

September 29, 2005

**CONFIDENTIAL**

***Via Overnight Courier and Filed by Edgar***

Mr. Jim B. Rosenberg  
Senior Assistant Chief Accountant  
Division of Corporate Finance  
United States Securities and Exchange Commission  
100 F Street, NE  
Washington, D.C. 20549

RE: DURECT Corporation  
Form 10-K for the fiscal year ended December 31, 2004  
File No. 000-31615

Dear Mr. Rosenberg,

This letter responds to your letter of September 22, 2005, which sets forth the Staff's comments on our response letter dated September 1, 2005 regarding Form 10-K for the fiscal year ended December 31, 2004 of DURECT Corporation ("DURECT" or the "Company"). For your convenience, we have numbered each response below so that it corresponds to the numbered paragraphs of your letter.

Management's Discussion and Analysis of Financial Condition and Results of Operations, page 25

Results of Operations, page 29

- 1. We acknowledge your response to comment 1 per our letter dated August 16, 2005, as well as the proposed disclosure that you provided. However, we request that you enhance your proposed disclosure with respect to your major research and development projects, which you have outlined on page 8. Specifically, please provide us, in a disclosure-type format, the information requested in point a) of our initial comment.**

Response:

a) In response to the Staff's comment, in future filings, we will provide costs incurred during each period presented on our major research and development programs, in the form of a table that shows our research and development expenses by product candidate in order to provide enhanced disclosure to our investors.

---

Attached please find a sample disclosure of Research and Development Expenses in the MD&A section of our Form 10-Q for the quarterly period ending September 30, 2005, incorporating the changes noted above.

Notes to Consolidated Financial Statements, page 63

Revenue Recognition, page 66

- 2. We acknowledge your response to comment 2 per our letter dated August 16, 2005, but do not believe that the disclosure in your Forms 10-Q for the periods ended March 31, 2005 and June 30, 2005 adequately addresses our comment. Please provide us with the following information, in a disclosure-type format:**
- **The revenue recognized in each period for each collaboration/development agreement, including amounts related to up-front fees; and**
  - **The specific development period used for recognizing the revenue, as well as the amortization methodology related to any up-front fees.**

Response:

In response to the Staff's comment, in future filings, the Company will include the following disclosure regarding the revenue recognized in each period presented, including up-front fees in the following disclosure-type format. The Company's amortization period for the up-front fees is determined at the execution of each respective agreement, and the period is based on the estimated level of the continuing involvement by the Company. Should there be a change to the assumptions underlying these estimates, the Company will report the nature of such changes in accordance with APB 20.

| Partner  | Three months ended<br>September 30, |         | Nine months ended<br>September 30, |         |
|--|-------------------------------------|---------|------------------------------------|---------|
|  | 2005                                | 2004    | 2005                               | 2004    |
| Endo Pharmaceuticals, Inc. (1)                       | \$X,XXX                             | \$X,XXX | \$X,XXX                            | \$X,XXX |
| Pain Therapeutics, Inc. (2)                          | X,XXX                               | X,XXX   | X,XXX                              | X,XXX   |
| Voyager Pharmaceutical Corporation                   | X,XXX                               | X,XXX   | X,XXX                              | X,XXX   |
| Others   | X,XXX                               | X,XXX   | X,XXX                              | X,XXX   |
| Total collaborative research and development revenue | \$X,XXX                             | \$X,XXX | \$X,XXX                            | \$X,XXX |

Notes:

1. Amounts related to up-front fees were \$X,XXX and \$X,XXX for the three months ended September 30, 2005 and 2004 and \$X,XXX and \$X,XXX for the nine months ended September 30, 2005 and 2004.

2. Amounts related to up-front fees were \$X,XXX and \$X,XXX for the three months ended September 30, 2005 and 2004 and \$X,XXX and \$X,XXX for the nine months ended September 30, 2005 and 2004.

