

September 1, 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 August 16, 2005, which sets forth the Staff's comments 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 table included in the section entitled "Product Research and Development Programs" on page 10. However, we believe that your disclosures about historical research and development expenses and estimated future expenses related to your major research and development projects could be enhanced for investors. Please refer to the Division of Corporation Finance "Current Issues and Rulemaking Projects Quarterly Update" under section VIII – Industry Specific Issues – Accounting and Disclosure by Companies Engaged in Research and Development Activities. You can find it at the following website address: [http: www.sec.gov/divisions/corpfin/cfcrq032001.htm#secviii](http://www.sec.gov/divisions/corpfin/cfcrq032001.htm#secviii).**

**Please disclose the following information for each of your major research and development projects:**

- a. The costs incurred during each period presented and to date on the project;**

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- b. The nature, timing and estimated costs of the efforts necessary to complete the project;**
  - c. The anticipated completion date;**
  - d. The risks and uncertainties associated with completing development on schedule and the consequences to your operations, financial position and liquidity if the project is not completed timely; and, finally**
  - e. The period in which material net cash inflows from your significant projects are expected to commence.**

**Regarding a., if you do not maintain research and development costs by project, please disclose why management does not maintain and evaluate research and development costs by project. Include other quantitative or qualitative analyses that indicate the amount of the company's resources being used on these projects.**

**Regarding b. and c., please disclose the amount or range of estimated costs and timing to complete the phase in process and each future phase. To the extent that information is not estimable, please disclose the facts and circumstances indicating the uncertainties that preclude you from making a reasonable estimate.**

Response:

a) In response to the Staff's comment, in future filings, we will provide research and development costs incurred during each period presented, in the form of two tables that show our research and development expenses by stage (earlier stage programs vs. later stage programs) and by type (internal programs vs. partnered programs) in order to provide meaningful and accurate disclosure to our investors. For purposes of this disclosure, "early stage programs" are programs that have not yet entered human clinical trials, and "later stage programs" are programs that have entered human clinical trials. A sample of how this disclosure would appear is attached to this letter. The Company believes that additional disclosure of expenses as allocated between earlier stage programs and later stage programs will provide investors with a better understanding of the overall risks associated with the Company's development pipeline (i.e., between programs that are earlier stage with more risk versus programs that are later stage with less risk). In addition, the proposed disclosure of expenses as allocated between internal programs and partnered programs provides investors with information about the proportion of expenses that are borne by the Company exclusively (i.e., internal programs) versus expenses that are potentially reimbursed by collaborative partners (i.e., partnered programs), thus providing investors with further meaningful information with respect to the risks associated with the Company's expenses.

The Company respectfully submits that detailed disclosure of research and development expenses incurred for each of its major research and development projects would be extremely deleterious to the Company's ability to conduct its business and have a negative impact on stockholder value, the costs of which outweigh the incremental

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information that investors would receive. In the Company's Form 10-K for the fiscal year ended December 31, 2004, the Company has disclosed the non-confidential business terms for each of its partnered research and development programs. In the Form 10-K and in each subsequent quarterly report on Form 10-Q, the Company also provides detailed disclosure regarding the status of each of the Company's significant partnered development programs, as well as disclosure regarding the collaborative research and development revenues from each such program that exceed 10% of the Company's revenues for the periods presented. As disclosed in these reports, revenues from these programs are from reimbursement of qualified expenses. Thus, investors already have detailed information regarding the development status and financial magnitude of each of the Company's significant partnered research and development programs. As noted above, in future filings, the Company will also disclose information about expenses for its internal research and development programs.

Additional specific disclosure about research and development expenses for the Company's development programs would harm the Company and its stockholders by revealing competitively sensitive confidential information of the Company and its collaborative partners. The Company and its partners are engaged in the research and development of products in highly competitive fields (e.g., pain therapies and related products), and, in fact, several other companies are pursuing similar products to those of the Company and its development partners. Disclosing specific information about development expenses for each specific program would enable competitors to infer with specificity the status of the Company's development activities. Competitors could better anticipate the Company's progress and plan counter-measures, such as increasing or decreasing the rate of their competing development programs accordingly. In addition, the Company negotiates the specific terms of each of its agreements with collaborative partners separately. These terms depend on a variety of factors and are the subject of intense negotiation. The disclosure of the Company's expenses by project would allow the Company's existing and potential collaborative partners to glean insight into confidential arrangements between the Company and other parties, thus potentially harming the Company's ability to effectively negotiate additional collaborative arrangements on the most favorable terms, to the detriment of the Company and its stockholders. DURECT's collaborative partners also closely guard information regarding their own development expenses and plans, and DURECT's ability to enter into future development agreements would be harmed if potential collaborators know that DURECT will reveal this information. Finally, agencies and third-parties that will be responsible for establishing medical reimbursement rates for the Company's or its partners' products, if approved, could use detailed information regarding the development expenses for those products against the Company or its partners to reduce reimbursement rates, effectively limiting the revenues that the Company or its partners can receive from the sale of the Company's products. Any such pricing pressure would harm the Company's growth and result in harm to the Company's stockholders. For these reasons, the Company submits that its now proposed disclosure provides the appropriate balance between disclosure to investors to enable them to evaluate the Company's prospects and risks while preserving confidentiality necessary for the Company to effectively run its business and maximize stockholder value.

