



## **Afferent Pharmaceuticals Presents Data Supporting Use of P2X3 Antagonists in Reducing Bone Cancer Pain**

Preclinical Findings Presented at the 13<sup>th</sup> World Congress on Pain in Montreal

**Montreal, Canada, September 1, 2010** – Afferent Pharmaceuticals, a clinical-stage biopharmaceutical company developing first-in-class, small molecules that target P2X3 receptors, today announced preclinical *in vivo* results demonstrating that an investigational P2X3 receptor antagonist significantly prevented and reversed bone cancer pain behavior in comparison to vehicle controls. These data expand on earlier findings and reveal that a marked reduction in apparent bone cancer pain occurs following oral administration of the proprietary P2X3 antagonist. Results from the study were presented in a poster session at the 13<sup>th</sup> World Congress on Pain in Montreal, Canada.

The study, co-authored by Anthony Ford, Ph.D., Founder and Chief Scientific Officer of Afferent Pharmaceuticals, was highlighted in a poster presentation titled, “P2X3 and P2X2/3 Antagonist as a Novel Bone Cancer Pain Treatment - In Vivo and In Vitro Mechanistic Insights.” According to Dr. Ford, the study showed P2X3 antagonists reduced bone cancer pain behavior by dampening down dorsal horn neuronal activity, in addition to reducing activation of extracellular-signal regulated kinase (ERK) in dorsal root ganglion (DRG) neurons. The effects of the proprietary P2X3 antagonist on dorsal horn neuronal pathophysiology were investigated using *in vivo* electrophysiology measures, which allowed characterization of neuronal responses to mechanical, thermal and electrical stimuli. To study the intracellular pain sensing mechanisms in primary afferent neurons, a novel, *in vitro* co-culture system was created, combining MRMT-1 carcinoma cells and DRG neurons. ERK activation was decreased in the presence of the antagonist, AF-353.

“The results of this study capture some of the mechanistic elements that may support the use of P2X3 antagonists to treat bone cancer pain,” commented Dr. Ford. “P2X3 receptors are preclinically well-validated targets, highly specific to unmyelinated, C fiber afferent nerves that have dense innervations in visceral organs, skin and joints. These small diameter fibers transmit sensations of pain and irritation via mechanisms that include ATP signaling. ATP released from cancer cells appears capable of driving peripheral sensitization, while P2X3 signaling in the dorsal horn is clearly adding central sensitization, and together these give rise to chronic cancer pain.”

Dr. Ford added, “P2X3 receptors have limited distribution beyond sensory nerves and no significant expression in the higher centers of the brain. A highly specific and targeted approach to chronic pain therapy, including bone cancer pain, is expected to provide patients with a safer and more effective alternative to current treatments. Clinical treatments of bone cancer pain remain limited and often result in significant adverse side effects.”

Authors of the poster were T. K. Kaan, P. K. Yip, S. Patel, M. Davies, F. Marchand, P. A. Nunn, A. H. Dickenson, A. P. Ford, Y. Zhong, M. Malcangio and S. B. McMahon.

Results from the study were simultaneously published in the September issue of *Brain*.

### **About Afferent Pharmaceuticals**

Afferent Pharmaceuticals is a clinical-stage biopharmaceutical company developing first-in-class, small molecule compounds that target P2X3 receptors for the treatment of chronic pain and irritative conditions. Validated in numerous preclinical models, P2X3 is highly specific to types of sensory nerves (C fiber afferents) that transmit sensations of pain and irritation via ATP signaling. Afferent’s singular focus and industry-leading position on P2X3 antagonism enables the Company to widely explore this novel mechanism of action and evaluate its utility in a broad range of indications. These indications include chronic pain in the joints and visceral organs and irritative conditions of the lungs and bladder.

Founded in December 2009, Afferent is building on over a decade of research on P2X3 antagonists. The Company currently has compounds in clinical and preclinical studies, in addition to a substantial and diverse library of small molecules that selectively target P2X3 receptors. Afferent’s lead compound, AF-219, is being prepared for entry into Phase 2 clinical testing in patients with osteoarthritis, interstitial cystitis/bladder pain syndrome and chronic cough.

Afferent Pharmaceuticals is located in San Mateo, California. Afferent is financed by the premier investors Domain Associates, New Leaf Venture Partners, Pappas Ventures and Third Rock Ventures.

For more information on the Company, please visit Afferent’s website at [www.afferentpharma.com](http://www.afferentpharma.com).

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