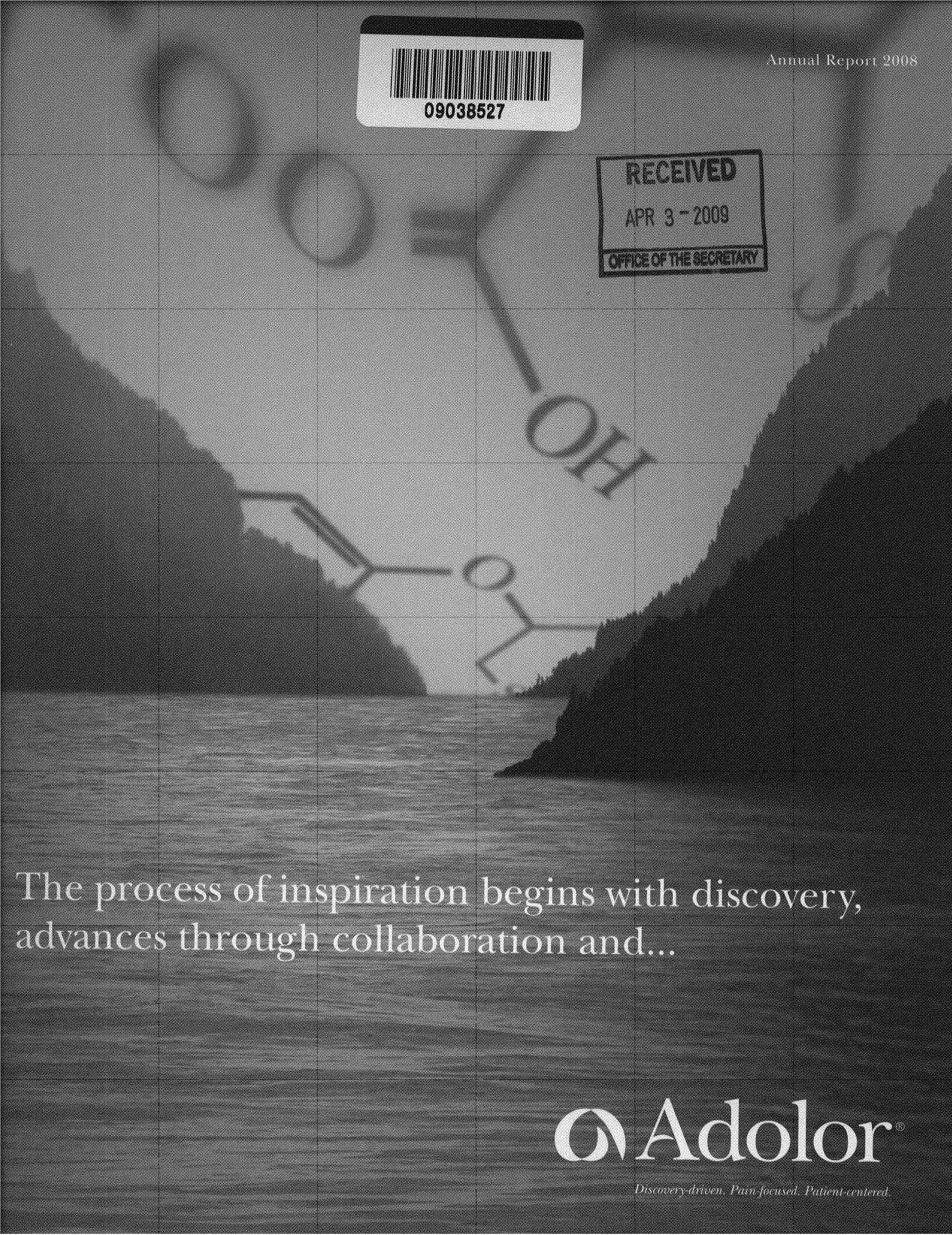
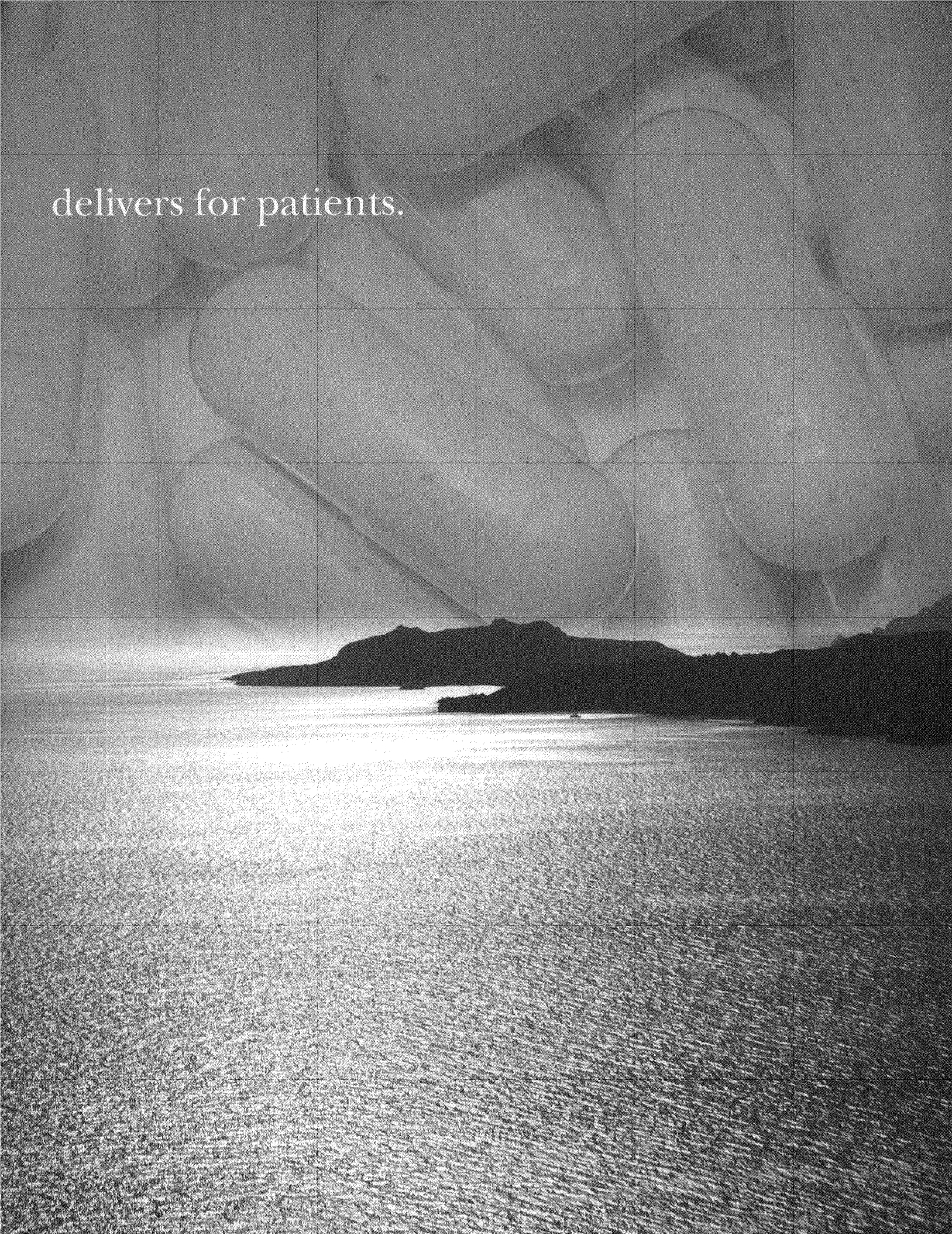


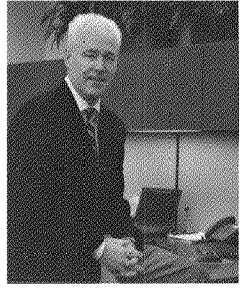

Annual Report 2008

The process of inspiration begins with discovery, advances through collaboration and...

Adolor®

*Discovery-driven. Pain-focused. Patient-centered.*


delivers for patients.



## Dear Stockholders

It is no exaggeration to say that Adolor is a different company today than it was at the beginning of last year. From receiving a long-awaited regulatory approval and entering the marketplace with our first product, ENTEREG® (alvimopan), to adapting our pipeline and our relationships with partners, 2008 was a year of fundamental change. These accomplishments have moved Adolor into a new era and left us in a strong position to advance our programs amid the unpredictable conditions in the economy and our industry.

We continue to pursue the commitment to our mission to improve the management of pain with an approach that consistently places new opportunities before us. We call it the *process of inspiration*, a phrase that recognizes that creativity and innovation in this industry require unique discipline, focused resources, and rigorous methods; that to achieve success, ideas and insights must be coupled with determined planning and sustained effort.

At Adolor, the process of inspiration begins with a robust discovery effort in our own labs, advances through strategic development collaborations with investigators and industry partners, and ultimately delivers new medicines for patients living with pain. In 2008, we made significant progress in all of these areas.

### Delivering New Medicines

The biggest news for Adolor last year was the U.S. Food and Drug Administration approval of ENTEREG for the management of postoperative ileus following bowel resection surgery. The first drug ever approved for this indication, ENTEREG is intended to accelerate gastrointestinal recovery and to reduce hospital stays for the approximately 500,000 Americans who undergo this common procedure each year. We launched ENTEREG in the second half of 2008 with our collaborator, GlaxoSmithKline (GSK). We focused initial efforts on registering hospitals in our ENTEREG Access Support and Education (E.A.S.E.™) Program and then shifted to the consideration for inclusion of ENTEREG on hospital formularies. Solid progress was made on both fronts by the end of last year.

The feedback about ENTEREG has been enthusiastic. Recently, a leading bowel resection surgeon told us that adoption of the drug was making a "huge difference" for his bowel resection patients, particularly the elderly. This kind of positive experience will help us build momentum as we work with healthcare providers to improve outcomes for their bowel resection patients.

### Advancing through Development

Last year, we also made important progress in our second major development program, as collaboration efforts with Pfizer Inc. on our proprietary family of *delta* opioid receptor agonist analgesic candidates began in earnest. Exploiting a different opioid pathway, *delta* agonists may avoid some of the negative side effects associated with currently available opioid pain relievers.

As can be expected for early stage compounds with a novel mechanism of action, the *delta* program produced some mixed results and valuable learnings in 2008. Last December, we announced results from two Phase 2a studies of ADL5859, one in diabetic neuropathic pain and the second in inflammatory pain associated with rheumatoid arthritis. Our analysis showed no statistical difference to placebo in either study, although ADL5859 was generally well tolerated. We noted a high degree of variability between patients in the way the drug was absorbed, which we believe impacted the results. We are working with Pfizer to improve the pharmacokinetics of the current formulation and anticipate initiating Phase 2a proof-of-concept clinical studies later in 2009.

For our second *delta* compound, ADL5747, we recently completed enrollment in a multiple ascending dose Phase 1 trial in healthy volunteers. To date, we've not observed any dose limiting toxicity or clinically serious adverse events. Later this year, we expect to initiate Phase 2a proof-of-concept trials with ADL5747 in osteoarthritis and neuropathic pain.

A significant transition occurred in 2008 in our chronic opioid bowel dysfunction (OBD) program, with our decision to discontinue development of alvimopan for chronic indications and focus exclusively on ADL7445. ADL7445 is the latest promising product candidate to emerge from our discovery efforts and, like alvimopan, is a *mu* opioid receptor antagonist. We expect to file an Investigational New Drug Application later this year to begin clinical testing for ADL7445 in OBD, still a large and unmet medical need. Our long-term success continues to rest on the productivity and performance of our discovery team.

### Financial and Managerial Strength

Behind all this activity, Adolor remains a well-capitalized company. In these uncertain economic times, balance sheet strength has never been more important. During 2008, we prudently managed our expenses and realized additional funding from our collaborators. We enter 2009 with $131.9 million in cash and investments, and remain debt-free.

Our list of accomplishments in 2008 wouldn't be complete without recognition of the new management and Board talent we attracted to Adolor. We appointed Dr. Eliseo O. Salinas as Senior Vice President Research & Development and CMO, John M. Limongelli, Esq., as Senior Vice President, General Counsel and Secretary and Stephen W. Webster as Senior Vice President, Finance and CFO. Seasoned industry executives John W. Wilson and Elizabeth V. Jobes, Esq., joined the company to oversee sales and marketing and compliance functions, respectively. We also welcomed Dr. Guido Magni, most recently the global head of drug development for F. Hoffman-La Roche, to our Board of Directors. These individuals bring a tremendous expertise to the company and support and strengthen key areas of our business.

In closing, it has been extremely gratifying for me to watch the process of inspiration transform Adolor over the past year. We are ready for the challenge of moving our business forward in 2009. I am grateful for your ongoing support and I hope you continue to share my enthusiasm for the process of inspiration that will be the hallmark of our future success.

Michael R. Dougherty
President and Chief Executive Officer
March 2, 2009

## Stockholder Information

### Corporate Headquarters

Adolor Corporation
700 Pennsylvania Drive
Exton, PA 19341

Telephone: 484-595-1500
Facsimile: 484-595-1520
www.adolor.com

### Adolor Common Stock Listing

The common stock of Adolor is listed on the Nasdaq Global Market under the symbol ADLR

### Form 10-K

A copy of Adolor's Annual Report on Form 10-K for the fiscal year ended December 31, 2008 is available without charge by contacting Adolor's Investor Relations department at 484-595-1500 or 700 Pennsylvania Drive, Exton, PA 19341.

### Annual Stockholders Meeting

The annual meeting of stockholders will be held at 8:30 a.m. on Tuesday, May 12, 2009 at The Desmond Great Valley Hotel and Conference Center, One Liberty Boulevard, Malvern, Pennsylvania 19355.

