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## **Cypress Bioscience Drug Milnacipran May Act through Multiple Mechanisms New Data Suggests Distinct Effects on Pain and Mood**

SAN DIEGO, CA – May 29, 2003 – Cypress Bioscience, Inc. (NASDAQ: CYPB) announced today that clinical results with its lead product, milnacipran, appear to demonstrate distinct mechanisms for the agent's effects on pain and mood in patients with Fibromyalgia Syndrome (FMS) as presented in a poster presentation by R. Michael Gendreau, M.D., Ph.D., Chief Medical Officer of Cypress Bioscience, Inc. The poster, entitled "Development of Milnacipran, A Dual Reuptake Inhibitor for the Treatment of Chronic Pain Associated with Fibromyalgia," is being presented today at the annual New Clinical Drug Evaluation Unit (NCDEU) meeting, sponsored by the National Institutes of Mental Health (NIMH) in Boca Raton, Florida.

In the study, twice-daily dosing of milnacipran was associated with statistically significant improvements in multiple measures of clinical pain. Other symptoms, including fatigue, mood and patient global improvement reports, were significantly improved in both the once-daily and twice-daily dosing groups, and achieved statistical significance on many of these secondary measures. These findings suggest different therapeutic mechanisms may be operative within different symptom domains of FMS.

Milnacipran is a first-in-class Norepinephrine Serotonin Reuptake Inhibitor (NSRI) in late-stage clinical development for the treatment of FMS. Pharmacologically, this agent is differentiated from the Selective Serotonin Reuptake Inhibitors (SSRIs), as well as from the Serotonin Norepinephrine Reuptake Inhibitors (SNRIs), by its preferential blockade of norepinephrine (NE) reuptake over serotonin (5-HT) reuptake. Milnacipran's NE/5-HT profile most closely mimics that of the tricyclic antidepressants (TCAs), a class of compounds with demonstrated effectiveness in FMS. One of milnacipran's potential benefits is that it lacks the other drug characteristics that underlie the TCAs' side effects and can limit their tolerability and usage.

The Phase II clinical trial results presented at NCDEU demonstrate the safety and efficacy of milnacipran in treating patients with FMS. A total of 125 patients were enrolled in the trial and were randomized to receive either placebo or milnacipran. Milnacipran was dosed either once or twice a day for four weeks of dose escalation, followed by eight weeks of constant dose. The study evaluated the efficacy and safety of milnacipran for the treatment of pain and associated symptoms such as fatigue, depressed mood, quality of life and ability to sleep.

A Phase III clinical program is currently being planned and is expected to commence before the end of the year.

### **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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