



DIVISION OF  
CORPORATION FINANCE

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

Mail Stop 3030

August 19, 2009

Via U.S. Mail and Fax (847) 400-9199

Mr. Roger Moody  
Chief Financial Officer  
Nanosphere, Inc.  
4088 Commercial Avenue  
Northbrook, Illinois 60062

**Re: Nanosphere, Inc.  
Form 10-K for the Fiscal Year Ended December 31, 2008  
Filed February 26, 2009  
Forms 10-Q for the Quarterly Periods Ended March 31, and  
June 30, 2009  
File No. 001-33775**

Dear Mr. Moody:

We have reviewed your filings and have the following comments. Where indicated, we think you should revise your documents in response to these comments. If you disagree, we will consider your explanation as to why our comments are inapplicable or a revision is unnecessary. Please be as detailed as necessary in your explanation. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure. After reviewing this information, we may raise additional comments.

Please understand that the purpose of our review process is to assist you in your compliance with the applicable disclosure requirements and to enhance the overall disclosure in your filing. We look forward to working with you in these respects. We welcome any questions you may have about our comments or any other aspect of our review. Feel free to call us at the telephone numbers listed at the end of this letter.

Form 10-K for the fiscal-year ended December 31, 2008

Item 1. Business

Overview, page 3

1. We note your disclosure on page 4 that "[c]urrently, our patent portfolio is comprised, on a worldwide basis, of 96 issued patents and over 163 pending patent applications which we own directly or for which we are the exclusive licensee." In your future filings, please clarify whether some of these patents and pending patent applications derive from a common parent patent application or are foreign counterpart patent applications and relate to similar or identical technological claims. Your disclosure in future filings should make it clearer how many different technological claims that you have protected by patents or are pending patent approval.
2. We note from your risk factor disclosure on page 18 that your "exclusive and non-exclusive licenses expire at various times, corresponding to the subject patents' expirations, which currently range from 2009 to 2025." In your future filings, please clarify the importance and duration and effect of all patents, licenses, etc., held. Refer to Item 101(c)(iv) of Regulation S-K. It should be clearer from your disclosure how your patent portfolio is structured in terms of which patents are more significant to your business and when those patents expire. For example, it is unclear from your current disclosure the effect, if any, that the patent(s) that expire in 2009 may have on your proprietary position.

Unparalleled Specificity, page 8

3. We note your disclosure that "[a] key property of the oligonucleotide-linked gold nanoparticle is an extremely sharp melting curve." Although we note your disclosure in the two sentences that follow, please revise your applicable future filings to explain more clearly the function of the sharp melt transition curves and the significance of those curves to the specificity of your product. In addition, please explain whether the sharp melting curves are a proprietary feature of your gold nanoparticles or whether the sharp melting curves, and therefore specificity, could be replicated by competitors using oligonucleotides labeled by gold or other types of nanoparticles, rather than fluorophore probes, that would not be covered by your patents or other forms of proprietary protections. Please update your "Competition" section in your future filings to disclose, to the extent then known, whether you have any competitors that are currently developing or marketing products with the oligonucleotide specificity you describe.

Assay Format, page 9

4. We understand from the first sentence of the first paragraph of this subsection that you intended to include a graphic in your filing that shows how your system detects and captures target molecules onto your microarrays. It does not appear, however, that such graphic was actually included in your filing. In your future filings, as applicable, please ensure that your graphic is included. If you intended to include the graphic that appeared on page 51 of your registration statement on Form S-1/A filed on October 29, 2007, please advise. Also, we understand that your graphic is intended to show genomic and proteonomic target capture, but the graphic included in the Form S-1/A referenced above only depicts genomic capture. Please advise.

Item 1A. Risk Factors, page 15

5. We understand from your disclosure on page 52 under "5. Equity Incentive Plan" that the number of shares available for issuance under your 2007 Long-Term Incentive Plan is increased each year by the least of (i) 900,000 shares of common stock, (ii) 4% of the total amount of your outstanding shares (or approximately 889,147 shares based on the number of outstanding shares as of December 31, 2008), which would pick up shares issued upon the exercise of previously granted options and shares issued in connection with future equity financings, or (iii) an amount determined by the board of directors. In your future filings, please include risk factor disclosure that clearly discloses the compounding effect of the yearly increases in the total number of shares available for issuance under your 2007 Plan and indicate the amount of shares that were added and made available for issuance under the 2007 Plan in the most recent fiscal year as a result of the evergreen provision. Please also disclose the dilution that may result from such increases in the amount of shares available to be issued under your 2007 Plan. Please also disclose that due to the evergreen provision, it is more likely that your shareholders will not be asked to approve or disapprove further additions to your current equity plan, or to approve or disapprove the adoption of new equity compensation plans in the future, given the presence of the evergreen provision in your current plan than if your plan did not contain such provision.

Item 7. Management's Discussion and Analysis...