### Transfer Agent and Registrar

StockTrans
44 West Lancaster Avenue
Ardmore, PA 19003
www.stocktrans.com

### Forward-Looking Statements

This annual report may contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements provide Adolor's current expectations or forecasts of future events. You may identify some of these forward-looking statements by the use of words such as "anticipate," "estimate," "expect," "project," "intend," "plan," "believe" or other words and terms of similar meaning or that otherwise express contingencies, goals, targets or future development. These statements are based upon management's current expectations and are subject to risks and uncertainties, known and unknown, that could cause actual results and developments to differ materially from those expressed or implied in such statements due to general financial, economic, regulatory and political conditions affecting the biotechnology and pharmaceutical industries, as well as more specific risks and uncertainties facing Adolor such as those set forth in its reports filed with the U.S. Securities and Exchange Commission. Adolor urges you to carefully review and consider the disclosures found in its filings which are available at www.sec.gov and from Adolor at www.adolor.com. Given the uncertainties affecting pharmaceutical companies such as Adolor, any or all of these forward-looking statements may prove to be incorrect. Therefore, you should not rely on any such factors or forward-looking statements. Adolor undertakes no obligation to publicly update or revise the statements made herein, except as may be required by law.

### Investor Relations

Updated information about Adolor Corporation is available on the company's home page located on the World Wide Web at http://www.adolor.com.

### Auditors

KPMG LLP
Philadelphia, PA

### Board of Directors

David M. Madden, Chairman
Founder and Principal, Narrow River Management, LP

Armando Anido
Chief Executive and President, Auxilium Pharmaceuticals, Inc.

Michael R. Dougherty
President and Chief Executive Officer, Adolor Corporation

Georges Gemayel, Ph.D.
President, Chief Executive Officer and Director, Altus Pharmaceuticals Inc.

Paul Goddard, Ph.D.
Chairman and Chief Executive Officer, ARYx Therapeutics, Inc.

George V. Hager, Jr.
Chairman and Chief Executive Officer, Genesis HealthCare

Guido Magni, M.D., Ph.D.
Former Global Head of Medical Science, Pharmaceutical Division, F. Hoffman-La Roche Ltd.

Claude H. Nash, Ph.D.
Chairman of the Board of Directors, BloodstoneVentures, plc

Donald E. Nickelson
Vice Chairman and Director, Harbour Group Industries Inc.

### Executive Officers

Michael R. Dougherty
President, Chief Executive Officer and Director

John M. Limongelli, Esq.
Senior Vice President, General Counsel and Secretary

George R. Maurer
Senior Vice President, Manufacturing and Pharmaceutical Technologies

Elisco O. Salinas, M.D., M.S.C.
Senior Vice President, Research and Development and Chief Medical Officer

Stephen W. Webster
Senior Vice President, Finance and Chief Financial Officer

### Management Team

Elizabeth V. Jobes, Esq.
Vice President, Chief Compliance Officer

Richard M. Mangano, Ph.D.
Vice President, Clinical Research and Development

David M. Stephon
Vice President, Quality Management

Kevin G. Taylor
Vice President, Business Development

Lee Techner, D.P.M.
Vice President, Medical Affairs and Medical Director

John P. Wilson
Vice President, Sales and Marketing

Richard M. Woodward, Ph.D.
Vice President, Discovery

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

# FORM 10-K

**(Mark One)**

☑ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
**For The Fiscal Year Ended December 31, 2008**

**OR**

**For the Transition Period from _____ to _____**

**Commission File 000-30039**



# ADOLOR CORPORATION
**(Exact name of registrant as specified in its charter)**

| **Delaware** | **31-1429198** |
|---|---|
| **(State or other jurisdiction of incorporation or organization)** | **(IRS Employer Identification Number)** |
| **700 Pennsylvania Drive, Exton, Pennsylvania** | **19341** |
| **(Address of principal executive offices)** | **(Zip code)** |

**(484) 595-1500**
**(Registrant's telephone number, including area code)**

**Securities registered pursuant to Section 12(b) of the Act:**

| **(Title of each class)** | **(Name of each exchange on which registered)** |
|---|---|
| **Common Stock, $0.0001 par value** | **NASDAQ** |
| **Series A Junior Participating Preferred Stock Purchase Rights** | **None** |

**Securities registered pursuant to Section 12(g) of the Act: None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☑

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes ☐ No ☑

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports) and (2) has been subject to such filing requirements for the past 90 days. Yes ☑ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☑

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. Check one:

Large accelerated filer ☐ Accelerated filer ☑ Non-accelerated filer ☐ Smaller reporting company ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☑

The aggregate market value of common stock held by non-affiliates of the registrant was $248,313,607 as of June 30, 2008, the last business day of the registrant's most recently completed second fiscal quarter. Such aggregate market value was computed by reference to the closing price of the common stock as reported on the NASDAQ Global Market on June 30, 2008. For purposes of determining this amount only, the registrant has defined affiliates as including (a) the executive officers of the registrant as of June 30, 2008 and (b) all directors of the registrant as of June 30, 2008.

The number of shares of the registrant's common stock outstanding as of February 19, 2009 was 46,333,735.

## DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive proxy statement (the "Definitive Proxy Statement") to be filed with the Securities and Exchange Commission in connection with the Company's Annual Meeting of Stockholders for the fiscal year ended December 31, 2008 are incorporated by reference into Items 10, 11, 12, 13 and 14 of Part III of this Form 10-K.

**ADOLOR CORPORATION**

**FORM 10-K**

**December 31, 2008**

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## CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

In addition to historical facts or statements of current condition, this report and the documents into which this report is and will be incorporated contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements contained in this report or incorporated herein by reference constitute our expectations or forecasts of future events as of the date this report was filed with the Securities and Exchange Commission and are not statements of historical fact. You can identify these statements by the fact that they do not relate strictly to historical or current facts. Such statements may include words such as "anticipate," "will," "estimate," "expect," "project," "intend," "should," "plan," "believe," "hope" and other words and terms of similar meaning in connection with any discussion of, among other things, sales, future operating or financial performance, strategic initiatives and business strategies, regulatory or competitive environments, our intellectual property and product development. In particular, these forward-looking statements include, among others, statements about:

- our dependence on sales of ENTEREG® (alvimopan) in the United States and the commercial prospects and future marketing efforts for this product;
- our anticipated scientific progress in our research programs and our development of potential pharmaceutical products, including our ongoing or planned clinical trials, the status, timing, costs and results of such trials, the ability to secure regulatory approval for our product candidates and the likelihood or timing of revenues from these products, if any;
- the scope and duration of our intellectual property protection for our products and product candidates, our ability to adequately protect our technologies and enforce our intellectual property rights and the future expiration of patent and/or regulatory exclusivity on alvimopan;
- our anticipated operating losses and cash requirements, projections regarding the levels of our cash, cash equivalents and investments and our ability to raise additional funds in light of our current and projected level of operations; and
- other statements regarding matters that are not historical facts or statements of current condition.

Any or all of our forward-looking statements in this report and in the documents to which we have referred you may turn out to be wrong. They can be affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties. Therefore, you should not place undue reliance on any such forward-looking statements. The factors that could cause actual results to differ from those expressed or implied by our forward-looking statements include, among others:

- the acceptance of ENTEREG by hospitals, physicians and patients in the marketplace;
- scientific or regulatory setbacks with respect to research programs, clinical trials, manufacturing activities or commercial activities;
- the timing and unpredictability of regulatory actions;
- our ability to develop and launch new products effectively;
- unanticipated cash requirements to support current operations, to expand our business or for capital expenditures;
- the inability to adequately protect our key intellectual property rights;
- the loss of key management or scientific personnel;
- the activities of our competitors;
- regulatory, legal or other setbacks with respect to our operations or business;

- market conditions in the capital markets and the biopharmaceutical industry that make raising capital or consummating acquisitions difficult, expensive or both; and
- enactment of new government laws, regulations, court decisions, regulatory interpretations or other initiatives that are adverse to us or our interests.

We do not intend to update publicly any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law. We discuss in more detail the risks that we anticipate in Part I, Item 1A of this report. This discussion is permitted by the Private Securities Litigation Reform Act of 1995.

## PART I

### ITEM 1. BUSINESS

### OVERVIEW

Adolor Corporation is a biopharmaceutical company focused on the discovery, development and commercialization of novel prescription pain management products. On May 20, 2008, the U.S. Food and Drug Administration (FDA) approved our first product, ENTEREG® (alvimopan), for the management of postoperative ileus following bowel resection surgery (POI). POI causes significant discomfort for patients and results in increased expense to healthcare providers. ENTEREG is specifically indicated to accelerate the time to upper and lower gastrointestinal (GI) recovery following partial large or small bowel resection surgery with primary anastomosis. In collaboration with Glaxo Group Limited (Glaxo), we launched ENTEREG in the United States in mid-2008.

We also have a number of product candidates in various stages of clinical and preclinical development. We are collaborating with Pfizer Inc. (Pfizer) for the development and commercialization of two *delta* opioid receptor agonist compounds, ADL5859 and ADL5747 (Pfizer compounds PF-04856880 and PF-04856881, respectively), for the treatment of pain. We recently completed three Phase 2a clinical trials of the initial formulation of ADL5859 and, based on the results of these trials, Pfizer and we are re-formulating ADL5859 before resuming clinical testing in 2009. We recently completed Phase 1 clinical testing of ADL5747 and have not observed any dose-limiting toxicity or serious adverse events with this compound. In addition to our *delta* compounds, we are developing ADL7445 to treat opioid bowel dysfunction (OBD), a condition that often results from chronic use of opioid analgesics to treat persistent pain conditions. ADL7445 is in preclinical development and we intend to submit an Investigational New Drug Application (IND) in the third quarter of 2009. Our other product candidates are in preclinical development for treating moderate-to-severe pain and other central nervous system (CNS) conditions.

For the year ended December 31, 2008, our total revenues and net loss were $49.5 million and $30.1 million, respectively. Net shipments of ENTEREG through December 31, 2008 were $2.2 million, of which we recognized $1.2 million as net product sales under our revenue recognition policy. We will need to grow sales of ENTEREG significantly beyond current levels before we will be able to achieve profitability and positive cash flows from operations. The rate of our future growth will depend on, among other things, the acceptance of ENTEREG in the marketplace, our ability to maintain adequate intellectual property protection for ENTEREG and our success in developing and commercializing additional product candidates. Ultimately, we may never generate significant product sales revenues, achieve profitable operations or generate positive cash flows from operations and, even if profitable operations are achieved, they may not be sustained on a continuing basis or sufficient to generate the operating cash flow to support our current or projected levels of operation.

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We are a Delaware corporation with our principal executive offices located at 700 Pennsylvania Drive, Exton, Pennsylvania, 19341. Our telephone number is (484) 595-1500 and our web site address is *www.adolor.com*. We include our web site address in this Annual Report on Form 10-K only as an inactive textual reference and do not intend it to be an active link to our web site. The information on our website is not incorporated by reference in this Annual Report on Form 10-K.

Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and all amendments to those reports, as well as other documents we file with the U.S. Securities and Exchange Commission (SEC), are available free of charge through the Investor Insights section of our web site as soon as reasonably practicable after such material is electronically filed with or furnished to the SEC. The public can obtain documents that we file with the SEC at *www.sec.gov*.

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## ENTEREG FOR POSTOPERATIVE ILEUS

ENTEREG (alvimopan) is a small molecule, peripherally-acting *mu*-opioid receptor antagonist intended to block the adverse side effects of opioid analgesics on the GI tract without affecting their beneficial analgesic effects. ENTEREG was approved by the FDA on May 20, 2008 for the management of POI and together with our partner, Glaxo, we launched the product in the United States in mid-2008. ENTEREG is specifically indicated to accelerate the time to upper and lower GI recovery following partial large or small bowel resection surgery with primary anastomosis. The recommended adult dose of ENTEREG is a single 12 milligram capsule administered orally 30 minutes to five hours prior to surgery followed by a 12 milligram capsule twice daily beginning the day after surgery for a maximum of seven days or until discharge, not to exceed a total of 15 doses.

In April 2007, Glaxo and we announced the results of Study 014, a Phase 3 long-term safety study of alvimopan in patients taking opioids for chronic non-cancer pain and experiencing OBD. Results from Study 014 showed numerically more myocardial infarctions and other cardiovascular serious adverse events reported by patients treated long-term with alvimopan in this study compared to placebo. As a result, ENTEREG was approved in POI subject to a Risk Evaluation and Mitigation Strategy (REMS) and the product labeling carries a boxed warning that ENTEREG is available only for short-term (15 doses) use in hospitalized patients. The REMS is designed to maintain the benefits associated with short-term use in the bowel resection population and prevent long-term, outpatient use.

Under the REMS, ENTEREG is available only to hospitals that perform bowel resection surgeries and that are enrolled in the ENTEREG Access Support and Education (E.A.S.E.™) Program. Hospitals can enroll in the E.A.S.E Program if they: have reviewed the E.A.S.E. Program educational materials, have systems in place to limit the use of ENTEREG to no more than 15 doses per patient, ensure in-hospital use only and will not transfer ENTEREG to an unregistered hospital. Upon enrollment, hospitals can order ENTEREG through wholesalers and on receipt and verification of the order, Glaxo will drop-ship ENTEREG directly to the hospital pharmacy. As of December 31, 2008, approximately 1,100 hospitals have registered.

*Market Opportunity and Commercialization*

Postoperative ileus is the impairment of GI motility after intra-abdominal surgery or other non-abdominal surgeries. It is associated with abdominal distension and bloating, persistent abdominal pain, nausea and vomiting, variable reduction of bowel sounds, delayed passage of or an inability to pass flatus (gas) or stool and an inability to tolerate oral intake or progress to a solid diet. POI may potentially delay GI recovery and hospital discharge until its resolution, resulting in decreased patient quality of life, increased medical care and an increased cost burden on healthcare providers.

