



DIVISION OF  
CORPORATION FINANCE

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

October 11, 2012

Via E-mail

William P. Moffitt III  
President and Chief Executive Officer  
Nanosphere, Inc.  
4088 Commercial Avenue  
Northbrook, Illinois 60062

**Re: Nanosphere, Inc.  
Amendment No. 1 to Registration Statement on Form S-3  
Filed October 2, 2012  
File No. 333-183916**

Dear Mr. Moffitt:

We have limited our review of your registration statement to those issues we have addressed in our comments. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure.

Please respond to this letter by amending your registration statement and providing the requested information. Where you do not believe our comments apply to your facts and circumstances or do not believe an amendment is appropriate, please tell us why in your response.

After reviewing any amendment to your registration statement and the information you provide in response to these comments, we may have additional comments.

Fee table

1. We note your response to prior comment 1; however, it remains unclear whether the fee table includes all of the securities underlying the offered securities. For example, we note your reference to debt obligations and "other securities" on page 17. Please revise or advise.

Explanatory Note

2. Please tell us the authority on which you rely to file a document consisting of only a facing page, explanatory note, signature page and partial exhibit index.

Exhibit 5.1 – Legality Opinion

3. From your revisions in response to prior comment 3, it remains unclear how this exhibit addresses whether the relevant securities are binding obligations of the registrant under the law of the jurisdiction governing those securities. This exhibit states that it addresses only the federal laws of the United States of America and Delaware General Corporation Law, applicable provisions of the Delaware Constitution and reported judicial decisions interpreting those laws. The exhibit appears to exclude relevant laws such as contract laws. Please advise or file a revised opinion.

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
- 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.

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You may contact Tim Buchmiller at (202) 551-3635 or me at (202) 551-3617 with any questions.

Sincerely,

/s/ Russell Mancuso

Russell Mancuso  
Branch Chief

cc: Blake Hornick  
Seyfarth Shaw LLP