

## **Pro-Pharmaceuticals Announces Dosing of Patients with DAVANAT® in Phase II, First Line, Colorectal Cancer Clinical Trial**

**Newton, Mass. (November 27, 2006) Pro-Pharmaceuticals, Inc. (Amex:PRW)**, a developer of novel carbohydrate compounds, today announces dosing of patients in its Phase II, first line, colorectal cancer trial. The Phase II trial is an open-label, multi-center trial of DAVANAT® with Avastin®, 5-Fluorouracil (5-FU) and Leucovorin in patients with locally advanced, unresectable or metastatic colorectal cancer and unable to tolerate intensive chemotherapy with an endpoint of tumor shrinkage.

“DAVANAT® is the first of a new class of drugs based on carbohydrate chemistry,” said David Platt, Ph.D., President and Chief Executive Officer, Pro-Pharmaceuticals, Inc. “When we combine the results from this front line trial, with the very positive results from our Phase I/II trials of end stage cancer patients, we believe it will conclusively prove the efficacy enhancing affect and toxicity reduction of DAVANAT® when co-administered with chemotherapeutics and biologics to treat cancer. We are actively enrolling patients in two first line Phase II cancer trials and expect preliminary results in the first quarter of 2007. We also are in discussions with a number of large bio-pharmaceutical companies who are evaluating our technology. Our goal is to facilitate collaborations that will enable us to get our compounds to market quickly in multiple indications.”

### **Phase I Trial for End Stage Patients with All Solid Tumors**

The Phase I clinical trial results for end stage cancer patients with all solid tumors show DAVANAT® was safe and well tolerated. All patients had progressive disease entering the study, tumor size that averaged 100mm, had a minimum of 12 weeks to live and were refractory to chemotherapy. The regimen called for 5-FU to be held constant (500mg/m<sup>2</sup>) for four consecutive days, while DAVANAT® was dose escalated from 30mg/m<sup>2</sup> to 280mg/m<sup>2</sup>. In the six cohorts, DAVANAT® was administered alone in the first cycle and in combination with 5-FU in the second cycle. The pharmacokinetic (PK) results show that 5-FU, in combination with DAVANAT®, remained significantly longer in the bloodstream (up to 8 times), without increasing 5-FU's toxicity in these fragile patients. The increased exposure to 5-FU may explain why 54% (14 of 26) of the end-stage cancer patients, who had measurable disease, were stabilized from 2 to 13 months and 70% (7 of 10) were stabilized at the highest DAVANAT® dose level. The PK data may indicate a trend for administering significantly higher dose levels of 5-FU.

### **Phase II Trial for End Stage Colorectal Cancer Patients**

In the Phase II clinical trial for end stage colorectal cancer patients, 30% (6 of 20) were stabilized from 2 to 8 months and 1 patient experienced a partial tumor response, as determined by an independent lab. These results from the Phase II trial are in the process of being audited. Patients had no increase in toxicity with increased exposure to 5-FU in the presence of DAVANAT®.

In the Phase I/II cancer trials, 36% (9 of 25) of the end stage colorectal cancer patients who received the highest dose level of DAVANAT®, were stabilized from 2 to 8 months. In the Phase I/II cancer trials, 43% (20 of 46) of end-stage cancer patients, who had measurable disease, were stabilized from 2 to 13 months. The results of these DAVANAT® studies compare very well and exceed results from recent studies in similar patient populations.

## **Phase II, First Line, Biliary Cancer Trial**

Additionally, the Company is actively recruiting patients in a Phase II study of DAVANAT<sup>®</sup> with 5-FU for first line treatment of advanced biliary cancer. The primary objectives of the trial are a partial or complete tumor response and stable disease. Secondary outcomes include progression-free survival and quality of life. The multi-center, open-label study will evaluate up to 42 patients treated with DAVANAT<sup>®</sup> and 5-FU for at least two cycles or to disease progression. A cholangiocarcinoma patient from the Phase I trial remained on study for 13 months, far exceeding expectations. Treatment of biliary cancer may represent an opportunity for orphan drug status approval.

