

## **PRO-PHARMACEUTICALS' ABSTRACT PUBLISHED IN ASCO ANNUAL MEETING *PROCEEDINGS***

### **Company Provides Clinical Trial Update**

**Newton, Mass. (June 5, 2006) -- Pro-Pharmaceuticals, Inc. (Amex: PRW)**, a developer of novel nanotechnology carbohydrate therapeutic compounds, today announced that its abstract, "*A Bio-distribution Study of DAVANAT®*" was published in The American Society of Cancer Oncology's (ASCO) 2006 Annual Meeting *Proceedings*. The ASCO Annual Meeting is being held in Atlanta, Georgia, June 2-6.

The abstract refers to Pro-Pharmaceuticals' research program to better understand the interaction of DAVANAT® and its effect on the pharmacokinetic profile of 5-fluorouracil (5-FU). The study used mice xenographic models with human colon tumor and used radio-labeled 5-FU to analyze the biodistribution of 5-FU in the blood, liver, lungs and other organs, as well as in the tumor, when co-administered with DAVANAT®.

The addition of DAVANAT® significantly increased the amount of 5-FU exposure as measured by area under the curve (AUC) between 1.5 and 24 hours post dose. Significant increases in AUC also were measured in the tumor when compared to 5-FU alone for the 1.5 to 24 hour duration. These findings confirm results obtained from a Phase I clinical trial where administering escalating doses of DAVANAT® (30 to 280 mg/m<sup>2</sup>) with a stable dose of 5-FU (500 mg/m<sup>2</sup>) also demonstrated an increase in 5-FU systemic exposure as the DAVANAT® dose increased to 280 mg/m<sup>2</sup>. The pharmacokinetic analysis of cancer patients in the sixth and final cohort of the Phase I trial indicates 5-FU remained in the blood significantly longer (28 to 137 minutes) when co-administered with DAVANAT®, compared with historical 5-FU data (8 to 20 minutes), thereby potentially increasing 5-FU's efficacy while lowering its toxicity.

#### **Area Under The Curve**

AUC is calculated by plotting 5-FU concentrations at various times during a 24-hour period. Increase of AUC value in the blood indicates higher availability of 5-FU. An increase of AUC in the tumor directly correlates to anti-tumor activity of 5-FU and confirms the target delivery mechanism of DAVANAT®.

#### **Phase I Trial for All Solid Tumors**

The Phase I multi-center, open-label trial was designed for cancer patients with advanced solid tumors that were not amenable to surgery, radiation, or chemotherapy, were refractory to 5-FU, and had a minimum of 12 weeks to live. Indications included colorectal, prostate, breast, liver, pancreatic, and cholangiocarcinoma. The objectives of the study were to determine the Maximum Tolerated Dose and Dose Limiting Toxicity of DAVANAT® as a single agent, and when administered in combination with 5-FU. In addition to safety, the study evaluated the pharmacokinetic profile of 5-FU in the presence of DAVANAT®, and the effect of DAVANAT®/5-FU on tumor size in patients with measurable disease. The trial was completed in 2005.

The third- and fourth-line cancer patients had solid tumors that averaged more than 100mm in size coming into the study, and had progressive disease. The disease was stabilized in 14 of 26 patients (54%) with measurable disease. Objective analysis shows that 70% of patients stabilized at the

highest dose level (280 mg/m<sup>2</sup>) compared with 44% of patients stabilized at lower dose levels (30-210 mg/m<sup>2</sup>), indicating the positive effect of DAVANAT<sup>®</sup>. Ten patients were treated from three to 13 months. The Phase I data also indicates that DAVANAT<sup>®</sup>/5-FU was well tolerated. Dose Limiting Toxicity and Maximum Tolerated Dose were not reached when DAVANAT<sup>®</sup> was administered alone or in combination with 5-FU.

### **Phase II Metastatic Colorectal Cancer Trial**

Preliminary data shows two patients with an objective partial tumor response and five with stabilized disease in a Phase II trial for third- and fourth-line treatment of colorectal cancer patients. Based on this positive preliminary data and the fact that the current standard of care for colorectal cancer now consists of combination therapies, the Company will not enroll additional patients. The Company received clearance from the European Medicines Agency (EMA) to initiate a Europe-based Phase III, line two colorectal cancer trial (see below) using combination therapies that include DAVANAT<sup>®</sup>, 5-FU, leucovorin, irinotecan and/or oxaliplatin. The Company expects to report additional Phase II results as patients continue to receive treatment.

In the Phase II trial, patients with colon cancer, which spread despite treatment with approved therapies, received DAVANAT<sup>®</sup> plus 5-FU in monthly cycles for at least two cycles or until their disease progressed. The study was designed to evaluate the safety and efficacy of DAVANAT<sup>®</sup> plus 5-FU to shrink tumors or prevent further growth. These patients are refractory to 5-FU and have a minimum of 12 weeks to live.

### **Phase II Cholangiocarcinoma Trial**

The Company initiated a U.S.-based Phase II study of its lead carbohydrate compound DAVANAT<sup>®</sup> with 5-FU for first line treatment of patients with Cholangiocarcinoma (cancer associated with the bile duct). The objectives of the trial are a complete or partial tumor response (RECIST) and progression-free survival. The multi-center, open-label study will evaluate approximately 30 patients treated with DAVANAT<sup>®</sup>/5-FU for at least two cycles or to disease progression. The Company expects to begin patient enrollment this quarter. Cholangiocarcinoma may represent an opportunity for orphan drug status approval.

### **Phase III Colorectal Cancer Trial**

The Company initiated a Europe-based Phase III clinical trial for second line treatment of patients with metastatic colorectal cancer. The trial is recruiting clinical sites in the European Union (EU) and countries outside of the EU following regulatory and ethics approval in each country. This study is a multi-center, double blind, randomized trial of 120 patients to evaluate the safety and efficacy of DAVANAT<sup>®</sup> with 5-FU and leucovorin in combination with irinotecan or oxaliplatin. The Company expects to begin patient enrollment this quarter.

### **About DAVANAT<sup>®</sup>**

DAVANAT<sup>®</sup>, the Company's lead product candidate, is a proprietary nanotechnology polysaccharide polymer comprised of mannose and galactose carbohydrates in a CARBOSOME<sup>™</sup> formation that enables the targeted delivery of chemotherapy drugs to protein receptors (lectins) on cancer cells.

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

Pro-Pharmaceuticals is a development stage company engaged in the discovery, development and commercialization of nanotechnology carbohydrate-based therapeutic compounds for advanced treatment of cancer, liver, infectious, 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 nanotechnology product candidate, 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. 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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