



DIVISION OF  
CORPORATION FINANCE

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 20549

September 27, 2010

Theodore D. Zucconi, Ph.D.  
Chief Executive Officer and President  
Pro-Pharmaceuticals, Inc.  
7 Wells Avenue  
Newton, Massachusetts 02459

**Re: Pro-Pharmaceuticals, Inc.  
Registration Statement on Form S-1  
Filed September 17, 2010  
File No. 333-169463**

Dear Dr. Zucconi:

We have limited our review of your registration statement to those issues we have addressed in our comments.

Please respond to this letter by providing the requested information, with a view toward disclosure in the prospectus. Where you do not believe our comments apply to your facts and circumstances, please tell us why in your response.

After reviewing the information you provide in response to these comments, we may have additional comments.

General

1. We note that you are registering the sale of 52,254,130 shares. Given the size relative to the number of shares outstanding held by non-affiliates, the nature of the offering and the selling shareholders, the transaction appears that it may be a primary offering. Because you would not be eligible to conduct a primary offering on Form S-3, you are not eligible to conduct a primary at-the-market offering under Rule 415(a)(4) on Form S-1. As a result, if this offering is deemed to be a primary offering, you must:
  - file a registration statement for the “resale” offering at the time of each conversion of preferred stock or exercise of warrants because you are not eligible to conduct the offering on a delayed or continuous basis under Rule 415(a)(1)(x);
  - identify the selling shareholders as underwriters in the registration statement; and
  - include the fixed price at which the deemed underwriters will sell the securities.

If you disagree with our analysis, please advise the staff of the company’s basis for determining that the transaction is appropriately characterized as a transaction that is eligible to be made

under Rule 415(a)(1)(i). In your analysis, please address the following, among any other relevant factors:

- The number of selling shareholders and the percentage of the overall offering made by each shareholder;
- The date on which and the manner in which each selling shareholder received the shares and/or the overlying securities;
- The relationship of each selling shareholder with the company, including an analysis of whether the selling shareholder is an affiliate of the company;
- Any relationships among the selling shareholders;
- The dollar value of the shares registered in relation to the proceeds that the company received from the selling shareholders for the securities, excluding amounts of proceeds that were returned (or will be returned) to the selling shareholders and/or their affiliates in fees or other payments;
- The discount at which the shareholders will purchase the common stock underlying the convertible preferred stock and warrants upon conversion and exercise, respectively; and
- Whether or not any of the selling shareholders is in the business of buying and selling securities.

#### Dollar value of underlying securities

2. Please provide us, with a view toward disclosure in the prospectus, with the total dollar value of the securities underlying the convertible preferred stock that you have registered for resale (using the number of underlying securities that you have registered for resale and the market price per share for those securities on the date of the sale of the convertible preferred stock).

#### Payments to the investor and affiliates

3. Please provide us, with a view toward disclosure in the prospectus, with tabular disclosure of the dollar amount of each payment (including the value of any payments to be made in common stock) in connection with the transaction that you have made or may be required to make to any selling shareholder, any affiliate of a selling shareholder, or any person with whom any selling shareholder has a contractual relationship regarding the transaction (including any interest payments, liquidated damages, payments made to “finders” or “placement agents,” and any other payments or potential payments). Please provide footnote disclosure of the terms of each such payment. Please do not include any repayment of the convertible preferred stock in this disclosure.

Further, please provide us, with a view toward disclosure in the prospectus, with disclosure of the net proceeds to the issuer from the sale of the convertible preferred stock and the total possible payments to all selling shareholders and any of their affiliates in the first year following the sale of the convertible preferred stock.

Potential profits on conversion

4. Please provide us, with a view toward disclosure in the prospectus, with tabular disclosure of:
- the total possible profit the selling shareholders could realize as a result of the conversion discount for the securities underlying the convertible preferred stock, presented in a table with the following information disclosed separately:
    - the market price per share of the securities underlying the convertible preferred stock on the date of the sale of the convertible preferred stock;
    - the conversion price per share of the underlying securities on the date of the sale of the convertible preferred stock, calculated as follows:
      - if the conversion price per share is set at a fixed price, use the price per share established by the convertible preferred stock; and
      - if the conversion price per share is not set at a fixed price and, instead, is set at a floating rate in relationship to the market price of the underlying security, use the conversion discount rate and the market rate per share on the date of the sale of the convertible preferred stock and determine the conversion price per share as of that date;
  - the total possible shares underlying the convertible preferred stock (assuming no interest payments and complete conversion throughout the term of the convertible preferred stock);
  - the combined market price of the total number of shares underlying the convertible preferred stock, calculated by using the market price per share on the date of the sale of the convertible preferred stock and the total possible shares underlying the convertible preferred stock;
  - the total possible shares the selling shareholders may receive and the combined conversion price of the total number of shares underlying the convertible preferred stock calculated by using the conversion price on the date of the sale of the convertible preferred stock and the total possible number of shares the selling shareholders may receive; and
  - the total possible discount to the market price as of the date of the sale of the convertible preferred stock, calculated by subtracting the total conversion price on the date of the sale of the convertible preferred stock from the combined market price of the total number of shares underlying the convertible preferred stock on that date.