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b) The nature of the effort to complete developing pharmaceutical product candidates is set forth in the "Business" section of the Company's annual report on Form 10-K for the fiscal year ended December 31, 2004. The Company cannot reasonably estimate the timing and estimated costs of our research and development projects due to the risks and uncertainties associated with developing pharmaceutical product candidates as outlined in the "Business" section as well as in the "Factors that May Affect Future Results" section of our annual report on Form 10-K. The duration of development of the Company's research and development projects 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 projects 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 projects. To address the risks associated with estimating the completion of developing pharmaceutical products, the Company will add appropriate risk factor language to the MD&A disclosure which specifically outlines the difficulty in determining estimated future costs or time to project completion of products in development.

c) The Company cannot reasonably estimate the anticipated completion date of our projects for the reasons outlined in section (b) above.

d) The Company has included discussions on the risks and uncertainties associated with completing development on schedule and the consequences to the Company's operations, financial position and liquidity if the project is not completed timely in the "Factors that May Affect Future Results" section in the Form 10-K for the fiscal year ended December 31, 2004. The Company will include reference to these risks as part of the MD&A disclosure.

e) As discussed above, it is virtually impossible for the Company to estimate the period in which material net cash inflows from the Company's significant research and development projects are expected to commence.

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.

**2. We note, per your disclosure in the “Strategy” section on page 8 and notes to your consolidated financial statements, that you are party to several collaboration/development agreements pursuant to which you have received up-front license fees. For example, we note that received a \$10.0 million up-front fee from Endo Pharmaceuticals related to your CHRONOGESIC license and development agreement. Please include disclosure for the periods presented, that outlines both the amount and accounting treatment related to each up-front fee that you have received under your significant collaboration/development agreements. In the instances, where you have recorded deferred revenue, please specify your amortization methodology and disclose the facts that support your methodology, including the recognition period.**

Response:

Consistent with the Staff's comment, we provided expanded disclosure related to up-front fees in the Company's Quarterly Reports on Form 10-Q filed on May 6, 2005 and August 4, 2005. The Company will continue to include such disclosure regarding up-front fees in future filings.

**3. Please disclose how you recognize milestone and royalty revenues. Stating that the amounts are “recognized as earned” is not clear.**

Response:

In response to the Staff's comment, we advise the staff that the Company has not received and does not anticipate receiving any royalties in the near future. In future filings we will amend our disclosures regarding revenue recognition policies related to milestone payments and exclude any discussion regarding future royalty revenues. For example, we will provide the following disclosure in future filings, as appropriate:

Milestone payments under collaborative arrangements are recognized as revenue upon achievement of the milestone events, which represent the culmination of the earnings process. Milestone payments are triggered either by the results of the Company's research and development efforts or by events external to the Company, such as regulatory approval to market a product or the achievement of specified sales levels by a collaboration partner. As such, the milestones are substantially at risk at the inception of the collaboration agreement, and the amounts of the payments assigned thereto are commensurate with the milestone achieved. In addition, upon the achievement of a milestone event, the Company has no future performance obligations related to that milestone payment.

**4. We note that you issued stock and warrants to ALZA Corporation, valued at \$13.5 million, which you recorded to a contra-equity account in your statement of stockholders' equity. Please provide us with additional information regarding the basis for your accounting treatment, including your valuation of the common stock and warrants, given that there was no market for your common stock at the time of the amendment to your development/commercialization agreement with ALZA. Please reference the applicable literature under U.S. GAAP. Additionally, please tell us what portion of this amendment consideration related to a reduction in "up-front payments" and specify your related accounting treatment, particularly given your on-going role in product development under this agreement.**

Response:

In response to the Staff's comment, we refer the Staff to the letter from Mr. Steven Duvall of August 21, 2000, which addressed this comment and set forth the Staff's view and direction with respect to this matter.

In connection with responding to the Staff's comments, the Company acknowledges 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.

Sincerely,

/s/ James E. Brown

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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.

Our research and development programs can be divided into earlier stage programs and later stage programs. Early stage programs include programs that have not yet entered into human clinical trials and generally include activities such as dosage form design, formulation development and pre-clinical animal studies. Later stage programs include programs that have entered human clinical trials, and expenses shown below include all program activities incurred for such programs in the periods presented, such as clinical trials, regulatory and medical affairs and clinical supplies manufacturing, as well as on-going non-clinical activities for such programs, such as toxicity studies or additional formulation development, that may be run in parallel. The research and development expenses associated with earlier stage programs and later stage programs approximate the following (in thousands):

	Three months ended September 30,		Nine months ended September 30,	
	2005	2004	2005	2004
Earlier Stage Programs	\$X,XXX	\$X,XXX	\$X,XXX	\$X,XXX
Later Stage Programs	X,XXX	X,XXX	X,XXX	X,XXX
Total Research and Development Expenses	\$X,XXX	\$X,XXX	\$X,XXX	\$X,XXX

Our research and development programs can also be divided into internal programs, for which we have not entered into an agreement with a third party collaborator and where we bear expenses exclusively, and partnered programs, for which we have entered into a third-party agreement and potentially may receive reimbursement for qualified research and development expenses from the collaborative third-party. The research and development expenses associated with internal programs and partnered programs approximate the following (in thousands):

	Three months ended September 30,		Nine months ended September 30,	
	2005	2004	2005	2004
Internal Programs	\$X,XXX	\$X,XXX	\$X,XXX	\$X,XXX
Partnered Programs	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.