



## **XTL Biopharmaceuticals Announces the In-Licensing of Bicifadine – A Late-Stage Clinical Compound for the Treatment of Neuropathic Pain**

**NEW YORK, NEW YORK, January 16, 2007** – XTL Biopharmaceuticals Ltd. (NASDAQ: XTLB, LSE: XTL, TASE: XTL) announced today that, through a wholly-owned subsidiary, it has signed an agreement with DOV Pharmaceutical, Inc. (PS: DOVP.PK) to in-license the worldwide rights for Bicifadine, a serotonin and norepinephrine reuptake inhibitor (SNRI).

XTL intends to develop Bicifadine for the treatment of neuropathic pain - a chronic condition resulting from damage to peripheral nerves. With 15 million people suffering from neuropathic pain in the United States alone, and limited treatment options available, neuropathic pain represents a significant unmet medical need. According to Datamonitor, the market for neuropathic pain drugs is expected to grow from \$1.8 billion in 2005 to \$5.5 billion by 2015.

Bicifadine is a serotonin and norepinephrine reuptake inhibitor (SNRI). Other members of the SNRI class include Cymbalta® (approved for depression and neuropathic pain), and Effexor® (approved only for depression). Both Cymbalta® and Effexor® have been shown to be efficacious in neuropathic pain. Activity on norepinephrine reuptake is thought to be necessary for anti-depressants to be effective in neuropathic pain.

Compared to the currently approved SNRI's, Bicifadine has a unique ratio of serotonin versus norepinephrine reuptake inhibition, which is weighted toward norepinephrine reuptake inhibition, providing a strong scientific rationale for using Bicifadine for the treatment neuropathic pain indications.

Bicifadine has been tested extensively in over 15 clinical trials involving over 3,000 patients, and has been shown to be safe and generally well tolerated. Bicifadine was evaluated in various pain indications, including two large, randomized clinical trials (n=750 and n=540) in patients suffering from acute (non-neuropathic) pain, where Bicifadine demonstrated statistically significant efficacy.

Dr. Christine Sang, Director of Translational Pain Research at the Brigham and Women's Hospital, Harvard Medical School, commented, "Neuropathic pain continues to be an area of growing unmet medical need, and I believe that Bicifadine represents an exciting potential treatment option. Clinical data clearly support the role of SNRI's for the treatment of neuropathic pain. Based on its mechanism of action that includes a unique ratio of serotonin versus norepinephrine reuptake inhibition, the demonstrated effect of other SNRI's in this disease area, and the activity it has demonstrated in acute pain studies, I have a high degree of confidence that Bicifadine could be successfully developed as a treatment for neuropathic pain."

Ron Bentsur, XTL's Chief Executive Officer, commented, "This is a very important event for XTL, as this in-license transforms us immediately into a late-stage development company. It is rare to come across an opportunity such as Bicifadine, a drug candidate that addresses a multi-billion dollar market, in a class with a proven mechanism of action, and with an established safety profile and clear evidence of activity in the treatment of pain." Mr. Bentsur added, "By re-directing the development of Bicifadine away from the novel indications in acute and chronic pain toward a proven area of efficacy of SNRI's in the treatment of neuropathic pain, we believe we can be the second approved SNRI for neuropathic pain, offering a differentiated efficacy and possibly safety profile based on the drug's emphasis on norepinephrine reuptake inhibition. We are excited to bring Bicifadine on board as our lead compound."

In accordance with the terms of the license agreement, XTL will make an up-front payment of \$7.5 million in cash. In addition, XTL will make milestone payments of up to \$126.5 million, in cash and/or XTL ordinary shares over the life of the license, of which up to \$115 million will be due upon or post approval of the product. XTL is also obligated to pay royalties on net sales of the product to



DOV. In addition, the Company has committed to pay a transaction advisory fee in the form of stock appreciation rights in the amount equivalent to 3% of the Company's current fully diluted ordinary shares, vesting after one year of the close of the transaction, and 7% of the Company's current fully diluted ordinary shares, vesting following successful Phase 3 clinical trial results or the acquisition of XTL. Payment of the stock appreciation rights by XTL can be satisfied, at XTL's discretion, in cash and/or by issuance of the Company's ordinary shares.

## **ABOUT BICIFADINE**

Bicifadine is a serotonin and norepinephrine reuptake inhibitor (SNRI) being developed by XTL for the treatment of neuropathic pain. Bicifadine was licensed by XTL from DOV Pharmaceutical, which originally licensed it from Wyeth Pharmaceuticals.