There are over 4,000 hospitals in the United States that perform bowel resection surgeries. Glaxo and we are initially targeting the approximately 1,400 hospitals that perform approximately 80% of the bowel resection surgeries in the United States. ENTEREG is detailed primarily by Glaxo's national hospital-based sales organization and we are co-promoting ENTEREG in certain hospitals with a field force that we expect will number 25 persons by mid-2009. Our initial launch efforts focused on registering hospitals in the E.A.S.E. Program and, as of December 31, 2008, approximately 1,100 hospitals have been registered, including approximately 45% of the target 1,400 hospitals.

In late 2008 and early 2009, the focus of our activity has shifted from registration to the consideration of ENTEREG by hospital pharmacy and therapeutics (P&T) committees. In the United States, each hospital's or hospital group's prescribing is influenced by a list of accepted drugs called a formulary. Most hospitals have a P&T committee which meets periodically to determine which pharmaceutical products to add to the formulary. Once a pharmaceutical is on formulary, it is easier for a physician within a hospital or hospital group to prescribe the drug. As such, we consider hospital formulary approval to be critical to the commercial success of ENTEREG. As of December 31, 2008, we estimate that approximately 300 hospitals, including approximately 200 of the target 1,400 hospitals, had approved ENTEREG for inclusion on their formularies.

*Market Expansion and Further Clinical Development*

In 2009, Glaxo and we are undertaking a number of initiatives to potentially increase the awareness and acceptance of ENTEREG among hospitals and physicians performing bowel resection surgeries. These efforts will include studies intending to address pharmacoeconomic and health outcomes associated with accelerated GI recovery. Longer-term, Glaxo and we are evaluating additional clinical studies of ENTEREG for POI resulting from pain management following surgical procedures other than bowel resection surgeries. As required by our FDA approval letter for ENTEREG, in February 2009, we began a Phase 4 clinical trial intended to evaluate the safety and efficacy of ENTEREG for POI in patients undergoing radical cystectomy for bladder cancer. Radical cystectomy is an extensive abdominal and pelvic surgical procedure that can be associated with a significant POI burden. The trial is expected to enroll approximately 300 patients over the next several years.

*Glaxo Collaboration and Other License Agreement*

In April 2002, we entered into our collaboration agreement with Glaxo for the exclusive worldwide development and commercialization of ENTEREG for certain indications. At that time, Glaxo paid us a non-refundable and non-creditable signing fee of $50 million. Since 2002, we have received and recognized $30 million of milestone revenue, including $20 million received following FDA approval of ENTEREG in May 2008. Under the agreement, we have a profit-sharing arrangement pursuant to which we receive 45% and Glaxo receives 55% of profits, as defined. Profits are calculated as net sales of ENTEREG for POI within the United States less certain agreed-upon costs, subject to certain adjustments. Beginning in mid-2011, the parties will share such profits equally.

The term of the collaboration agreement for the POI indication in the United States is ten years from the first commercial sale of ENTEREG in that indication, which occurred in June 2008. Glaxo has the right, upon notice, to terminate its rights and obligations with respect to POI. Glaxo also has the right to terminate the collaboration agreement for breach of the agreement by us or for safety related reasons as defined in the collaboration agreement.

We also have a distribution agreement with Glaxo under which it performs certain distribution and contracting services for ENTEREG on our behalf for a fee. External expenses for research and development and marketing activities incurred in the United States by each company are reimbursed by the other party pursuant to contractually agreed percentages. Contract reimbursement amounts owed to us by Glaxo are recorded gross on our statements of operations as cost reimbursement under collaborative agreement. Amounts reimbursable to Glaxo by us are recorded as research and development or marketing expense, as appropriate, on our statements of operations.

In September 2008, Glaxo returned to us all worldwide rights to alvimopan for the treatment of chronic OBD. Following an internal evaluation and an exploration of partnering opportunities, in December 2008, we ceased further development of alvimopan to treat chronic OBD. Based on discussions with Glaxo, we expect that they also will return to us the rights to alvimopan outside of the United States for the treatment of POI. We currently do not have any plans to seek approval to market alvimopan outside of the United States for the treatment of chronic OBD or POI.

In November 1996, Roberts Laboratories Inc. (Roberts) licensed from Eli Lilly and Company (Eli Lilly) certain intellectual property rights relating to ENTEREG. In June 1998, we entered into an option and license agreement with Roberts under which we sublicensed these rights from Roberts. In December 2000, Shire U.S. Inc. became the successor in interests to Roberts under our option and license agreement with Roberts. We have made license and milestone payments under this agreement totaling $2.5 million, including $0.9 million paid during the year ended December 31, 2008 as a result of ENTEREG receiving regulatory approval. Our license to ENTEREG and our obligations to pay royalties to Shire and Eli Lilly expire on the later of either the date of the last to expire of the licensed Eli Lilly patents or November 5, 2011.

*Intellectual Property Position*

We have rights to patents related to ENTEREG that will expire between 2011 and 2020, including U.S. patents claiming the composition of alvimopan that will expire in 2011 and 2013. After the approval of ENTEREG in May 2008, we filed for a patent term extension to extend the term of one of these patents by five years. There can be no assurance that our application for patent term extension will be granted or that, if granted, the term extension will be five years. If we are granted patent term extension for an ENTEREG patent, we cannot be assured that any such extension will provide meaningful proprietary protection during the period of extension. We have rights to other patents and patent applications that also may protect ENTEREG until 2025 or 2026. These patents include U.S. patents claiming the use of ENTEREG in POI that expire in 2020 and various formulation patents.

*Manufacturing and Product Supply*

We depend on Piramal Healthcare (Canada) Limited (formerly Torcan Chemical Ltd.) as the sole approved supplier under our New Drug Application (NDA) of the active pharmaceutical ingredient (API) in ENTEREG. We also depend on Pharmaceutics International, Inc. to manufacture ENTEREG finished capsules. We seek to maintain inventories of finished products to protect against supply disruptions. Any future change in manufacturers or manufacturing process requires regulatory approval.

*Competition*

Currently, ENTEREG is the only FDA-approved product for the treatment of POI. We are aware of other products in clinical development for the treatment of POI, including methylnaltrexone, which was developed by Progenics Pharmaceuticals, Inc. (Progenics) in collaboration with Wyeth. In April 2008, methylnaltrexone as a subcutaneous injection was approved by the FDA for sale in the United States for the treatment of opioid-induced constipation (OIC) in patients with advanced illness who are receiving palliative care, when response to laxative therapy has not been sufficient. In addition, Tranzyme Pharma is currently developing TZP-101, an intravenous ghrelin agonist that is currently in Phase 2b clinical testing, for the treatment of POI.

*Customers*

Our principal customers are wholesale drug distributors. These customers comprise a significant part of the distribution network for all pharmaceutical products in the United States. Three large wholesale drug distributors, Cardinal Health, Inc., McKesson Corporation and AmerisourceBergen Corporation, control a significant share of this network. These three wholesale customers, in the aggregate, accounted for 93% of our total gross shipments for the year ended December 31, 2008. Under the E.A.S.E. Program, hospital orders are processed through wholesalers; however, ENTEREG is drop-shipped from Glaxo's warehouse directly to registered hospitals.

## RESEARCH AND DEVELOPMENT PROGRAMS

### Delta Opioid Receptor Agonists Program

Opioid receptors located in the brain and on the surface of nerves that modulate pain signals alter transmission of these pain signals when activated by drugs specific for those receptors. There are three major classes of opioid receptors—*mu*, *kappa* and *delta*. Virtually all marketed opioid analgesic drugs used to control moderate-to-severe pain interact with *mu*-opioid receptors in the brain and spinal cord. However, activating these opioid receptors in the central nervous system with morphine-like *mu* opioid analgesics often results in serious side effects such as sedation, decreased respiratory function, nausea and vomiting, euphoria and addiction.

Through a proprietary research platform based on cloned human opioid receptors, we have identified a series of novel, orally-active *delta* agonists that selectively stimulate the *delta* opioid receptor. We are pursuing development of these compounds as a potential new class of opioid analgesics that produce pain relief similar to

traditional *mu* opioids, while reducing or eliminating some typical narcotic side effects. In addition, *delta* agonists may have a role in modulating other biological processes that may manifest themselves in disease states or conditions such as depression, cognitive disorders and overactive bladder.

In December 2007, we entered into an exclusive worldwide license and collaboration with Pfizer to develop and commercialize our two proprietary *delta* opioid receptor agonist compounds, ADL5859 and ADL5747 (Pfizer compounds PF-04856880 and PF-04856881, respectively), for the treatment of pain.

*Clinical Development*

*ADL5859.* In 2007, we completed Phase 1 clinical testing of the initial formulation of ADL5859 in single- and multi-dose administration in healthy volunteers to investigate the safety, tolerability and pharmacokinetics of this formulation of ADL5859. We recently completed three Phase 2a clinical trials of the initial formulation of ADL5859 in patients in three different models of pain: acute pain after surgical removal of impacted third molars; neuropathic pain associated with diabetic peripheral neuropathy; and inflammatory pain associated with rheumatoid arthritis.

Study 33CL230 was a randomized, double-blind, single-dose, active and placebo controlled parallel group study of the initial formulation of ADL5859 for the treatment of acute pain after surgical removal of impacted third molars. The active control in Study 33CL230 was ibuprofen. The study enrolled 201 patients, and the primary endpoint was a measure of pain relief. Top-line results from Study 33CL230 indicated that ADL5859 was well tolerated, but that ADL5859 showed no efficacy signal in this model.

Study 33CL231 was a randomized, double-blind, placebo- and active-controlled parallel group study of the initial formulation of ADL5859 conducted to assess the safety and efficacy of ADL5859 in patients with neuropathic pain associated with diabetic peripheral neuropathy. The study enrolled 226 patients, randomized to placebo, 60 milligrams of duloxetine (once daily) and 100 milligrams of ADL5859 (twice daily). The primary outcome measure was change from baseline to week four in the pain intensity score via the Numeric Pain Rating Scale assessment measured three times daily. Top-line results of the study showed no statistically significant difference between ADL5859 and placebo. In addition, there was no statistically significant difference between patients treated with duloxetine and placebo. There was a large variability in response seen in all three arms of this trial. In addition, a high degree of variability was observed in plasma levels of ADL5859. ADL5859 was well-tolerated, with no serious adverse events reported during the study.

Study 33CL232 was a two-part study designed to assess the safety and efficacy of the initial formulation of ADL5859 in patients with inflammatory pain associated with rheumatoid arthritis. The study enrolled 46 patients. Part A was a single-dose, randomized, double-blind, placebo- and active-controlled, three-period crossover phase using a model of evoked pain produced by physical activity. Each subject received 200 milligrams of ADL5859, 500 milligrams of naproxen and placebo. The primary outcome measure of efficacy in Part A was the average difference between baseline and post-dose Evoked Lower Extremity Pain Intensity (ELEPI) after a treadmill walk over the six hours after dosing. Part B was a multiple-dose, randomized, double-blind, placebo-controlled, parallel group phase. Patients were re-randomized to receive either 100 milligrams of ADL5859 or matching placebo twice daily for 14 consecutive days. The primary measure of efficacy was the mean daily Lower Extremity Pain Intensity score measured three times daily over the two-week period. There were no statistically significant differences between ADL5859 200 milligrams and placebo in Part A of the study or between ADL5859 100 milligrams and placebo in Part B of the study. In Part A, there was a statistically significant decrease in ELEPI over six hours for patients receiving 500 milligrams of naproxen versus placebo. In this study, ADL5859 was well-tolerated, with no serious adverse events reported during the study.

Before commencing additional clinical trials for ADL5859 planned for later in 2009, Pfizer and we will re-formulate ADL5859 to address the pharmacokinetic variability observed in the Phase 2a trials.

*ADL5747.* We also are developing the *delta* opioid receptor agonist ADL5747 in collaboration with Pfizer. We recently completed enrollment in a multiple ascending dose Phase 1 trial in 32 healthy volunteers, and did not observe any dose-limiting toxicity or serious adverse events. Pfizer and we intend to initiate later in 2009 proof-of-concept trials of ADL5747.

*Collaboration Agreement with Pfizer*

Under our collaboration agreement with Pfizer, we are responsible for IND filings and Phase 1 and Phase 2a clinical studies and Pfizer is responsible for subsequent worldwide development, securing all regulatory approvals and for commercialization of the products. The development and commercialization of the products are managed by a joint steering committee consisting of representatives from both companies. The companies share external development expenses in support of regulatory filings in the United States with 60% paid by Pfizer and 40% paid by us. Expenses for development activities required for regulatory filings outside the United States are the responsibility of Pfizer.

Upon commercialization of any products, we will share in the net profits/net losses, as defined in the agreement, in the United States with 60% paid to Pfizer and 40% paid to us, and we will be entitled to receive royalty payments for net sales (as defined in the agreement) of products outside of the United States. We also retained an option to co-promote the products in the United States or convert our share of net profits, if any, into a royalty. Additional *delta* compounds and additional indications for compounds may be added to the collaboration on terms specified in the agreement.

We received an upfront payment of $30 million from Pfizer and reimbursement of $1.9 million for Phase 2a development costs that we had incurred prior to entering into the collaboration agreement. The agreement also provides that we may receive milestone payments of up to $155 million for the first compound and $77.5 million for a second compound. The milestone payments would become payable upon achievement of certain clinical, regulatory and commercial milestones defined in the agreement. The first milestone event defined is commencement of Phase 2b clinical testing.

The agreement expires on a country-by-country basis upon expiration of the royalty term in each country, which term is a minimum of ten years following first commercial sale of a licensed product, if any. Pfizer and we each have the right to terminate the agreement upon a material default of the other party. Pfizer also has the right to terminate the agreement for certain clinical study results as set forth in the agreement. Following completion of Phase 2b studies for ADL5859 and ADL5747, Pfizer has the right to terminate the agreement without cause upon one hundred eighty (180) days written notice to us.