If there are provisions in the convertible preferred stock that could result in a change in the price per share upon the occurrence of certain events, please provide additional tabular disclosure as appropriate. For example, if the conversion price per share is fixed unless and until the market price falls below a stated price, at which point the conversion price per share drops to a lower price, please provide additional disclosure.

Total potential profit from other securities

5. Please provide us, with a view toward disclosure in the prospectus, with tabular disclosure of:
- the total possible profit to be realized as a result of any conversion discounts for securities underlying any other warrants, options, notes, or other securities of the issuer that are held by the selling shareholders or any affiliates of the selling shareholders, presented in a table with the following information disclosed separately:
    - market price per share of the underlying securities on the date of the sale of that other security;
    - the conversion/exercise price per share as of the date of the sale of that other security, calculated as follows:
      - if the conversion/exercise price per share is set at a fixed price, use the price per share on the date of the sale of that other security; and
      - if the conversion/exercise price per share is not set at a fixed price and, instead, is set at a floating rate in relationship to the market price of the underlying security, use the conversion/exercise discount rate and the market rate per share on the date of the sale of that other security and determine the conversion price per share as of that date;
    - the total possible shares to be received under the particular securities (assuming complete conversion/exercise);
    - the combined market price of the total number of underlying shares, calculated by using the market price per share on the date of the sale of that other security and the total possible shares to be received;
    - the total possible shares to be received and the combined conversion price of the total number of shares underlying that other security calculated by using the conversion price on the date of the sale of that other security and the total possible number of underlying shares; and
    - the total possible discount to the market price as of the date of the sale of that other security, calculated by subtracting the total conversion/exercise price on the date of the sale of that other security from the combined market price of the total number of underlying shares on that date.

Comparison of issuer proceeds to potential investor profit

6. Please provide us, with a view toward disclosure in the prospectus, with tabular disclosure of:
- the gross proceeds paid or payable to the issuer in the convertible preferred stock transaction;

- all payments that have been made or that may be required to be made by the issuer that are disclosed in response to comment 2;
- the resulting net proceeds to the issuer; and
- the combined total possible profit to be realized as a result of any conversion discounts regarding the securities underlying the convertible preferred stock and any other warrants, options, notes, or other securities of the issuer that are held by the selling shareholders or any affiliates of the selling shareholders that is disclosed in response to comments 3 and 4.

Further, please provide us, with a view toward disclosure in the prospectus, with disclosure – as a percentage – of the total amount of all possible payments as disclosed in response to comment 2 and the total possible discount to the market price of the shares underlying the convertible preferred stock as disclosed in response to comment 3 divided by the net proceeds to the issuer from the sale of the convertible preferred stock, as well as the amount of that resulting percentage averaged over the term of the convertible preferred stock.

Prior transactions between the issuer and the selling shareholders

7. Please provide us, with a view toward disclosure in the prospectus, with tabular disclosure of all prior securities transactions between the issuer (or any of its predecessors) and the selling shareholders, any affiliates of the selling shareholders, or any person with whom any selling shareholder has a contractual relationship regarding the transaction (or any predecessors of those persons), with the table including the following information disclosed separately for each transaction:
  - the date of the transaction;
  - the number of shares of the class of securities subject to the transaction that were outstanding prior to the transaction;
  - the number of shares of the class of securities subject to the transaction that were outstanding prior to the transaction and held by persons other than the selling shareholders, affiliates of the company, or affiliates of the selling shareholders;
  - the number of shares of the class of securities subject to the transaction that were issued or issuable in connection with the transaction;
  - the percentage of total issued and outstanding securities that were issued or issuable in the transaction (assuming full issuance), with the percentage calculated by taking the number of shares issued and outstanding prior to the applicable transaction and held by persons other than the selling shareholders, affiliates of the company, or affiliates of the selling shareholders, and dividing that number by the number of shares issued or issuable in connection with the applicable transaction;
  - the market price per share of the class of securities subject to the transaction

- immediately prior to the transaction (reverse split adjusted, if necessary); and
- the current market price per share of the class of securities subject to the transaction (reverse split adjusted, if necessary).