Four Phase 1 clinical trials and 14 Phase 2 clinical trials involving more than 1,000 patients were conducted by Wyeth or DOV with an IR (immediate release) formulation of Bicifadine. In five exploratory double-blind, placebo-controlled Phase 2 clinical trials of the IR formulation conducted by Wyeth, Bicifadine demonstrated a statistically significant reduction in pain versus placebo, in some cases with an outcome suggesting it might be comparable to or better than positive controls such as codeine. In addition to these trials with the IR formulation, eight Phase 1 clinical trials using the SR (sustained release) formulation have been conducted, a formulation that permits less frequent daily dosing, improves tolerability and for which patents have been filed. It is intended that the SR formulation will be used in future clinical development and for commercial use.

In two additional and larger (n=750 and n=540) single-dose, double-blind, placebo-controlled clinical trials with Bicifadine in the treatment of moderate to severe post-surgical acute dental pain, Bicifadine produced a highly statistically significant, dose-related reduction in pain compared to placebo, and which was comparable to a positive control arm (codeine or Tramadol). Both trials demonstrated Bicifadine to be safe and generally well-tolerated without producing any serious adverse events.

In a Phase 3 double-blind, placebo-controlled, clinical trial (n=325) with Bicifadine in the treatment of moderate to severe acute pain following bunionectomy surgery, statistically significant increases in analgesia were measured as early as 30 minutes after administration and these effects were sustained for the balance of the eight-hour measurement period. In this study, Bicifadine was safe and generally well-tolerated. The complete assessment of the analgesic action of Bicifadine under repeat dosing conditions could not be fully elucidated due to the high level of "rescue" analgesic medication used in both the placebo and active drug groups.

Due to the highly competitive nature of the market for acute pain drugs, and the FDA requirement to complete two repeat-dosing clinical trials in two different acute pain indications, no further studies in acute pain are planned.

Bicifadine has been further evaluated in three Phase 3 trials in Chronic Lower Back Pain (CLBP). The primary efficacy endpoint in these trials was the change in pain severity rating score between baseline and the end of dosing. In these trials, Bicifadine was safe and generally well tolerated, but did not show a statistically significant effect relative to placebo on the primary endpoint of the study at any of the doses tested.

XTL believes that the failure of Bicifadine in the CLBP trials was a result of the inherent heterogeneity of the studied patient population (i.e. the varying causes of CLBP pain), uncontrolled physical activities in what is largely an activity-dependent pain indication, and a high placebo response.

XTL believes that by re-directing the development of Bicifadine away from the novel indications in acute and chronic pain toward a proven area of efficacy of SNRI's in the treatment of neuropathic pain, Bicifadine could be successfully developed to be the second approved SNRI for neuropathic



pain, offering a differentiated efficacy and possibly safety profile based on the drug's emphasis on norepinephrine reuptake inhibition.

## **ABOUT XTL BIOPHARMACEUTICALS LTD.**

XTL Biopharmaceuticals Ltd. ("XTL") is engaged in the acquisition, development and commercialization of therapeutics for the treatment of neuropathic pain and hepatitis C. XTL is developing Bicifadine, a serotonin and norepinephrine reuptake inhibitor, for the treatment of neuropathic pain. In addition, XTL is developing XTL-2125 - a small molecule, non-nucleoside inhibitor of the hepatitis C virus polymerase. XTL-2125 is currently in a Phase 1 clinical trial in patients with chronic hepatitis C. XTL is also developing XTL-6865 - a combination of two monoclonal antibodies against the hepatitis C virus - presently in Phase 1 clinical trials in patients with chronic hepatitis C. XTL's hepatitis C pipeline also includes several families of pre-clinical hepatitis C small molecule inhibitors. XTL also has an active in-licensing and acquisition program designed to identify and acquire additional drug candidates. XTL is publicly traded on the NASDAQ, London, and Tel-Aviv Stock Exchanges (NASDAQ: XTLB; LSE: XTL; TASE: XTL).

### *Contact:*

Ron Bentsur, Chief Executive Officer  
Tel: +1-(212)-531-5960

## **Cautionary Statement**

*Some of the statements included in this press release, particularly those anticipating future clinical and business prospects for our clinical compound for neuropathic pain, Bicifadine, operating strategies and similar matters, may be forward-looking statements that involve a number of risks and uncertainties. For those statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995. Among the factors that could cause our actual results to differ materially are the following: our ability to successfully complete cost-effective clinical trials for the drug candidates in our pipeline which would affect our ability to continue to fund our operations with our available cash reserves, our ability to meet anticipated development timelines for the drug candidates in our pipeline due to recruitment, clinical trial results, manufacturing capabilities or other factors; and other risk factors identified from time to time in our reports filed with the Securities and Exchange Commission and the London Stock Exchange, including our annual report on Form 20-F filed with the Securities and Exchange Commission on May 25, 2006. Any forward-looking statements set forth in this press release speak only as of the date of this press release. We do not intend to update any of these forward-looking statements to reflect events or circumstances that occur after the date hereof. This press release and prior releases are available at <http://www.xtlbio.com>. The information in our website is not incorporated by reference into this press release and is included as an inactive textual reference only.*