



**CYPRESS BIOSCIENCE, INC. ANNOUNCES RESULTS DEMONSTRATING THE  
SUPERIORITY OF ELECTRONIC DIARY AS A METHOD TO RECORD PAIN  
ASSESSMENTS**

**Traditional diary methodologies shown to elevate the placebo response**

**FOR IMMEDIATE RELEASE**

San Diego, California, March 24, 2003 – Cypress Bioscience, Inc. (NASDAQ: CYPB) today announced data demonstrating the superiority of electronic diaries over traditional pen and paper diaries for obtaining patient self-report information on pain in a clinical trial setting. These results were presented at the 22<sup>nd</sup> Annual Scientific Meeting of the American Pain Society in Chicago.

Paper diaries have been used for many years to obtain patient self-report data on a wide range of symptoms and conditions. Compliance to diary protocols is paramount to ensuring accurate and unbiased data. If subjects fail to complete their diary reports in a timely fashion, or if they back-fill reports after the fact, the data will be subject to recall bias. Electronic diaries show promise as superior tools for the recording of reliable pain data in patients with chronic pain conditions. Electronic diaries offer many advantages that are not available with traditional paper based systems, such as the ability to time and date stamp the entry, to only allow entries within defined time windows, and to upload the data to the clinic so that early intervention is possible in the case of a non-compliant patient. Based on previous studies suggesting that electronic diaries would allow the collection of data that more accurately reflects subjects' pain during a clinical trial, participants in Cypress' Phase II trial evaluating milnacipran as a treatment for fibromyalgia syndrome carried an electronic diary for the frequent recording of pain and other symptoms. Traditional pain assessments were also performed for comparison purposes.

The results presented at the American Pain Society meeting confirmed that the frequent sampling possible with the electronic diary lead to lower baseline pain scores than those obtained from the infrequent sampling of the traditional pen and paper approach. However, this difference becomes less pronounced over the course of the study. As a result, by virtue of the artificially high scoring of pain at baseline, there is a measure of "placebo response" intrinsic to the sampling methodology.

"Our successful experience with electronic diaries in measuring the improvement of pain scores in fibromyalgia patients treated with milnacipran supports the case for adopting this technology as the gold standard for future clinical trials in analgesic drug development," commented R. Michael Gendreau, MD, PhD, Chief Medical Officer of Cypress Bioscience, Inc.

Milnacipran is the first in a new class of oral therapeutics known as Norepinephrine Serotonin Reuptake Inhibitors (NSRIs) that decrease the uptake of both norepinephrine

and serotonin, but with a preference for norepinephrine. These two neurotransmitters are known to play an essential role in regulating pain and mood. In the recently completed double-blind, placebo-controlled, flexible dose escalation monotherapy trial evaluating the safety and efficacy of milnacipran in treating patients with fibromyalgia syndrome, milnacipran was shown to statistically improve a number of primary and secondary hallmark symptoms of fibromyalgia syndrome, including occurrence/intensity of pain and overall well-being.

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

Cypress is committed to be the innovator and commercial leader in providing products for the diagnosis and treatment of patients with Functional Somatic Syndromes, such as Fibromyalgia Syndrome, or FMS, and other related chronic pain and central nervous system disorders. In August 2001, Cypress licensed from Pierre Fabre Medicament its first product for clinical development, milnacipran. Milnacipran, the first of a new class of agents known as NSRIs, or Norepinephrine Serotonin Reuptake Inhibitors, shares a pharmacological profile with the tricyclic antidepressants (TCAs), considered the most effective drugs for treatment of FMS, while appearing to lack the side effects associated with the latter. Cypress recently completed a Phase II trial in which milnacipran is being evaluated as a potential treatment for FMS. For more information about Cypress, please visit the Company's web site at [www.cypressbio.com](http://www.cypressbio.com). For more information about FMS, please visit [www.FMSresource.com](http://www.FMSresource.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. 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 and any subsequent SEC filings. In addition, there is the risk that we 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; that our clinical development plan or timeline for milnacipran may be delayed; that our current working capital will not allow us to execute our business plans into 2003; that we may encounter regulatory or other difficulties in the development of milnacipran for FMS; and that milnacipran may not significantly improve the treatment of FMS or any other related Functional Somatic Syndrome. 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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