

PROSPECTUS SUPPLEMENT NO. 2
(to Prospectus dated March 29, 2006, as supplemented by
Prospectus Supplement No. 1 dated May 31, 2006)

PRO-PHARMACEUTICALS, INC.

7,300,000 SHARES OF COMMON STOCK

This Prospectus Supplement No. 2 supplements the Prospectus dated March 29, 2006 (as supplemented by Prospectus Supplement No. 1 dated May 31, 2006) relating to the offer and sale of (i) up to 5,150,000 shares of our Common Stock, par value \$0.001 per share, issuable upon the conversion or redemption of, or as interest payments on, our 7% Convertible Debentures (the "Debentures") and (ii) up to 2,150,000 shares of our Common Stock issuable upon the exercise of Common Stock Purchase Warrants (the "Warrants"). We issued and sold the Debentures and Warrants on February 14, 2006.

The Debentures state that we may elect to make redemption and interest payments thereunder in cash or shares of our Common Stock. On June 27, 2006, we provided notice to the initial holders of the Debentures that we have elected to pay the interest and principal due August 1, 2006 in shares of our Common Stock.

This Prospectus Supplement No. 2 should be read in conjunction with the Prospectus dated March 29, 2006, which is to be delivered with this Prospectus Supplement No. 2. All capitalized terms used but not defined in this Prospectus Supplement No. 2 shall have the meanings given them in the Prospectus.

Investing in the shares of Common Stock issued pursuant to the Debentures or upon exercise of the Warrants involves substantial risks. See "Risk Factors" beginning on page 4 of the Prospectus dated March 29, 2006.

Our Common Stock is quoted on the American Stock Exchange under the symbol "PRW". The last reported price of our Common Stock on June 29, 2006 was \$3.13 per share.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined whether this prospectus supplement or the Prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this Prospectus Supplement No. 2 is June 30, 2006.