*Intellectual Property*

We own a patent claiming the composition of ADL5859 and ADL5747. We project that this patent, which was issued on March 4, 2008, will expire in 2027. Currently, we have a number of pending patent applications that also claim our *delta* agonist product candidates both in the United States and in certain foreign countries.

**Opioid Bowel Dysfunction Program**

Just as there are opioid receptors in the central and peripheral nervous system that regulate the transmission of signals into the spinal cord, there are opioid receptors in the GI tract, or peripheral opioid receptors, that regulate functions such as motility and water secretion and absorption. Stimulation of these GI *mu* opioid receptors by morphine, or other *mu* opioid analgesics, can slow gut motility and disrupt normal GI function that allows for the passage, absorption and excretion of ingested solid materials. In patients who take opioid analgesics to treat chronic and persistent pain, this condition is known as OBD.

We are developing ADL7445 to treat OBD. ADL7445 is a proprietary, small molecule, peripherally-acting *mu* opioid receptor antagonist intended to block the adverse effects of opioid analgesics on the GI tract without

affecting analgesia. ADL7445 has demonstrated safety and efficacy in preclinical models and we are targeting the third quarter of 2009 for the submission of an IND.

We previously were developing alvimopan with Glaxo to treat OBD. In September 2008, Glaxo returned to us all worldwide rights to alvimopan for the chronic OBD indication and, following an internal evaluation and an exploration of partnering opportunities, we announced in December 2008 that we will not pursue further development of alvimopan to treat chronic OBD.

### Other Preclinical Programs

Our pain research efforts initially focused on designing small molecules to target opioid receptors as a means of improving the benefit-to-risk profile of currently available opioid analgesics. While work continues on the selective targeting of opioid receptors, we also are seeking to use advancements in molecular biology and medicinal chemistry to design molecules that target other, non-opioid, pain receptors and other central nervous system targets. Through our internal discovery effort, we have several product candidates in preclinical development intended to address the treatment of moderate-to-severe pain.

We believe there may be opportunities to expand our product portfolio through the acquisition or in-licensing of products and/or product development candidates and intend to continue to explore and evaluate such opportunities.

## INTELLECTUAL PROPERTY

We seek United States and international patent protection for important and strategic components of our technology. There can be no assurance that any of our patents will guarantee protection or market exclusivity for our products and product candidates. We also rely on trade secret protection for certain of our confidential and proprietary information, and we use license agreements both to access external technologies and assets and to convey certain intellectual property rights to others. Our success will be dependent in part on our ability to obtain commercially valuable patent claims and to protect our intellectual property rights and to operate without infringing upon the proprietary rights of others.

The patent positions of pharmaceutical and biotechnology companies, including ours, are generally uncertain and involve complex legal and factual questions. Our business could be negatively impacted by any of the following:

- the claims of any patents that are issued may not provide meaningful protection, may not provide a basis for commercially viable products or may not provide us with any competitive advantages;
- our patents may be challenged by third parties;
- others may have patents that relate to our technology or business that may prevent us from marketing our product candidates unless we are able to obtain a license to those patents;
- the pending patent applications to which we have rights may not result in issued patents; and
- we may not be successful in developing additional proprietary technologies that are patentable.

In addition, patent law relating to the scope of claims in the field in which we operate is still evolving. The degree of future protection for some of our rights, therefore, is uncertain. Furthermore, others may independently develop similar or alternative technologies, duplicate any of our technologies and, if patents are licensed or issued to us, design around the patented technologies licensed to or developed by us. In addition, we could incur substantial costs in litigation if we have to defend ourselves in patent suits brought by third parties or if we initiate such suits.

With respect to proprietary know-how that is not patentable and for processes for which patents are difficult to enforce, we rely on trade secret protection and confidentiality agreements to protect our interests. While we

require all employees, consultants and potential business partners to enter into confidentiality agreements, we may not be able to protect adequately our trade secrets or other proprietary information. Others may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets.

## COMPETITION

In addition to the competition we face for ENTEREG as discussed above, we face intense competition and rapid technological change in the pharmaceutical marketplace. Large and small companies, academic institutions and other public and private research organizations conduct research, seek patent protection and establish collaborative arrangements for product development in competition with us. Products developed by any of these entities may compete directly with those we may develop or sell. In addition, many of the companies and institutions that compete with us have substantially greater capital resources, research and development staffs and facilities than we have, and substantially greater experience in conducting clinical trials, obtaining regulatory approvals and manufacturing and marketing pharmaceutical products. These entities represent significant competition for us. In addition, competitors who are developing prescription pain management products might succeed in developing technologies and products that are more effective than any that we develop or sell or that would render our technology and products obsolete or noncompetitive. Competition and innovation from these or other sources potentially could negatively affect sales of our products or make them obsolete. Advances in current treatment methods also may adversely affect the market for such products. In addition, we may be at a competitive marketing disadvantage against companies that have broader product lines and whose sales personnel are able to offer more complementary products than we can. Any failure to maintain our competitive position could adversely affect our business and results of operations.

Our competitive position also will depend upon our ability to attract and retain qualified personnel, obtain patent protection or otherwise develop proprietary products or processes and secure sufficient capital resources for the typically substantial period between technological conception and commercial sales. Competitive disadvantages in any of these factors could materially harm our business and financial condition.

## MANUFACTURING

We presently do not maintain our own manufacturing facilities. We maintain a small manufacturing organization to manage our relationships with third parties for the manufacture and supply of products for preclinical, clinical and commercial purposes. We have contracted with certain of these third-party manufacturers for the supply of certain amounts of material to meet our needs for commercial and developmental purposes. Commercial quantities of any products that we develop will need to be manufactured in facilities, and by processes, that comply with FDA regulations and other federal, state and local regulations.

## GOVERNMENT REGULATION

*Approval Process*

In the United States, pharmaceutical and diagnostic products intended for use in humans are subject to rigorous FDA regulation. The process of completing clinical trials and obtaining FDA approval for a new drug is likely to take a number of years and require the expenditure of substantial resources. There can be no assurance that any of our product candidates will receive FDA approval.

The process of drug development is complex and lengthy and the activities undertaken before a new pharmaceutical product may be marketed in the United States include:

- discovery research;
- preclinical studies;
- submission to the FDA of an IND, which must become effective before human clinical trials commence;

- adequate and well-controlled human clinical trials to establish the safety and efficacy of the product candidate;
- submission to the FDA of a NDA; and
- FDA approval of the NDA prior to any commercial sale of the product.

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as *in vivo* studies and other studies to assess the potential safety and efficacy of the product candidate. The results of preclinical studies are then submitted to the FDA as a part of an IND and are reviewed by the FDA prior to the commencement of human clinical trials. Unless the FDA objects to, or otherwise responds to, an IND submission, the IND becomes effective 30 days following its receipt by the FDA.

Human clinical trials are typically conducted in three sequential phases that may overlap:

- Phase 1: The drug is initially introduced into healthy human volunteers or patients and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and clinical pharmacology. In addition, it is sometimes possible to conduct a preliminary evaluation of efficacy in Phase 1 trials.
- Phase 2: This phase involves studies in a limited patient population to identify possible adverse effects and safety risks, to evaluate the efficacy of the product for specific targeted diseases and to determine optimal dosage and tolerance.
- Phase 3: When Phase 2 evaluations demonstrate that a dose range of the product is effective and has an acceptable safety profile, Phase 3 trials are undertaken to further evaluate dosage and clinical efficacy, to further test for safety in an expanded patient population at geographically dispersed clinical study sites and to determine the overall risk-benefit ratio of the drug and to provide an adequate basis for product labeling.

Each trial is conducted in accordance with certain standards under protocols that detail the objectives of the study, the parameters to be used to monitor safety and the efficacy criteria to be evaluated. In the United States, each protocol must be submitted to the FDA as part of the NDA. Further, one or more independent Institutional Review Boards must evaluate each clinical study. The Institutional Review Board considers, among other things, ethical factors, the safety of the study, the adequacy of informed consent by human subjects and the possible liability of the institution.

Data from preclinical and clinical trials are submitted to the FDA in an NDA for marketing approval. Preparing an NDA involves considerable data collection, verification, analyses and expense and there can be no assurance that the FDA will accept the application or grant an approval on a timely basis, if at all. The marketing or sale of pharmaceuticals in the United States may not begin without FDA approval. The approval process is affected by a number of factors, including primarily the safety and efficacy demonstrated in clinical trials and the severity of the disease. The FDA may deny an application if, in its sole discretion, it determines that applicable regulatory criteria have not been satisfied or if, in its judgment, additional testing or information is required to ensure the efficacy and safety of the product. One of the conditions for initial marketing approval, as well as continued post-approval marketing, is that a prospective manufacturer's quality control and manufacturing procedures conform to the current Good Manufacturing Practices (cGMPs) regulations of the FDA. In complying with these regulations, a manufacturer must continue to expend time, money and effort in the area of production, quality control and quality assurance to ensure full compliance. Manufacturing establishments, both foreign and domestic, are subject to inspections by or under the authority of the FDA and by other federal, state, local or foreign agencies. Discovery of previously unknown problems with a product or manufacturer may result in restrictions on such product or manufacturer, including withdrawal of the product from the market.

*Post-marketing Regulations*

After FDA approval has been obtained, further studies, including Phase 4 post-marketing studies, may be required to provide additional data on safety, to validate surrogate efficacy endpoints or for other reasons, and the

failure of such studies can result in a range of regulatory actions, including withdrawal of the product from the market. Further studies will be required to gain approval for the use of a product as a treatment for clinical indications other than those for which the product was initially approved. As required by our FDA approval letter for ENTEREG, in February 2009, we began a Phase 4 clinical trial intended to evaluate the safety and efficacy of ENTEREG for POI in patients undergoing radical cystectomy for bladder cancer.

Results of post-marketing programs may limit or expand the further marketing of the products. Further, if there are any modifications to the drug, including any change in indication, manufacturing process, labeling or manufacturing facility, it may be necessary to submit an application seeking approval of such changes to the FDA. Also, the FDA can place restrictions on approval and marketing utilizing its authority under applicable regulations. For example, ENTEREG was approved subject to a REMS under which the product is available only to hospitals that perform bowel resection surgeries and are enrolled in the E.A.S.E. Program.

Additionally, the FDA regulates the labeling, storage, record keeping, advertising and promotion of prescription pharmaceuticals. Marketed products also are subject to continued regulatory oversight by the Office of Medical Policy Division of Drug Marketing, Advertising, and Communications, and the failure to comply with applicable regulations could result in marketing restrictions, financial penalties and/or other sanctions. Certain products approved by the FDA may only be marketed if the promotional materials advertising such products carry a so-called boxed warning. ENTEREG has a boxed warning that alerts prescribers to the restriction on ENTEREG imposed by the REMS—in particular, that no more than 15 doses of ENTEREG should be prescribed to any patient and ENTEREG should only be used in the hospital and not in an outpatient population.

The Controlled Substances Act imposes various registration, record-keeping and reporting requirements, procurement and manufacturing quotas, labeling and packaging requirements, security controls and a restriction on prescription refills on certain pharmaceutical products. A principal factor in determining the particular requirements of this act, if any, applicable to a product is its actual or potential abuse profile. A pharmaceutical product may be listed as a Schedule I, II, III, IV or V substance, with Schedule I substances considered to present the highest risk of substance abuse and Schedule V substances the lowest. Because of the potential for abuse, drugs that are able to activate *mu*-opioid receptors in the brain (morphine-like opioid analgesics) are regulated, or scheduled, under the Controlled Substances Act.

Since we sell ENTEREG to the Department of Veterans Affairs (VA) and other governmental agencies, we are subject to additional legal requirements arising out of our status as a government contractor. In addition, we also are subject to healthcare anti-kickback statutes and false claims statutes as well as regulation under the Occupational Safety and Health Act, the Environmental Protection Act, the Clean Air Act and other federal, state and local regulations. Failure to comply with these requirements could result, among other things, in suspension of regulatory approval, recalls, injunctions, product seizures, non-coverage of our products under government healthcare programs or civil or criminal sanctions.

*Hatch-Waxman Act*

Under the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, Congress created an abbreviated FDA review process for generic versions of pioneer (brand name) drug products. The law also provides incentives by awarding, in certain circumstances, non-patent marketing exclusivities to pioneer drug manufacturers. Newly approved drug products and changes to the conditions of use of approved products may benefit from periods of non-patent marketing exclusivity in addition to any patent protection the drug product may have. The Hatch-Waxman Act provides five years of "new chemical entity," or NCE, marketing exclusivity to the first applicant to gain approval of an NDA for a product that does not contain an active ingredient found in any other approved product. We have five years of NCE exclusivity for ENTEREG that expires on May 20, 2013. The NCE exclusivity prevents the submission to the FDA of any Abbreviated New Drug Application, or ANDA, for any pharmaceutical product containing alvimopan until May 2013 (or May 2012 if the ANDA applicant certifies that the patents covering ENTEREG are invalid or will not be infringed by the ANDA product).

The Hatch-Waxman Act also provides three years of exclusivity for applications containing the results of new clinical investigations (other than bioavailability studies) essential to the FDA's approval of new uses of approved products, such as new indications, dosage forms, strengths or conditions of use.

The Hatch-Waxman Act requires NDA applicants and NDA holders to provide certain patent information for listing in "Approved Drug Products with Therapeutic Equivalence Evaluations," also known as the "Orange Book." ANDA and 505(b)(2) applicants must then certify regarding each of the patents listed with the FDA for the reference product(s). A certification that each listed patent is invalid or will not be infringed by the marketing of the applicant's product is called a "Paragraph IV certification." If the ANDA or 505(b)(2) applicant provides such a notification of patent invalidity or noninfringement, then the FDA may accept the ANDA or 505(b)(2) application four years after approval of the NDA.

