



**Cypress’ “Pain Assessment in Patients with Fibromyalgia Syndrome: A Consideration of Methods for Clinical Trials”  
Published in *Clinical Journal of Pain***

**Electronic Diaries Demonstrate Improved Patient Compliance When Used in Fibromyalgia Clinical Trials**

San Diego, California, October 11, 2004 – Cypress Bioscience, Inc. (Nasdaq:CYPB) announced today that a publication of a study in the *Clinical Journal of Pain* showed that, in clinical trials, pain assessment methods relying on recall could contribute to an apparent improvement in pain over time in the absence of a true therapeutic effect; such a methodological characteristic would constitute a component of a placebo response. Future clinical trials should consider using a real-time approach to pain assessment, which in this study appeared to mitigate against elevated baseline pain scores. In addition, patient compliance was also better when using the real-time approach to pain assessment.

“We find that the electronic diary approach to pain assessment is consistent and reliable, providing what we believe to be a more accurate depiction of a patient’s true pain status, eliminating the psychological impact of the visit to the doctor’s office,” commented Dr. Gendreau.

For conditions like fibromyalgia syndrome, the accurate assessment of patient reported pain over time is an essential component of the clinical trials. Cypress’ clinical studies in fibromyalgia syndrome are distinguished by the use of novel assessment tools developed by the company in conjunction with invivodata™.

The publication summarizes a pilot study comparing multiple approaches to the assessment of clinical pain during trials involving patients diagnosed with fibromyalgia syndrome. Patient’s self-report of pain was assessed with: 1) an electronic pain diary (ED), in which the patients recorded their symptoms on a “real time” basis – this provides greater ability to receive accurate information rather than having the patient try and remember how they felt at periodic time points; 2) end-of-week reports collected on a recall basis on Friday evenings using the ED, and 3) on a monthly basis during in-clinic visits using traditional pencil and paper scoring.

The average compliance to patient pain reporting using the electronic diary was 85%, meaning that on average, patients completed 85% of prompted inquiries about their pain on the electronic diary. This compliance level was superior to the compliance measured for the in-clinic based methods when considering missed or rescheduled clinic visits.

Results of the study showed that significantly different baseline (initial) values were obtained when using each of these approaches. Paper and pencil produced the highest baseline pain scores, and real-time pain reports produced the lowest baseline pain scores. Over time, the difference in scoring between the ED and paper and pencil methods decreased. When comparing baseline to endpoint pain scores, this led to an apparent improvement in pain over time when comparing the recall based methods to the real time ED methodology.

The publication, entitled “Pain Assessment in Patients With Fibromyalgia Syndrome: A Consideration of Methods for Clinical Trials”, appeared in the September-October 2004 issue of Clinical Journal of Pain [Sep-Oct;20(5):348-356], and was co-authored by R. Michael Gendreau, MD, PhD, Cypress’ Chief Medical Officer, and David A. Williams, PhD, Michael R. Hufford, PhD, Kimberly Groner, MSN, Richard H Gracely, PhD, and Daniel J. Clauw, MD.

Earlier this year Cypress Bioscience, Inc. (NASDAQ: CYPB) and Forest Laboratories, Inc. (NYSE: [FRX](#)) announced that they entered into a collaboration agreement for the development and marketing for Cypress’ product, milnacipran, licensed from the product’s originator, Pierre Fabre Médicament, for indications in the United States market. Milnacipran is currently being evaluated in a Phase III program that was commenced in October 2003 for the treatment of Fibromyalgia Syndrome (FMS). Fibromyalgia is a frequent cause of chronic, widespread pain, and there are currently no products approved for the treatment of FMS.

### **About Milnacipran**

Milnacipran is a novel compound that exerts its effect by inhibiting the reuptake of norepinephrine, known to play an essential role in regulating pain, and other neurotransmitters, including serotonin and NMDA. It has been approved for the treatment of non-pain indications in 32 countries and has been used safely by more than 3 million patients during more than six years of commercial availability outside the U.S.

### **About Fibromyalgia**

FMS is considered one of a group of related chronic pain syndromes characterized by both physical and psychiatric symptoms that include conditions such as irritable bowel syndrome (IBS), chronic tension headache, non-cardiac chest pain, and certain types of lower back pain. FMS is estimated to affect six to twelve million people in the United States. FMS is most often diagnosed in the primary care setting and in addition is the second most commonly diagnosed condition in rheumatology clinics in the United States after osteoarthritis.

### **About Cypress Bioscience, Inc.**

Cypress is committed to be the innovator and leader in providing products that improve the treatment of Functional Somatic Syndromes, including Fibromyalgia Syndrome (FMS), and other related Pain and Central Nervous System conditions. Cypress’ strategy involves acquiring/in-licensing undervalued central nervous system active compounds and developing them for new indications.

In August 2001, Cypress licensed from Pierre Fabre Medicament its first product for clinical development, milnacipran. The license agreement provides Cypress with an exclusive license to develop and sell any products with the compound milnacipran as an active ingredient for any indication in the United States and Canada. On January 9, 2004, Cypress entered into a collaboration agreement with Forest Laboratories for the development and marketing of milnacipran. In October 2003, Cypress began initiating its Phase III clinical trials for the use of milnacipran as a potential treatment for FMS. We are continuing to evaluate various potential strategic transactions, including the potential acquisition of products and companies, and other alternatives that we believe may enhance stockholder value.

For more information about Cypress, please visit the Company's web site at [www.cypressbio.com](http://www.cypressbio.com).

*This press release, as well as Cypress' SEC filings and web site at <http://www.cypressbio.com>, contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 including statements about the potential of milnacipran to treat FMS and other related Functional Somatic Syndromes and entering into a strategic transaction. Actual results could vary materially from those described as a result of a number of factors, including those set forth in Cypress Annual Report on Form 10-K, the most recent Quarterly Report on Form 10-Q and any subsequent SEC filings. In addition,*

*there is the risk that we and Forest Laboratories may not be able to successfully develop or market milnacipran or any other products for the treatment of FMS and other related Functional Somatic Syndromes, and, as a result, would not receive any milestone or royalty payments from Forest Laboratories; that we and Forest Laboratories may encounter regulatory or other difficulties in the development of milnacipran for FMS, including delays in completing Phase III trials; that we may not be able to protect our patents or proprietary technology; that milnacipran may not significantly improve the treatment of FMS or any other related Functional Somatic Syndrome; that we may not be successful in identifying, licensing and developing any additional products or companies and even if we complete any such transaction, it may not enhance stockholder value. Cypress undertakes no obligation to revise or update these forward-looking statements to reflect events or circumstances after the date of this press release, except as required by law.*

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