Fiscal 2008 Compared to 2007, page 33

6. We note your disclosure that your product revenues increased over the periods compared due to sales and rentals of your system. In your future filings, to the extent material to an investor's understanding of your operating results and trends related thereto, please disclose the portion of your revenues that were due to

rentals or sales for the periods presented. If a significant portion of your revenues are due to rentals, please disclose whether there are any additional demands on your capital resources as a result of entering into rental arrangements (where you bear the upfront cost of goods sold) rather than consummating upfront sales of your systems (where you would immediately recognize revenue that would approximate or exceed your cost of goods sold), and any risk related thereto. Please also disclose, to the extent then material, the portion of your revenues due to sales of consummables as opposed to revenues derived from sales or rentals of your systems.

Item 11. Executive Compensation, page 60

7. We note the discussion under the heading “Stock Option Awards” on page 17 of your proxy statement that you have incorporated by reference into your annual report on Form 10-K. In your future filings, as applicable, please provide an enhanced discussion of your policies for allocating between options that have gradual and cliff-vesting schedules. Also, in your future filings, please ensure that your disclosure regarding awards of options clearly identifies the type of vesting for that award, why that vesting schedule was selected and the basis for awarding the option to the named executive officer. In this regard, it is unclear from your current disclosure on page 18 of the proxy statement which vesting schedule applies to the options you awarded during 2008, why that vesting schedule was selected or what was the basis for the option awards.

Signatures, page 63

8. Please amend your filing to include the correct second paragraph of the text required on the signatures page of Form 10-K. The second paragraph currently included on this page indicates that each person listed below that paragraph only signed the document on behalf of the registrant, rather than on behalf of the registrant and in that person’s capacity as indicated in the signature blocks. When you amend your filing, please ensure that, in addition to identifying which officer signed in their capacity as principal executive officer, you also identify which officers signed in their capacities as (i) principal financial officer and (ii) principal accounting officer or controller. Refer to General Instruction D(2)(a) to Form 10-K.

Form 10-Q for the Quarterly Period Ended June 30, 2009

Contractual Obligations and Commitments, page 16

9. We note the vague reference here that your commitments have not changed significantly “[o]ther than disclosed elsewhere in this Quarterly Report.” In your applicable future filings, rather than requiring investors to piece together information from other portions of your document to figure out how your contractual obligations have changed since the fiscal-year end, please describe in your MD&A the significant changes to such obligations and provide the tabular disclosure required by Item 303(a)(5) of Regulation S-K.

Forms 10-Q for the Quarterly Period Ended March 31, 2009 and June 30, 2009

Certifications Exhibit 31.1

10. We note that your annual report contains management’s internal control report as required by Item 308T of Regulation S-K. As such, your certifications should include the introductory language in paragraph 4 of the certification that refers to the certifying officers' responsibility for establishing and maintaining internal control over financial reporting for the company as required by Item 601(b)(31) of Regulation S-K. Please amend your Forms 10-Q for the periods ended March 31, 2009 and June 30, 2009 to include corrected certifications that include the required language. You may provide abbreviated amendments that consist of a cover page, explanatory note, signature page and paragraphs 1, 2, 4 and 5 of the certification.

As appropriate, please amend your Form 10-K and Forms 10-Q and respond to these comments within 10 business days or tell us when you will provide us with a response. You may wish to provide us with marked copies of the amendments to expedite our review. Please furnish a cover letter with your amendments that keys your responses to our comments and provides any requested information. Detailed cover letters greatly facilitate our review. Please understand that we may have additional comments after reviewing your amendments and responses to our comments.

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 all information required under the Securities Exchange Act of 1934 and that they have provided all information investors require for an informed investment decision. 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.

Mr. Roger Moody  
Nanosphere, Inc.  
August 19, 2009  
Page 6

In connection with responding to our comments, please provide, in writing, a statement from the company acknowledging that:

- the company is responsible for the adequacy and accuracy of the disclosure in the filing;
- staff comments or changes to disclosure in response to staff comments do not foreclose the Commission from taking any action with respect to the filing; and
- the company may not assert staff comments as a defense in any proceeding initiated by the Commission or any person under the federal securities laws of the United States.

In addition, please be advised that the Division of Enforcement has access to all information you provide to the staff of the Division of Corporation Finance in our review of your filing or in response to our comments on your filing.

You may contact Julie Sherman, Staff Accountant, at (202) 551-3640 or me at (202) 551-3604 if you have any questions regarding comments on the financial statements and related matters. Please contact Geoffrey Kruczek, Staff Attorney, at (202) 551-3641 or Tim Buchmiller, Reviewing Attorney, at (202) 551-3635 if you have questions on any other comments. In this regard, do not hesitate to contact Martin James, Senior Assistant Chief Accountant, at (202) 551-3671.

Sincerely,

Kate Tillan  
Assistant Chief Accountant