If a Paragraph IV certification is filed and the ANDA has been accepted as a reviewable filing by the FDA, the ANDA or 505(b)(2) applicant must then within 30 days provide notice to the NDA holder and patent owner stating that the application has been submitted and providing the factual and legal basis for the applicant's opinion that the patent is invalid or not infringed. If the NDA holder or patent owner files suit against the ANDA or 505(b)(2) applicant for patent infringement within 45 days of receiving notice of the Paragraph IV certification, a one-time 30-month stay of the FDA's ability to approve the ANDA or 505(b)(2) application is triggered. The 30- month stay begins at the end of the NDA holder's five years of data exclusivity or, if data exclusivity has expired, on the date that the patent holder is notified. The FDA may approve the proposed product before the expiration of the 30-month stay if a court finds the patent invalid or not infringed, or if the court shortens the period because the parties have failed to cooperate in expediting the litigation.

*Foreign Regulation*

Whether or not FDA approval has been obtained, approval of a product by regulatory authorities in foreign countries must be obtained prior to the commencement of commercial sales of the product in such countries. The requirements governing the conduct of clinical trials and product approvals vary widely from country to country, and the time required for approval may be longer or shorter than that required for FDA approval. Although there are procedures for unified filings for most European countries, in general, each country also has its own additional procedures and requirements, especially related to pricing of new pharmaceuticals. Further, the FDA and other federal agencies regulate the export of products produced in the United States and, in some circumstances, may prohibit or restrict the export even if such products are approved for sale in other countries.

## LEGAL MATTERS

For a summary of legal matters, see Note 10 of the Financial Statements included in Part II, Item 8 of this Annual Report on Form 10-K, which is incorporated herein by reference.

## EMPLOYEES

As of December 31, 2008, we had 128 full-time employees and one part-time employee. Most of our senior management and professional employees have had prior experience in pharmaceutical or biotechnology companies. None of our employees is covered by collective bargaining agreements. We believe that our relations with our employees are good.

## ITEM 1A. RISK FACTORS

*You should carefully consider the risks described below, in addition to the other information contained in this Annual Report, before making an investment decision. Our business, financial condition or results of operations could be harmed by any of these risks. The risks and uncertainties described below are not the only ones we face. Additional risks not presently known to us or other factors not perceived by us to present significant risks to our business at this time also may impair our business operations.*

**During the next several years, we will be highly dependent on the commercial success of ENTEREG for POI, and we may be unable to attain profitability and positive cash flow from operations based solely on product sales of ENTEREG.**

In May 2008, the FDA approved ENTEREG for use in the treatment of POI. ENTEREG is for hospital use only and is available only to hospitals that have been registered under our E.A.S.E. Program. The commercial success of ENTEREG will depend on several factors, including the following:

- the number of hospitals that register for the E.A.S.E. Program;
- the ability to obtain formulary acceptance for ENTEREG at registered hospitals;
- the effectiveness of Glaxo's and our sales and marketing efforts;
- the acceptance of ENTEREG in the medical community, particularly with respect to whether physicians, patients and healthcare payors view ENTEREG as safe and effective for its labeled indication, and whether it carries with it an acceptable benefit-to-risk profile;
- the occurrence of any side effects, adverse reactions or misuse (or any unfavorable publicity relating thereto) stemming from the use of ENTEREG; and
- the development of competing products or therapies for the treatment of POI.

Ultimately, we may never generate sufficient revenues from ENTEREG for us to reach profitability or sustain our current or projected levels of operations.

**Restrictions on ENTEREG may have the effect of limiting the commercial prospects for the product.**

In April 2007, Glaxo and we announced the results of Study 014, a Phase 3 long-term safety study of alvimopan in patients taking opioids for chronic non-cancer pain and experiencing OBD. Results from Study 014 showed numerically more myocardial infarctions and other cardiovascular serious adverse events reported by patients treated long-term with alvimopan in this study compared to placebo. As a result, ENTEREG was approved by the FDA subject to a REMS. The FDA has determined that a REMS is necessary to ensure that the benefits of ENTEREG in POI outweigh the risks. Our ENTEREG product labeling carries a boxed warning that ENTEREG is available only for short-term (15 doses) use in hospitalized patients. The REMS and the boxed warning may make it more difficult to market and sell ENTEREG. We will not be able to market and sell ENTEREG to hospitals that do not register for the E.A.S.E. Program. Hospitals may be unwilling or unable to comply with the requirements for registration in the E.A.S.E. Program. For example, hospitals may not have systems, order sets, protocols or other measures in place to limit the use of ENTEREG to no more than 15 doses per patient and to ensure in-hospital use only. Hospitals also may not have controls in place to ensure that ENTEREG will neither be dispensed for outpatient use nor be transferred to unregistered hospitals. In such cases, we will be unable to register these hospitals in the E.A.S.E. Program. Further, even if we are successful in registering hospitals, there can be no assurance that such hospitals will order ENTEREG in meaningful amounts, if at all.

Selling a pharmaceutical product in the hospital setting presents certain challenges. Each hospital environment is different, and each hospital's or hospital group's prescribing is influenced by a list of accepted drugs called a formulary. Most hospitals have a committee, often called a pharmacy and therapeutics (P&T) committee, which meets periodically to determine which pharmaceutical products to add to the formulary. Many factors are assessed by such committees, including the cost of the drug and its pharmacoeconomic profile. Once a pharmaceutical is on formulary, it is easier for a physician within a hospital or hospital group to prescribe the drug. Hospital formulary approval is critical to the commercial success of ENTEREG and we cannot assure you that a sufficient number of hospitals will include ENTEREG on their formulary.

**Our product sales revenues from ENTEREG and related financial results will likely fluctuate and may fail to meet market expectations, which may adversely affect our stock price.**

Forecasting revenue is difficult, especially when there is little commercial history, the product is the first product approved for a particular indication and when the level of market acceptance of the product is uncertain. For ENTEREG, the registration process required under the E.A.S.E. Program, as well as the P&T committee and formulary approval process, is likely to slow uptake of the product. As a result of these factors, it is likely that we will experience significant fluctuations in ENTEREG product sales from period to period and/or that product sales may not meet market expectations, which may adversely affect our stock price. Other factors that may cause our financial results to fluctuate include the achievement and timing of research and development milestones and other collaboration revenues, the cost and timing of clinical trials, marketing and other expenses and manufacturing or supply disruption.

**Our delta opioid receptor agonist program may not lead to successful drug candidates.**

To date, no selective *delta* opioid receptor agonist compounds have been successfully developed and approved by the FDA or any other regulatory authority. We are developing our *delta* agonists, ADL5859 and ADL5747, in collaboration with Pfizer. These product candidates are in clinical development. Drug development is a highly uncertain process; our *delta* agonist product candidates may not be safe or effective and we may not be successful in our *delta* agonist development program. Development of *delta* agonists may not lead to commercially successful products. ADL5859 has not achieved a statistically significant difference versus placebo in three Phase 2a clinical trials in three different models of pain.

**If we continue to incur significant operating losses, we may be unable to continue our operations.**

We have generated operating losses in each year since we began operations in November 1994, and our accumulated deficit as of December 31, 2008 was $455.1 million. Our losses have resulted principally from costs incurred in research and development, including clinical trials, and from selling, general and administrative expenses associated with our operations. We expect to continue to generate substantial losses for at least the next several years to fund our sales and marketing and research and development activities. We cannot be sure that we will ever achieve significant product revenue from ENTEREG or any of our other product candidates sufficient for us to generate positive cash flows from operations. Even if we achieve profitability, we may be unable to maintain profitability on a continuing basis or at a level sufficient to support our current or projected levels of continuing investment. We may need to obtain funding for our future operational needs, and we cannot be certain that such funding will be available on terms acceptable to us, if at all, particularly in light of current economic conditions. Any capital raising necessary to continue our operations may be through one or a combination of approaches, which could include public and/or private financing, sale and/or partnering of one or more of our development programs or other strategic initiatives. Any public or private financings may involve issuances of debt or common stock or other classes of our equity, which could further dilute existing stockholders' percentage ownership. If we are unable to obtain funding to support operations, we will be forced to curtail our operations and we will be unable to develop products successfully.

**Our stock price has been highly volatile, and your investment in our stock could decline significantly in value.**

The market price for our common stock has been, and may continue to be in the future, highly volatile. For example, during the period January 1, 2006 through January 31, 2009, the price of our common stock reached a low of $1.27 per share on December 19, 2008 and a high of $27.80 per share on March 1, 2006.

The market price for our common stock is highly dependent on the performance of ENTEREG in the market and the success of our product development efforts. Negative announcements, including, among others:

- disappointing sales of ENTEREG;
- disappointing developments concerning our collaborations;

- negative clinical trial results or adverse regulatory decisions for our product candidates;
- adverse period-to-period fluctuations in our sales or operating results or financial results that fall below the market's expectations; or
- legal challenges, disputes and/or other adverse developments impacting our patents or other proprietary products,

could trigger a significant decline in the price of our common stock. In addition, external events, such as news concerning economic or market conditions in the general economy or within our industry, the activities of our competitors or our customers, changes in U.S. or foreign government regulations impacting our industry or the movement of capital into or out of our industry, also are likely to affect the price of our common stock, regardless of our operating performance.

**Our success is highly dependent on the efforts of our collaborators, the efforts of our third party contractors and on our ability to secure future partnerships.**

Because we have limited resources, we have entered into a number of agreements with other pharmaceutical companies. These agreements may call for our partner to control or play a significant role in, among other things:

- the development of a product candidate, including, among other things, toxicology, formulation and clinical research efforts;
- the design and execution of clinical studies;
- the process of obtaining regulatory approval to market the product; and
- the manufacturing, marketing and selling of any approved product.

In each of these areas, our partners may not support fully our research and commercial interests since our program may compete for time, attention and resources with the internal programs of our corporate collaborators. As such, we cannot be sure that our corporate collaborators will share our perspectives on the relative importance of our program, that they will commit sufficient resources to our program to move it forward effectively or that the program will advance as rapidly as it might if we had retained complete control of all research, development, regulatory and commercialization decisions. For example, we are highly dependent on the efforts and expertise of Glaxo in the distribution, marketing and selling of ENTEREG. Presently, ENTEREG is detailed primarily by Glaxo's national hospital-based sales organization. We are co-promoting ENTEREG in certain hospitals with a contract-based field force that we expect will number 25 persons by mid-2009. The ultimate commercial success of ENTEREG will depend, to a large degree, on the success of the efforts of Glaxo and our contract-based field force.

We also have a development and commercialization agreement with Pfizer for ADL5859 and ADL5747, our proprietary *delta* opioid receptor agonist compounds, for the treatment of pain. Under the Pfizer agreement, we are responsible for IND filings and Phase 1 and Phase 2a clinical studies and Pfizer is responsible for subsequent worldwide development, for securing regulatory approvals and for commercialization of the products.

Any failure by our collaborators to perform their obligations or any decision by our collaborators to terminate these agreements under the terms provided for in their respective agreements could negatively impact our ability to successfully develop, obtain regulatory approvals for and commercialize our product and product candidates, which would likely materially impact our financial condition, results of operations and our outlook. In addition, any termination of our collaboration agreements will terminate the funding we may receive under the relevant collaboration agreement and may materially and adversely impact our ability to fund further development efforts and may materially and adversely impact our progress in our development programs.

In the future, we may enter into other collaborative arrangements for the development, marketing, sale and/or distribution of certain of our product candidates, which may require us to share profits or revenues. For

example, we currently have limited marketing, sales and distribution capabilities, and also have limited resources. Despite our efforts, we may be unable to enter into additional collaborative licensing or other arrangements that we need to develop and commercialize our product candidates. Moreover, we may not realize the contemplated benefits from such collaborative licensing or other arrangements. These arrangements may place responsibility on our collaborative partners for preclinical testing, human clinical trials, the preparation and submission of applications for regulatory approval, or for marketing, sales and distribution support for product commercialization. These arrangements may also require us to transfer certain material rights or issue our equity securities to corporate partners, licensees or others. Any license or sublicense of our commercial rights may reduce our product revenue. Moreover, we may not derive any revenues or profits from these arrangements.

**We have limited commercial manufacturing capability and expertise, and we rely on third parties to manufacture our products in sufficient quantities, at an acceptable cost and in compliance with regulatory requirements.**

We depend on Piramal Healthcare (Canada) Limited (formerly Torcan Chemical Ltd.) as the sole approved supplier under our New Drug Application (NDA) of the API in ENTEREG. We also depend on Pharmaceutics International, Inc. to manufacture ENTEREG finished capsules. Changes to our approved suppliers and manufacturers will require FDA approval and could result in delays that disrupt the supply of the product. While we seek to maintain inventory to protect against supply disruptions, if they were to occur they could materially and adversely affect the commercial success of ENTEREG.

Completion of our clinical trials and commercialization of our product candidates require access to, or development of, facilities to manufacture a sufficient supply of our product candidates. We have depended, and expect to continue to depend, on third parties for the manufacture of our product candidates for preclinical, clinical and commercial purposes. We may not be able to contract for the manufacture of sufficient quantities of the products we develop, or even to meet our needs for preclinical or clinical development. Our products may be in competition with other products for access to facilities of third parties and suitable alternatives may be unavailable. Consequently, our products may be subject to manufacturing delays if outside contractors give their own or other products greater priority than ours. It is difficult and expensive to change contract manufacturers for pharmaceutical products. Our dependence upon others for the manufacture of our products may adversely affect our future profit margin and our ability to commercialize products, if additional products are approved, on a timely and competitive basis.