Additional information on the two first line Phase II clinical trials and participating sites can be found at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) website, key word: DAVANAT<sup>®</sup>.

## **About DAVANAT<sup>®</sup>**

DAVANAT<sup>®</sup>, the Company's lead drug candidate, is a carbohydrate (polysaccharide) polymer derived from plant sources composed of mannose and galactose. The Company believes DAVANAT<sup>®</sup>'s mechanism of action is based upon binding to lectins on cell surface proteins. Lectins are carbohydrate binding proteins found in increased amounts on cell surfaces. DAVANAT<sup>®</sup>, when injected into humans, recognizes and attaches to lectins. It is theorized that DAVANAT<sup>®</sup> targets specific lectin receptors (Galectins) that are over-expressed on cancer cells. Current research indicates that Galectins affect cell development and play important roles in cancer, including tumor cell survival, angiogenesis and tumor metastasis. This form of targeted delivery may allow for higher doses of chemotherapy administration with no increase in toxicity.

## **Pro-Pharmaceuticals, Inc. – Advancing Drugs Through Glycoscience<sup>®</sup>**

Pro-Pharmaceuticals is a development stage pharmaceutical company engaged in the discovery, development and commercialization of carbohydrate-based therapeutic compounds for advanced treatment of cancer, liver, microbial, cardiovascular and inflammatory diseases. Initially, the product pipeline is principally focused on increasing the efficacy and decreasing the toxicity of approved chemotherapy drugs. The Company has been conducting clinical and pre-clinical studies with its lead compound, DAVANAT<sup>®</sup>, in combination with 5-FU, leucovorin, irinotecan, doxorubicin, oxaliplatin, paclitaxel, cisplatin, and bevacizumab (Avastin<sup>®</sup>). Results show that DAVANAT<sup>®</sup> exhibits a broad spectrum of activity with tested drugs. The Company is developing other carbohydrate-based therapeutic compounds that are currently in the pre-clinical stage of development. Founded in 2000, the Company is headquartered in Newton, Mass. Additional information is available at [www.pro-pharmaceuticals.com](http://www.pro-pharmaceuticals.com).

**FORWARD LOOKING STATEMENTS:** Any statements in this news release about future expectations, plans and prospects for the Company, including without limitation statements containing the words "believes," "anticipates," "plans," "expects," and similar expressions, constitute forward-looking statements as defined in the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are based on management's current expectations and are subject to a number of factors and uncertainties, which could cause actual results to differ materially from those described in such statements. We caution investors that actual results or business conditions may differ materially from those projected or suggested in forward-looking statements as a result of various factors including, but not limited to, the following: uncertainties as to the utility and market for our potential products; uncertainties associated with pre-clinical and clinical trials of our product candidates; our limited experience in product development and expected dependence on potential licensees and collaborators for commercial manufacturing, sales, distribution and marketing of our potential products; possible development by competitors of competing products and technologies; lack of assurance regarding patent and other protection of our proprietary technology; compliance with and change of government regulation of our activities, facilities and personnel; uncertainties as to the extent of reimbursement for our potential products by

government and private health insurers; our dependence on key personnel; our history of operating losses and accumulated deficit; and economic conditions related to the biotechnology and biopharmaceutical industry. We cannot assure you that we have identified all the factors that create uncertainties. Readers should not place undue reliance on forward-looking statements.

More information about those risks and uncertainties is contained and discussed in the "Management Discussion and Analysis of Financial Condition and Results of Operations" and "Risk Factors" sections of the Company's most recent quarterly or annual report and in the Company's other reports filed with the Securities and Exchange Commission. The forward-looking statements represent the Company's views as of the date of this news release and should not be relied upon to represent the Company's views as of a subsequent date. While the Company anticipates that subsequent events may cause the Company's views to change, the Company disclaims any obligation to update such forward-looking statements.

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