degree of specificity to the nociceptive system (the system in the human body that perceives pain). As a result, there is a lower likelihood of adverse effects in the brain or cardiovascular tissues, effects which have been limiting factors for many existing therapeutics. In the periphery, ATP (the factor that triggers P2X3 receptor activation) can be released from various cells as a result of tissue inflammation, injury or visceral distension and may stimulate these local nociceptors. The highly selective distribution of P2X3 and P2X2/3 receptors within the nociceptive system has led to various efforts to clarify the potential role of ATP as a pain mediator. P2X receptor-mediated afferent activation has been implicated in inflammatory, visceral and neuropathic pain, as well as migraine and cancer pain. Additional information regarding P2X3 and Afferent can be found on the company's website at [www.afferentpharma.com](http://www.afferentpharma.com).

### **About Afferent**

Afferent Pharmaceuticals is focused on developing first-in-class medicines to treat chronic pain by targeting P2X3 receptors in nerve fibers. Research shows that P2X3-containing receptors are highly specific to nerve fibers that transmit the sensations of pain and discomfort in response to inflammation or injury, particularly in chronic conditions. P2X3 antagonism represents a breakthrough and potentially transformative approach to treating chronic pain associated with conditions such as osteoarthritis, back pain, visceral pain and neuropathy. The company's lead compound, AF-219, has successfully completed two Phase 1 clinical studies, and is expected to

undergo efficacy testing in several indications starting in 2010. Afferent was launched in December 2009 by Pappas Ventures, Third Rock Ventures, Domain Associates and New Leaf Ventures, and is led by Anthony P. Ford, Ph.D., chief scientific officer and a recognized expert in the P2X3 field.

### **About Roche**

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's largest biotech company with truly differentiated medicines in oncology, virology, inflammation, metabolism and CNS. Roche is also the world leader in in-vitro diagnostics, tissue-based cancer diagnostics and a pioneer in diabetes management. Roche's personalised healthcare strategy aims at providing medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2008, Roche had over 80,000 employees worldwide and invested almost 9 billion Swiss francs in R&D. The company posted sales of 45.6 billion Swiss francs. Genentech, United States, is a wholly owned member of the Roche Group. Roche has a majority stake in Chugai Pharmaceutical of Japan. For more information: [www.roche.com](http://www.roche.com).

### **About Third Rock Ventures**

Third Rock Ventures is a premier venture firm focused on life sciences, investing and launching companies that make a difference in people's lives. Collaborating with entrepreneurs, the Third Rock team applies its deep expertise to establish the roadmap and building blocks for a rapidly-growing and highly-successful life sciences company. The Third Rock team has a unique vision and experience in building great companies, extensive academic and industry networks and a collective track record for creatively managing the value creation path to deliver exceptional performance. For more information, please visit [www.thirdrockventures.com](http://www.thirdrockventures.com).

### **About Pappas Venture**

Founded in 1994, Pappas Ventures invests exclusively in the life sciences sector – biotechnology, biopharmaceuticals, drug delivery, medical devices and related ventures. Pappas Ventures has more than \$350 million in capital under management, and has guided the launch and/or development of more than 50 life sciences companies, including Cerexa (acquired by Forest Laboratories), Peninsula Pharmaceuticals (acquired by Johnson & Johnson), Syntonix (acquired by Biogen IDEC), NuVasive (IPO), and Arena Pharmaceuticals (IPO). For more information about Pappas Ventures, please visit [www.pappasventures.com](http://www.pappasventures.com).

### **About New Leaf Venture (NLV) Partners**

NLV Partners is a life science-dedicated venture capital firm with offices in Menlo Park and New York. Founded by an experienced team of venture capitalists with deep healthcare industry experience, NLV Partners invests primarily in companies focused on clinical-stage biopharmaceutical products, early-stage medical devices and molecular diagnostics. NLV Partners manages over \$1.3 billion of assets, including NLV-I, NLV-II and the healthcare technology portfolio of Sprout Group. For further information, visit the NLV Partners website at [www.nlvpartners.com](http://www.nlvpartners.com).

### **About Domain Associates**

Founded in 1985, Domain Associates, L.L.C. is a venture capital firm with an exclusive focus on life sciences. With \$2.5 billion of capital under management, Domain has offices in Princeton, NJ and San Diego, CA. Domain's three major investment segments are pharmaceuticals, specialty pharmaceuticals, and medical devices, while additional areas of interest include biomaterials, bioinstrumentation, and diagnostics. The Partners of Domain have a total of close to 200 person-years of experience among them in the healthcare/venture capital industries and have been involved in the formation and growth of more than 210 life-sciences companies. For further information, visit [www.domainvc.com](http://www.domainvc.com).

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<sup>i</sup> The lead compound licensed to Afferent was RO 4926219, is in Phase 1 and otherwise known as RG1646

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