To receive regulatory approval for a product, our contract manufacturers will be required to obtain approval for their manufacturing facilities to manufacture that product, and there is a risk that such approval may not be obtained. We are required to submit, in an NDA, information and data regarding chemistry, manufacturing and controls which satisfy the FDA that our contract manufacturers are able to make that product in accordance with cGMPs. Under cGMPs, our manufacturers and we will be required to manufacture our products and maintain records in a prescribed manner with respect to manufacturing, testing and quality control activities. We are dependent on our third-party manufacturers to comply with these regulations in the manufacture of our products and these parties may have difficulties complying with cGMPs. The failure of any third-party manufacturer to comply with applicable government regulations could substantially harm and delay or prevent regulatory approval and marketing of our products.

**It is difficult and costly to protect our intellectual property rights, and we cannot ensure the protection of these rights; we may be sued by others for infringing their intellectual property.**

Our commercial success will depend, in part, on obtaining patent protection for new technologies, products and processes and successfully defending these patents against third-party challenges. To that end, we file applications for patents covering the compositions, uses and proprietary processes for the manufacture of our product candidates. The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal, scientific and factual questions. Accordingly, we cannot predict the breadth of claims

allowed in our patents or those of our collaborators. The patents and patent applications relating to our products, product candidates and technologies may be challenged, invalidated or circumvented by third parties and might not protect us against competitors with similar products or technology. Patent disputes in our industry are frequent and can preclude commercialization of products. If we ultimately engage in and lose any such disputes, we could be subject to competition and/or significant liabilities, we could be required to enter into third-party licenses or we could be required to cease using the technology or product in dispute. In addition, even if such licenses are available, the terms of any license requested by a third party could be unacceptable to us.

Others have filed, and in the future are likely to file, patent applications covering products and technologies that are similar, identical or competitive to ours, or important to our business. We cannot be certain that any patent application owned by a third party will not have priority over patent applications filed or in-licensed by us, or that we or our licensors will not be involved in interference proceedings before U.S. or foreign patent offices.

Although no third party has asserted a claim of infringement against us, others may hold proprietary rights that could prevent our product candidates from being marketed unless we can obtain a license to those proprietary rights. Any patent-related legal action against our collaborators or us claiming damages and seeking to enjoin commercial activities relating to our products and processes could subject us to potential liability for damages and require our collaborators or us to obtain a license to continue to manufacture or market the affected products and processes. We cannot predict whether our collaborators or we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all.

There has been, and we believe that there will continue to be, significant litigation in the industry regarding patent and other intellectual property rights. The results of patent litigation among third parties has caused, and may continue to cause, changes to the ways patents are interpreted, enforced and/or challenged. These changes may adversely affect our ability to protect our products. If we become involved in litigation, it could consume substantial managerial and financial resources.

We also rely on trade secrets to protect technology in cases when we believe patent protection is not appropriate or obtainable. However, trade secrets are difficult to protect. While we require employees, academic collaborators, consultants and other contractors to enter into confidentiality agreements, we may not be able to adequately protect our trade secrets or other proprietary information. Our research collaborators and scientific advisors have rights to publish data and information in which we have rights. If we cannot maintain the confidentiality of our technology and other confidential information in connection with our collaborators and advisors, our ability to receive patent protection or protect our proprietary information may be imperiled.

We are a party to various license agreements that give us rights to use specified technologies in our research and development processes. If we are not able to continue to license such technology on commercially reasonable terms, our product development and research may be delayed. In addition, we generally do not fully control the prosecution of patents relating to in-licensed technology (or technology subject to a collaboration) and, accordingly, are unable to exercise the same degree of control over this intellectual property as we exercise over our internally developed technology.

**The results and timing of future clinical trials cannot be predicted and future setbacks may materially and adversely affect our business.**

We must demonstrate through preclinical testing and clinical trials that a product candidate is safe and efficacious. The results from preclinical testing and early clinical trials may not be predictive of results obtained in subsequent clinical trials, and we cannot be sure that these clinical trials will demonstrate the safety and efficacy necessary to obtain regulatory approval for any product candidates.

Many companies in the biotechnology and pharmaceutical industries have suffered significant setbacks in advanced clinical trials. Product candidates that appear to be promising at earlier stages of development may not reach the market or be marketed successfully for a number of reasons, including, but not limited to, the following:

- researchers may find during later preclinical testing or clinical trials that the product candidate is ineffective or has harmful side effects;
- the number and types of patients available for extensive clinical trials may vary;
- new information about the mechanisms by which a drug candidate works may adversely affect its development;
- one or more competing products may be approved for the same or a similar condition, raising the hurdles to approval of the product candidate;
- the product candidate may fail to receive necessary regulatory approval or clearance; or
- competitors may market equivalent or superior products.

The completion of clinical trials of our product candidates may be delayed by many factors, one of which is the rate of enrollment of patients. Neither we nor our collaborators can control the rate at which patients present themselves for enrollment, and we cannot be sure that the rate of patient enrollment will be consistent with our expectations or be sufficient to enable clinical trials of our product candidates to be completed in a timely manner. In addition, we often contract with third parties to conduct our clinical trials, and are subject to the risk that these third parties fail to perform their obligations properly and in compliance with applicable FDA and other governmental regulations. Any significant delays in, or termination of, clinical trials of our product candidates may have a material adverse effect on our business.

We cannot be sure that we will be permitted by regulatory authorities to undertake additional clinical trials for any of our product candidates, or that if such trials are conducted, any of our product candidates will prove to be safe and efficacious or will receive regulatory approvals. In addition, we, or a regulatory authority, may suspend ongoing clinical trials at any time if the subjects participating in the trial are exposed to unacceptable health risks or if the regulatory agency finds deficiencies in the conduct of the trials. Any delays in or termination of these clinical trial efforts could have a material and adverse effect on our business.

**Our long-term success depends upon our ability to develop, receive regulatory approval for and commercialize our product candidates and, if we are not successful, our ability to generate revenue from the commercialization of any products resulting from our development efforts will be limited.**

Our product candidates will require governmental approvals prior to commercialization. Because these product candidates are in development, we face the substantial risks of failure inherent in developing drugs based on new technologies. Our product candidates must satisfy rigorous standards of safety and efficacy before the FDA and foreign regulatory authorities will approve them for commercial use. There can be no assurance that these standards will remain consistent over time, further complicating our ability to obtain marketing approvals for our product candidates. To satisfy these standards, we will need to conduct significant additional research, preclinical testing and clinical trials.

Preclinical testing and clinical development are long, expensive and uncertain processes. Failure can occur at any stage of testing. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful. Based on results at any stage of clinical trials, we may decide to discontinue development of our product candidates. Even if we obtain approval and begin marketing a product, ongoing clinical trials, including for other indications, may result in additional information that could affect our ability or decision to continue marketing the product. Even if we receive regulatory approval for our product candidates, we must comply with applicable FDA post-marketing regulations governing manufacturing, promotion, labeling,

risk management and reporting of adverse events and other information, as well as other regulatory requirements. Failure to comply with applicable regulatory requirements could subject us to criminal penalties, civil penalties, recall or seizure of products, withdrawal of marketing approval, total or partial suspension of production or injunction, as well as other regulatory actions against our product or us.

We intend to explore opportunities to expand our product portfolio by acquiring or in-licensing product candidates. Although we conduct extensive evaluations of product candidate opportunities as part of our due diligence efforts, there can be no assurance that our product candidate development efforts related thereto will be successful or that we will not become aware of issues or complications that will cause us to alter, delay or terminate our product candidate development efforts.

**If we market products in a manner that violates healthcare fraud and abuse laws, or if we violate government price reporting laws, we may be subject to civil or criminal penalties.**

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal healthcare fraud and abuse laws have been applied in recent years to restrict certain marketing practices in the pharmaceutical industry. These laws include anti-kickback statutes and false claims statutes. Because of the breadth of these laws and the narrowness of the safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of these laws.

The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Although there are several statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, or causing to be made, a false statement to get a false claim paid.

Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for a variety of alleged promotional and marketing activities, such as: allegedly providing free trips, free goods, sham consulting fees and grants and other monetary benefits to prescribers; reporting to pricing services inflated average wholesale prices that were then used by federal programs to set reimbursement rates; engaging in off-label promotion that caused claims to be submitted to Medicaid for non-covered, off-label uses; and submitting inflated best price information to the Medicaid Rebate Program to reduce liability for Medicaid rebates. Most states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Sanctions under these federal and state laws may include civil monetary penalties, exclusion of a manufacturer's products from reimbursement under government programs, criminal fines and imprisonment.

We are required to submit pricing data to the federal government as a condition of selling ENTEREG to healthcare facilities of the VA, the Department of Defense (DoD) and other federal agencies and of having ENTEREG covered under Medicaid. These price reports are used to determine the amount of discounts that must be provided to the VA and DoD healthcare networks. Pharmaceutical manufacturers have been prosecuted under false claims laws for knowingly submitting inaccurate pricing information to the government to reduce their

liability for providing discounts. The rules governing the calculation of these reported prices are complex. We depend upon Glaxo to calculate these prices for ENTEREG, and it is possible that Glaxo's methodologies for calculating these prices could be challenged under false claims laws or other laws. If this were to occur, we could face substantial liability.

**We face product liability risks, which may have a negative effect on our financial performance.**

The administration of drugs to humans, whether in clinical trials or commercially, can result in product liability claims regardless of whether or not the drugs are actually at fault for causing an injury. The product labeling for ENTEREG includes a boxed warning that ENTEREG is available only for short-term (15 doses) use in hospitalized patients. The product label informs physicians that there were more reports of myocardial infarctions in patients treated with alvimopan 0.5 milligrams twice daily compared with placebo-treated patients in a 12-month study of patients treated with opioids for chronic pain. ENTEREG also is marketed and sold under a REMS.

If ENTEREG is used more widely or if physicians prescribe the product for conditions other than its labeled indication, the likelihood of an adverse drug reaction, unintended side effect or incident of misuse may increase. Product liability claims can be expensive to defend and may result in large judgments or settlements against us, which could have a negative effect on our financial performance. The cost of product liability insurance has increased in recent years, and the availability of coverage has decreased. We maintain product liability insurance and self-insurance retentions in amounts we believe to be commercially reasonable, but which may not cover the potential liability associated with significant product liability claims. Even if a product liability claim is not successful, the adverse publicity and time and expense of defending such a claim may interfere with our business.

Additionally, we enter into various agreements where we indemnify third parties such as manufacturers and investigators for certain product liability claims related to our products. These indemnification obligations may require us to pay significant sums of money for claims that are covered by these indemnifications.

**Our ability to generate product sales could diminish if we fail to obtain acceptable prices or an adequate level of reimbursement for our products from third-party payors.**

Our ability to successfully commercialize pharmaceutical products, alone or with collaborators, may depend in part on the extent to which reimbursement is available from government and health administration authorities or private health insurers and third-party payors.

The continuing efforts of government and third-party payors to contain or reduce the costs of healthcare through various means may limit our commercial opportunity. For example, in some foreign markets, pricing and profitability of prescription pharmaceuticals are subject to government control. In the United States, we expect that there will continue to be a number of federal and state proposals to implement pharmaceutical pricing and cost control measures under government healthcare programs such as Medicare and Medicaid. Increasing emphasis on managed care in the United States will continue to put pressure on the pricing of in-patient hospital procedures and pharmaceutical products. Significant uncertainty exists as to the reimbursement status of newly approved healthcare products. Cost control initiatives could adversely affect the commercialization of our products, decrease the price received for any products in the future and may impede patients' ability to obtain reimbursement under their insurance programs for our products.

In the case of partial large or small bowel resection surgery, a hospital typically will be reimbursed a fixed fee for the procedure by a private health insurer or Medicare. Pharmaceutical products such as ENTEREG that may be used in connection with the surgery are not separately reimbursed and therefore a hospital must assess the cost of ENTEREG relative to its pharmacoeconomic benefit. Current and future efforts to limit the level of reimbursement for in-patient hospital procedures could cause a hospital to decide to not use ENTEREG or to discontinue use of the product.

**If competitors develop and market products that are more effective, have fewer side effects, are less expensive than our product candidates or offer other advantages, our commercial opportunities will be limited.**

Other companies have product candidates in development to treat the conditions we are seeking to treat and they may develop effective and commercially successful products. Our competitors may succeed in developing products that are more effective than those that we may develop, that have fewer side effects, that are less expensive or that they market before we market any products we may develop.

We are aware of other products in clinical development for the treatment of POI, including methylnaltrexone, which was developed by Progenics in collaboration with Wyeth. In April 2008, methylnaltrexone as a subcutaneous injection was approved by the FDA for sale in the United States for the treatment of OIC in patients with advanced illness who are receiving palliative care, when response to laxative therapy has not been sufficient. In addition, Tranzyme Pharma is currently developing TZP-101, an intravenous ghrelin agonist that is currently in Phase 2b clinical testing, for the treatment of POI. If Wyeth and Progenics are able to successfully develop methylnaltrexone for the treatment of POI, and/or Tranzyme Pharma is able to successfully develop TZP-101, our business could be adversely affected. In addition, there are products already on the market for use in treating other GI conditions that also are being developed for use in opioid induced bowel dysfunction. There may be additional competitive products being developed that could have a material adverse effect on our ability to successfully market and sell our products.

Our competitors include fully-integrated pharmaceutical companies and biotechnology companies, universities and public and private research institutions. Many of the organizations competing with us have substantially greater capital resources, larger research and development staffs and facilities, greater experience in drug development and in obtaining regulatory approvals, and greater manufacturing and marketing capabilities than we do. These organizations also compete with us to:

- attract qualified personnel;
- attract partners for acquisitions, joint ventures or other collaborations; and
- license proprietary technology.