The Company amortizes up-front fees on a straight-line basis over the period in which the Company has continuing involvement with the third-party collaborator pursuant to the applicable agreement. Such period generally represents the research and development period set forth in the work plan under each collaboration agreement between the Company and its third-party collaborator.

Note 2. Strategic Agreements, page 69

**3. Please provide us, in a disclosure-type format, the information required by paragraph 14b. of SFAS No. 68 for each of your “partnered” collaboration and development agreements.**

Response:

In response to the Staff's comment, in future filings, we will revise our disclosure set forth in our response for comment 2 to address the information required by paragraph 14b. of SFAS No. 68.

---

Sincerely,

/s/ James E. Brown

---

James E. Brown  
Chief Executive Officer

cc: Jian Li, DURECT Corporation  
Jean Liu, DURECT Corporation  
Fran Schulz, Ernst & Young LLP  
Mark Weeks, Heller Ehrman LLP  
Stephen Thau, Heller Ehrman LLP

Attachment – Sample Disclosure of Research and Development Expenses in Form 10-Q for the quarterly period ending September 30, 2005

*Research and Development.* Research and development expenses were \$XX million and \$XX million for the three and nine months ended September 30, 2005, respectively, compared with \$XX million and \$XX million for the corresponding periods in 2004. The [increase] [decrease] in the three and nine months ended September 30, 2005 was primarily attributable to [LIST OF FACTORS FOR PROGRAMS], partially offset by [OTHER FACTORS].

In the three and nine months ended September 30, 2005, we continued with [UPDATE TO STATUS OF PROGRAMS]. In addition, we incurred [higher] [lower] expenses for [ACTIVITIES RELATED TO PROGRAMS]. As of September 30, 2005, we had XX research and development employees compared with XX as of the corresponding date in 2004. We expect research and development expenses to [increase] [decrease] in the near future as we continue product development efforts for our internal and partnered product candidates.

The research and development expenses associated with our major product candidates approximate the following (in thousands):

|   | Three months ended<br>September 30, |         | Nine months ended<br>September 30, |         |
|---|-------------------------------------|---------|------------------------------------|---------|
|   | 2005                                | 2004    | 2005                               | 2004    |
| SABER™-Bupivacaine                      | \$X,XXX                             | \$X,XXX | \$X,XXX                            | \$X,XXX |
| ORADUR™ (Remoxy)                        | X,XXX                               | X,XXX   | X,XXX                              | X,XXX   |
| TRANSDUR™ Sufentanil                    | X,XXX                               | X,XXX   | X,XXX                              | X,XXX   |
| DURIN™-Leuprolide                       | X,XXX                               | X,XXX   | X,XXX                              | X,XXX   |
| CHRONOGESIC                             | X,XXX                               | X,XXX   | X,XXX                              | X,XXX   |
| Others                                  | X,XXX                               | X,XXX   | X,XXX                              | X,XXX   |
| Total Research and Development Expenses | \$X,XXX                             | \$X,XXX | \$X,XXX                            | \$X,XXX |

The Company cannot reasonably estimate the timing and estimated costs of our research and development programs due to the risks and uncertainties associated with developing pharmaceutical product candidates as outlined in the “Factors that May Affect Future Results” section of this report. The duration of development of the Company’s research and development programs may span as many as ten years or more, and estimation of completion dates or costs to complete would be highly speculative and subjective due to the numerous risks and uncertainties associated with developing pharmaceutical products, including significant and changing government regulation, the

---

uncertainties of future preclinical and clinical study results, the uncertainties with our partners' commitment and progress to the programs and the uncertainties associated with process development and manufacturing as well as sales and marketing. In addition, with respect to our partnered development programs, the timing and expenditures to complete the programs are subject to the control of our partners. Therefore, the Company cannot reasonably estimate the timing and estimated costs of the efforts necessary to complete the research and development programs. For additional information regarding these risks and uncertainties, see "Factors that May Affect Future Results" below.