Comparison of registered shares to outstanding shares

8. Please provide us, with a view toward disclosure in the prospectus, with tabular disclosure comparing:
  - the number of shares outstanding prior to the convertible preferred stock transaction that are held by persons other than the selling shareholders, affiliates of the company, and affiliates of the selling shareholders;
  - the number of shares registered for resale by the selling shareholders or affiliates of the selling shareholders in prior registration statements;
  - the number of shares registered for resale by the selling shareholders or affiliates of the selling shareholders that continue to be held by the selling shareholders or affiliates of the selling shareholders;
  - the number of shares that have been sold in registered resale transactions by the selling shareholders or affiliates of the selling shareholders; and
  - the number of shares registered for resale on behalf of the selling shareholders or affiliates of the selling shareholders in the current transaction.

In this analysis, the calculation of the number of outstanding shares should not include any securities underlying any outstanding convertible securities, options, or warrants.

The presence or absence of short selling by the selling shareholders

9. Please provide us, with a view toward disclosure in the prospectus, with the following information:
  - whether – based on information obtained from the selling shareholders – any of the selling shareholders have an existing short position in the company's common stock and, if any of the selling shareholders have an existing short position in the company's stock, the following additional information:
    - the date on which each such selling shareholder entered into that short position; and
    - the relationship of the date on which each such selling shareholder entered into that short position to the date of the announcement of the convertible preferred stock transaction and the filing of the registration statement (e.g., before or after the announcement of the convertible preferred stock transaction, before the filing or after the filing of the registration statement, etc.).

Relationships between the issuer and selling shareholders

10. Please provide us, with a view toward disclosure in the prospectus, with:

- a materially complete description of the relationships and arrangements that have existed in the past three years or are to be performed in the future between the issuer (or any of its predecessors) and the selling shareholders, any affiliates of the selling shareholders, or any person with whom any selling shareholder has a contractual relationship regarding the transaction (or any predecessors of those persons) – the information provided should include, in reasonable detail, a complete description of the rights and obligations of the parties in connection with the sale of the convertible preferred stock; and
- copies of all agreements between the issuer (or any of its predecessors) and the selling shareholders, any affiliates of the selling shareholders, or any person with whom any selling shareholder has a contractual relationship regarding the transaction (or any predecessors of those persons) in connection with the sale of the convertible preferred stock.

If it is your view that such a description of the relationships and arrangements between and among those parties already is presented in the prospectus and that all agreements between and/or among those parties are included as exhibits to the registration statement, please provide us with confirmation of your view in this regard.

We urge all persons who are responsible for the accuracy and adequacy of the disclosure in the filing to be certain that the filing includes the information the Securities Act of 1933 and all applicable Securities Act rules require. Since the company and its management are in possession of all facts relating to a company's disclosure, they are responsible for the accuracy and adequacy of the disclosures they have made.

Notwithstanding our comments, in the event you request acceleration of the effective date of the pending registration statement please provide a written statement from the company acknowledging that:

- should the Commission or the staff, acting pursuant to delegated authority, declare the filing effective, it does not foreclose the Commission from taking any action with respect to the filing;
- the action of the Commission or the staff, acting pursuant to delegated authority, in declaring the filing effective, does not relieve the company from its full responsibility for the adequacy and accuracy of the disclosure in the filing; and

Theodore D. Zucconi, Ph.D.  
Pro-Pharmaceuticals, Inc.  
September 27, 2010  
Page 8

- the company may not assert staff comments and the declaration of effectiveness as a defense in any proceeding initiated by the Commission or any person under the federal securities laws of the United States.

Please refer to Rules 460 and 461 regarding requests for acceleration. We will consider a written request for acceleration of the effective date of the registration statement as confirmation of the fact that those requesting acceleration are aware of their respective responsibilities under the Securities Act of 1933 and the Securities Exchange Act of 1934 as they relate to the proposed public offering of the securities specified in the above registration statement. Please allow adequate time for us to review any amendment prior to the requested effective date of the registration statement.

Please contact Sebastian Gomez Abero at (202) 551-3578 or Daniel Greenspan at (202) 551-3623 with any other questions.

Sincerely,

Jeffrey Riedler  
Assistant Director