**Reduction in the use of opioid analgesics would reduce the potential market for ENTEREG for POI and any products developed to treat OBD.**

If the use of drugs or techniques that reduce the requirement for *mu*-opioid analgesics becomes more widespread, the market for ENTEREG for POI and our OBD product candidate would decrease. Various techniques to reduce the use of opioids are being utilized in an attempt to reduce the impact of opioid side effects. The use of local anesthetics in epidural catheters during and after surgery with the continuation of the epidural into the postoperative period can reduce or eliminate the use of opioids. Non-steroidal anti-inflammatory agents also may reduce total opioid requirements. Continuous infusion of local anesthetic into a wound or near major nerves can reduce the use of opioids in limited types of procedures and pain states. Novel analgesics that act at receptors other than *mu*-opioid receptors also are under development. Many companies have developed and are developing analgesic products that compete with opioids or which, if approved, would compete with opioids. If these analgesics reduce the use of opioids, it would have a negative impact on the potential market for ENTEREG for POI and our OBD product candidate.

**We are or may become involved in legal proceedings that, if adversely adjudicated or settled, could materially impact our financial condition.**

As a public biopharmaceutical company, we are or may become a party to litigation in the ordinary course of our business, including, among others, matters alleging product liability, patent or other intellectual property rights infringement, patent invalidity, violations of securities laws, employment discrimination or breach of commercial contract. In general, litigation claims can be expensive and time consuming to bring or defend

against and could result in settlements or damages that could significantly impact our results of operations and financial condition.

We have been named in a purported class action lawsuit and related derivative lawsuits. On April 21, 2004, a lawsuit was filed in the U.S. District Court for the Eastern District of Pennsylvania against us, one of our directors and certain of our officers seeking unspecified damages on behalf of a putative class of persons who purchased Adolor common stock between September 23, 2003 and January 14, 2004. The complaint alleges violations of Section 10(b) and Section 20(a) of the Securities Exchange Act of 1934, in connection with the announcement of the results of certain studies in our Phase 3 clinical trials for alvimopan, which allegedly had the effect of artificially inflating the price of our common stock. This suit has been consolidated with three subsequent actions asserting similar claims under the caption *In re Adolor Corporation Securities Litigation*, No. 2:04-cv-01728. On December 29, 2004, the District Court issued an order appointing the Greater Pennsylvania Carpenters' Pension Fund as Lead Plaintiff. The appointed Lead Plaintiff filed a consolidated amended complaint on February 28, 2005. That complaint purported to extend the class period, so as to bring claims on behalf of a putative class of Adolor shareholders who purchased stock between September 23, 2003 and December 22, 2004. The complaint also adds as defendants our Board of Directors asserting claims against them and the other defendants for violation of Section 11 and Section 15 of the Securities Act of 1933 in connection with our public offering of stock in November 2003. Together with the management and director defendants, we moved to dismiss the complaint on April 29, 2005. The plaintiffs responded to the motion to dismiss on June 28, 2005, and our reply was filed on August 12, 2005.

On August 2, 2004, two shareholder derivative lawsuits were filed in the U.S. District Court for the Eastern District of Pennsylvania, purportedly on behalf of the Company, against our directors and certain of our officers seeking unspecified damages for various alleged breaches of fiduciary duty and waste. The allegations are similar to those set forth in the class action complaints, involving the announcement of the results of certain studies in our Phase 3 clinical trials for ENTEREG. On November 12, 2004, the derivative plaintiff filed an amended complaint. On December 13, 2004, we filed a motion challenging the standing of the derivative plaintiff to file the derivative litigation on its behalf. On December 13, 2004, our directors and officers moved to dismiss the complaint for the failure to state a claim. Plaintiffs responded to these motions on January 27, 2005 and we filed reply briefs on February 18, 2005.

We have not accrued any amount in our financial statements as of December 31, 2008 for these matters, and we await the decision of the District Court in each matter.

**Our business could suffer if we are unable to attract, retain and motivate skilled personnel and cultivate key academic collaborations.**

We are a small company, and our success depends on our continued ability to attract, retain and motivate highly-qualified management and scientific personnel. We may not be successful in attracting or retaining qualified individuals. Our success also depends on our ability to develop and maintain important relationships with leading academic institutions and scientists. Competition for personnel and academic collaborations is intense. In particular, our product development programs depend on our ability to attract and retain highly-skilled chemists, biologists and clinical development personnel. If we lose the services of any of these personnel, it could impede significantly the achievement of our research and development objectives. In addition, we will need to hire additional personnel and develop additional academic collaborations as we continue to expand our research and development activities. We do not know if we will be able to attract, retain or motivate personnel or maintain relationships. We do not maintain key man life insurance on any of our employees.

**If we use biological and hazardous materials in a manner that causes injury or violates laws, we may be liable for damages.**

Our research and development activities involve the controlled use of potentially harmful biological materials as well as hazardous materials, chemicals and various radioactive compounds. We use radioactivity in

conducting biological assays and we use solvents that could be flammable in conducting our research and development activities. We cannot completely eliminate the risk of accidental contamination or injury from the use, storage, handling or disposal of these materials. We do not maintain a separate insurance policy for these types of risks. In the event of contamination or injury, we could be held liable for damages that result, and any liability could exceed our resources. We are subject to federal, state and local laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. The cost of compliance with these laws and regulations could be significant.

**If we engage in an acquisition, reorganization or business combination, we will incur a variety of risks that could adversely affect our business operations or our stockholders.**

From time to time we have considered, and we will continue to consider in the future, if and when any appropriate opportunities become available, strategic business initiatives intended to further the development of our business. These initiatives may include acquiring businesses, technologies or products or entering into a business combination with another company. If we do pursue such a strategy, we could, among other things:

- issue equity securities that would dilute our current stockholders' percentage ownership;
- incur substantial debt that may place strains on our operations;
- spend substantial operational, financial and management resources in integrating new businesses, technologies and products;
- assume substantial actual or contingent liabilities; or
- merge with, or otherwise enter into a business combination with, another company in which our stockholders would receive cash or shares of the other company or a combination of both on terms that our stockholders may not deem desirable.

We are not in a position to predict what, if any, collaborations, alliances or other transactions may result or how, when or if these activities would have a material effect on us or the development of our business.

**Certain provisions of both our charter documents and Delaware law, our adoption of a shareholder rights plan and certain limitations within our collaboration agreements may make an acquisition of us, which may be beneficial to our stockholders, more difficult.**

Provisions of our amended and restated certificate of incorporation and restated bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us, even if doing so would benefit our stockholders.

Authorized shares of our common stock and preferred stock are available for future issuance without stockholder approval. The existence of unissued common stock and preferred stock may enable our Board of Directors to issue shares to persons friendly to current management or to issue preferred stock with terms that could render more difficult or discourage a third-party attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise, which would protect the continuity of our management. In addition, we adopted a shareholder rights plan, the effect of which may be to make an acquisition of us more difficult.

Our amended and restated certificate of incorporation provides for our Board of Directors to be divided into three classes, with the term of one such class expiring each year, and we have eliminated the ability of our stockholders to consent in writing to the taking of any action pursuant to Section 228 of the Delaware General Corporation Law.

Under our collaboration agreements with Glaxo and Pfizer, there are certain limitations on the ability of Glaxo and Pfizer to acquire our securities. These limitations make it more difficult for Glaxo or Pfizer to acquire us, even if such an acquisition would benefit our stockholders. The limitations do not prevent Glaxo or Pfizer,

among other things, from acquiring our securities in certain circumstances following initiation by a third party of an unsolicited tender offer to purchase more than a certain percentage of any class of our publicly traded securities.

## ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

## ITEM 2. PROPERTIES

We lease our corporate headquarters in Exton, Pennsylvania, under a ten-year lease agreement expiring in July 2013. The lease includes a renewal option for two consecutive additional five-year periods and we have a purchase option exercisable at the fifth and tenth year of the lease term. The building has approximately 80,000 square feet of space consisting of approximately 30,000 square feet of administrative office space, 25,000 square feet of laboratory space and 25,000 square feet of unfinished space that is available for potential future expansion.

## ITEM 3. LEGAL PROCEEDINGS

The information set forth in Note 10 of the Financial Statements included in Part II, Item 8 of this Annual Report on Form 10-K is incorporated herein by reference.

## ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS

No matters were submitted to a vote of our stockholders, through the solicitation of proxies or otherwise, during the fourth quarter of the year ended December 31, 2008.

### Executive Officers of the Registrant

The names, ages and positions held by our executive officers as of the filing date of this Annual Report on Form 10-K are as follows:

| Name | Age | Title |
|---|---|---|
| Michael R. Dougherty | 51 | President, Chief Executive Officer and Director |
| John M. Limongelli, Esq. | 39 | Senior Vice President, General Counsel and Secretary |
| George R. Maurer | 53 | Senior Vice President, Manufacturing and Pharmaceutical Technologies |
| Eliseo O. Salinas, MD, MSc | 53 | Senior Vice President, Research and Development and Chief Medical Officer |
| Stephen W. Webster | 47 | Senior Vice President, Finance and Chief Financial Officer |

*Michael R. Dougherty.* Mr. Dougherty was named as our President and Chief Executive Officer and appointed as a member of the Board of Directors on December 14, 2006. Mr. Dougherty served as our Senior Vice President, Chief Operating Officer and Treasurer from October 31, 2005 until December 14, 2006. From April 2003 until October 31, 2005, he was Chief Financial Officer. He joined us as our Senior Vice President of Commercial Operations in November 2002. From November 2000 to November 2002, Mr. Dougherty was President and Chief Operating Officer of Genomics Collaborative, Inc., a privately-held functional genomics company. Previously, Mr. Dougherty served as President and Chief Executive Officer at Genaera Corporation, formerly Magainin Pharmaceuticals Inc., a publicly-traded biotechnology company, and as Senior Vice President and Chief Financial Officer at Centocor, Inc., a publicly-traded biotechnology company. Mr. Dougherty received a B.S. from Villanova University. Mr. Dougherty has served on the Board of Directors of ViroPharma Incorporated since January 2004.

*John M. Limongelli, Esq.* Mr. Limongelli joined us as our Senior Vice President, General Counsel and Secretary in September 2008. From 2002 until joining the Company, Mr. Limongelli held several roles of increasing responsibility with Cephalon, Inc., most recently serving as Vice President and Associate General Counsel. Prior to joining Cephalon in 2002, Mr. Limongelli was an associate with Morgan, Lewis & Bockius, LLP, in Philadelphia. From 1995 to 1997, Mr. Limongelli worked as a financial analyst for Bell Atlantic Corp., and from 1991 to 1995 he was an auditor with KPMG LLP. Mr. Limongelli obtained both his Juris Doctor and Masters in Business Administration from Temple University.

*George R. Maurer.* Mr. Maurer was named as our Senior Vice President, Manufacturing and Pharmaceutical Technologies, on January 7, 2009. Mr. Maurer joined Adolor in 2002 as Senior Director, Commercial Manufacturing, and then served as Vice President, Commercial Manufacturing since 2005. Prior to joining Adolor, Mr. Maurer was Director, Commercial Manufacturing at ViroPharma Incorporated. Prior to ViroPharma, for 22 years Mr. Maurer held positions of increasing responsibility with Schering-Plough Corporation, including directing production planning of manufacturing functions supporting domestic sales and management of manufacturing operations in Puerto Rico and New Jersey. Mr. Maurer earned his B.S. in Biology from Rensselaer Polytechnic Institute.

*Dr. Eliseo Oreste Salinas, MD, MSc.* Dr. Salinas joined us as our Senior Vice President Research and Development and Chief Medical Officer in June 2008. From June 2004 until May 2008, Dr. Salinas served as Executive Vice President Global Research & Development and Chief Scientific Officer for Shire, a specialty biopharmaceutical company. Between 1993 and June 2004, Dr. Salinas served in several positions of increased responsibility at Wyeth Research, including Vice President of Headquarters for Japan Research & Development, Vice President of Regional Research North and South America and Head of Worldwide Central Nervous System Clinical Research and Development. Dr. Salinas received his Doctor of Medicine from the University of Buenos Aires, Argentina, in 1980, received a Masters in Pharmacology in 1990 and completed his Residency in Psychiatry from the University of Paris, France.

*Stephen W. Webster.* Mr. Webster joined us as our Senior Vice President, Finance and Chief Financial Officer in June 2008. From 2007 until joining Adolor, Mr. Webster was Managing Director, Investment Banking Division, Health Care Group for Broadpoint Capital (formerly First Albany Capital). From 2000 to 2006, he was with Neuronyx, Inc., a development-stage biotechnology company he co-founded, as President from 2000 to 2006 and Chief Executive Officer from 2003 to 2006. From 1987 to 2000, he served in positions of increased responsibility including as Director, Investment Banking Division, Health Care Group for PaineWebber Incorporated. He received his A.B. in Economics *cum laude* from Dartmouth College in 1983 and his Master of Business Administration in Finance from The Wharton School, The University of Pennsylvania in 1987. Mr. Webster serves on the Board of Directors of HearUSA Inc. and Pennsylvania Bio.

## PART II

### ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Our common stock is traded on NASDAQ Global Market under the symbol "ADLR." The price range per share reflected in the table below is the highest and lowest per share sales price for our stock as reported by The NASDAQ Global Market during each quarter of the two most recent years.

| | High | Low |
|---|---|---|
| **2008** | | |
| First Quarter | $5.20 | $3.75 |
| Second Quarter | 6.09 | 4.39 |
| Third Quarter | 5.58 | 2.92 |
| Fourth Quarter | 3.69 | 1.27 |
| **2007** | | |
| First Quarter | $9.45 | $6.53 |
| Second Quarter | 8.97 | 3.51 |
| Third Quarter | 4.30 | 3.09 |
| Fourth Quarter | 5.34 | 3.05 |

As of February 19, 2009, there were 127 holders of record of our common stock. This does not reflect beneficial stockholders who hold their stock in nominee or "street" name through various brokerage firms. On February 19, 2009, the last reported sale price of our common stock as reported on the NASDAQ Global Market was $2.27 per share.

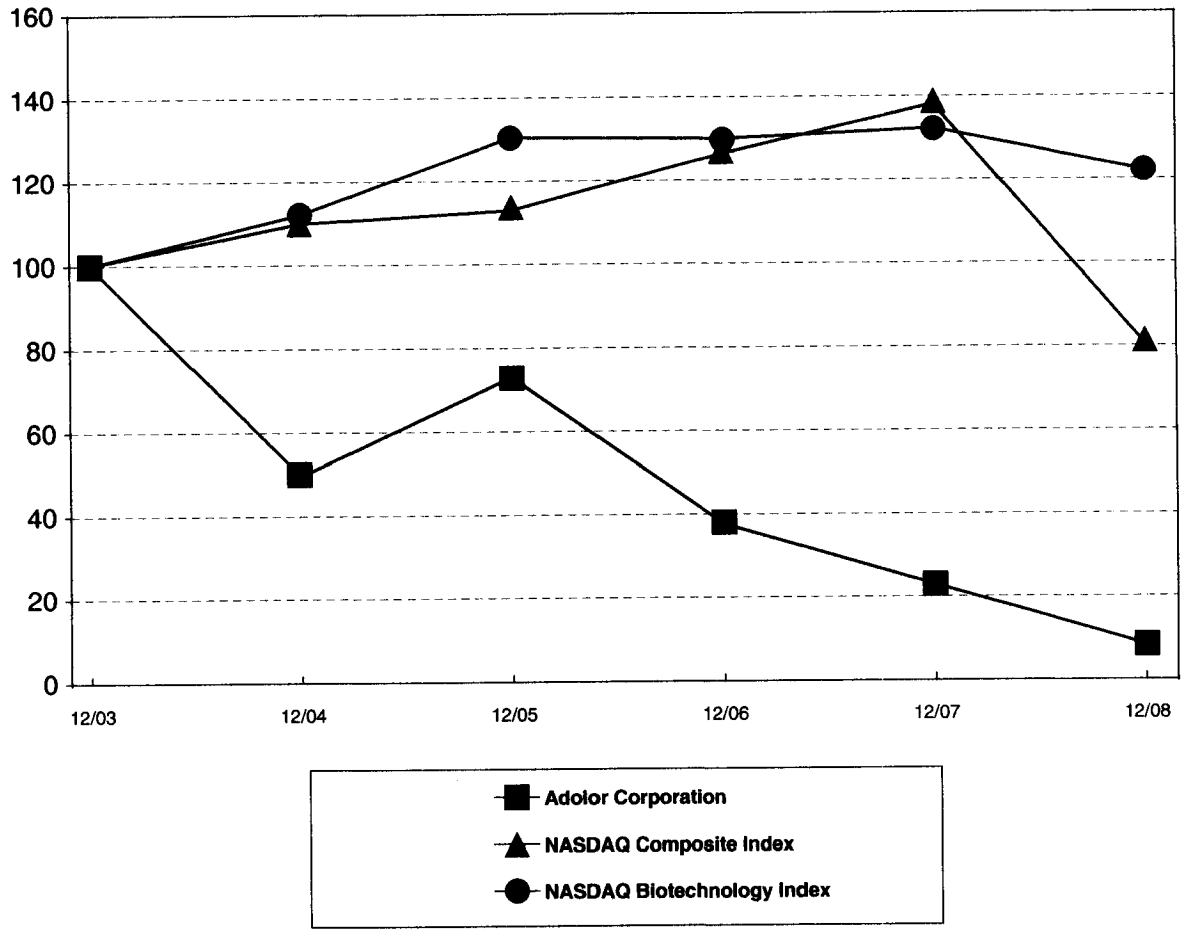
We have never declared or paid cash dividends on our capital stock, and we do not intend to pay cash dividends in the foreseeable future. We plan to retain earnings, if any, for use in the operation of our business and to fund future growth.

**Performance Graph**

The following graph compares the cumulative five-year total return on our common stock relative to the cumulative total returns of the NASDAQ Composite Index and the NASDAQ Biotechnology Index. An investment of $100 (with reinvestment of all dividends) is assumed to have been made in our common stock and in each of the indexes on December 31, 2003 and its relative performance is tracked through December 31, 2008.

**COMPARISON OF 5 YEAR CUMULATIVE TOTAL RETURN***

Among Adolor Corporation, The NASDAQ Composite Index
and The NASDAQ Biotechnology Index




* $100 invested on 12/31/03 in Adolor stock, NASDAQ Composite Index and NASDAQ Biotechnology Index, in each case with reinvestment of dividends.

| | Fiscal year ended December 31, | | | | | |
|---|---|---|---|---|---|---|
| | 12/03 | 12/04 | 12/05 | 12/06 | 12/07 | 12/08 |
| **Adolor Corporation** | $100.00 | $ 49.62 | $ 73.04 | $ 37.62 | $ 23.01 | $ 8.30 |
| **NASDAQ Composite Index** | 100.00 | 110.08 | 112.88 | 126.51 | 138.13 | 80.47 |
| **NASDAQ Biotechnology Index** | 100.00 | 112.17 | 130.53 | 130.05 | 132.24 | 122.10 |

The stock price performance included in this graph is not necessarily indicative of future stock price performance.

## ITEM 6. SELECTED FINANCIAL DATA

The following selected financial data should be read in conjunction with our financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in Part II, Item 7 in this Annual Report. The Statements of Operations data for the years ended December 31, 2008, 2007 and 2006, and the Balance Sheet data as of December 31, 2008 and 2007, are derived from our audited financial statements which are included elsewhere in this Annual Report. The Statements of Operations data for the years ended December 31, 2005 and 2004 and the Balance Sheet data as of December 31, 2006, 2005 and 2004 are derived from audited financial statements not included in this Annual Report. Historical results are not necessarily indicative of the results to be expected in the future.

| | Years Ended December 31, | | | | |
|---|---|---|---|---|---|
| | 2008 | 2007 | 2006 | 2005 | 2004 |
| | (in thousands, except per share data) | | | | |
| **Statements of Operations** | | | | | |
| Product sales, net | $ 1,248 | $ — | $ — | $ — | $ — |
| Contract revenues | 48,208 | 9,120 | 15,087 | 15,719 | 25,542 |
| Total revenues, net | 49,456 | 9,120 | 15,087 | 15,719 | 25,542 |
| Operating expenses incurred: | | | | | |
| Cost of product sales | 204 | — | — | — | — |
| Research and development | 52,664 | 41,610 | 56,660 | 49,631 | 48,766 |
| Selling, general and administrative | 31,115 | 23,970 | 37,689 | 26,293 | 22,870 |
| Total operating expenses | 83,983 | 65,580 | 94,349 | 75,924 | 71,636 |
| Loss from operations | (34,527) | (56,460) | (79,262) | (60,205) | (46,094) |
| Other income, net | 4,405 | 8,017 | 9,524 | 3,408 | 2,508 |
| Net loss | $ (30,122) | $ (48,443) | $ (69,738) | $ (56,797) | $ (43,586) |
| Basic and diluted net loss per share | $ (0.65) | $ (1.05) | $ (1.56) | $ (1.45) | $ (1.12) |
| Shares used in computing basic and diluted net loss per share | 46,158 | 45,933 | 44,731 | 39,088 | 38,924 |

| | As of December 31, | | | | |
|---|---|---|---|---|---|
| | 2008 | 2007 | 2006 | 2005 | 2004 |
| | | | (in thousands) | | |
| **Balance Sheet** | | | | | |
| Cash, cash equivalents and short-term investments | $ 131,910 | $ 167,189 | $ 185,562 | $ 103,075 | $ 162,324 |
| Working capital | 112,250 | 147,543 | 173,130 | 89,664 | 149,081 |
| Total assets | 144,427 | 178,677 | 200,598 | 117,237 | 178,103 |
| Accumulated deficit | (455,067) | (424,944) | (376,502) | (306,763) | (249,967) |
| Total stockholders' equity | 88,619 | 112,353 | 153,181 | 66,693 | 123,160 |

## ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

Management's Discussion and Analysis of Financial Condition and Results of Operations (MD&A) is intended to provide information to assist you in better understanding and evaluating our financial condition and results of operations. We encourage you to read this MD&A in conjunction with our financial statements included in Part II, Item 8 of this Annual Report on Form 10-K and the "Risk Factors" contained in Part I, Item 1A of this Annual Report on Form 10-K.

### EXECUTIVE SUMMARY

We are a biopharmaceutical company focused on the discovery, development and commercialization of novel prescription pain management products. On May 20, 2008, the U.S. Food and Drug Administration (FDA) approved our first product, ENTEREG® (alvimopan), for the management of postoperative ileus following bowel resection surgery (POI). POI causes significant discomfort for patients and results in increased expense to healthcare providers. ENTEREG is specifically indicated to accelerate the time to upper and lower gastrointestinal (GI) recovery following partial large or small bowel resection surgery with primary anastomosis. We also have a number of product candidates in various stages of clinical and preclinical development.

For the year ended December 31, 2008, our total revenues and net loss were $49.5 million and $30.1 million, respectively. Net shipments of ENTEREG through December 31, 2008 were $2.2 million, of which we recognized $1.2 million as net product sales under our revenue recognition policy. We will need to grow sales of ENTEREG significantly beyond current levels before we will be able to achieve profitability and positive cash flow from operations. The rate of our future growth will depend on, among other things, the acceptance of ENTEREG in the marketplace, our ability to maintain adequate intellectual property protection for ENTEREG and our success in developing and commercializing additional product candidates. Ultimately, we may never generate significant product sales revenues, achieve profitable operations or generate positive cash flows from operations and, even if profitable operations are achieved, they may not be sustained on a continuing basis or sufficient to generate the operating cash flow to support our current or projected levels of operation.

### ENTEREG for POI

Together with our partner, Glaxo Group Limited (Glaxo), we launched ENTEREG in the United States in mid-2008. ENTEREG is detailed primarily by Glaxo's national hospital-based sales organization. We are co-promoting ENTEREG in certain hospitals with a field force that we expect will number 25 persons by mid-2009. ENTEREG was approved in POI subject to a Risk Evaluation and Mitigation Strategy (REMS) under which the product is available only to hospitals that perform bowel resections and are enrolled in the ENTEREG Access Support and Education (E.A.S.E.) Program. Our initial launch efforts focused on registering hospitals in the E.A.S.E. Program. As of December 31, 2008, approximately 1,100 hospitals had registered, and of those 1,100, approximately 300 had approved ENTEREG for inclusion on their formularies.

Under our agreement with Glaxo, we have a profit-sharing arrangement under which we receive 45% and Glaxo receives 55% of profits, as defined. Profits are calculated as net sales of ENTEREG for POI less certain agreed-upon costs and is subject to certain adjustments. Beginning in mid-2011, the parties will share such profits equally.

In 2009, Glaxo and we are undertaking a number of initiatives to potentially increase the awareness and acceptance of ENTEREG among hospitals and physicians performing bowel resection surgeries. These efforts will include studies intending to address pharmacoeconomic and health outcomes associated with accelerated GI recovery. Longer-term, Glaxo and we are evaluating additional clinical studies of ENTEREG for POI resulting from pain management following surgical procedures other than bowel resection surgeries. As required by our FDA approval letter for ENTEREG, in February 2009, we began a Phase 4 clinical trial intended to evaluate the safety and efficacy of ENTEREG for POI in patients undergoing radical cystectomy for bladder cancer.

### *Delta* Opioid Receptor Agonists

We are collaborating with Pfizer Inc. (Pfizer) for the development and commercialization of the delta opioid receptor agonist compounds, ADL5859 and ADL5747 (Pfizer compounds PF-04856880 and PF-04856881), for the treatment of pain. The delta receptor is one of three opioid receptors that modulate pain. Today, all marketed opioid drugs interact primarily with the mu receptor. We have identified a series of novel, orally-active *delta* agonists that selectively stimulate the *delta* opioid receptor. Our goal is to develop medications that produce pain relief similar to traditional *mu* opioids, while reducing or eliminating some typical narcotic side effects.

We have completed three Phase 2a studies of the initial formulation of ADL5859 in (i) acute pain after surgical removal of impacted third molars, (ii) pain associated with rheumatoid arthritis and (iii) pain associated with diabetic peripheral neuropathy. While ADL5859 was well tolerated in these studies, ADL5859 showed no statistically significant difference versus placebo in these trials. Before commencing additional clinical trials for ADL5859, Pfizer and we plan to re-formulate ADL5859 to address the pharmacokinetic variability observed in these Phase 2a trials.

We recently completed enrollment in an ADL5747 multiple ascending dose Phase 1 trial in 32 healthy volunteers, and did not observe any dose-limiting toxicity or serious adverse events. Pfizer and we intend to initiate proof-of-concept trials of ADL5747 later in 2009.

### Opioid Bowel Dysfunction Program

There are opioid receptors in the GI tract, or peripheral opioid receptors, that regulate functions such as motility and water secretion and absorption. Stimulation of these GI *mu*-opioid receptors by morphine, or other opioid analgesics, can slow gut motility and disrupt normal GI function that allows for the passage, absorption and excretion of ingested solid materials. In patients who take opioid analgesics to treat chronic and persistent pain, this condition is known as OBD.

We are developing ADL7445 to treat OBD. ADL7445 is a proprietary, small molecule, peripherally-acting *mu*-opioid receptor antagonist intended to block the adverse effects of opioid analgesics on the GI tract without affecting analgesia. ADL7445 has demonstrated safety and efficacy in preclinical models and we are targeting the third quarter of 2009 for the submission of an Investigational New Drug Application (IND).

We previously were developing alvimopan with Glaxo to treat OBD. In September 2008, Glaxo returned to us all worldwide rights to alvimopan for the chronic OBD indication and, following an internal evaluation and an exploration of partnering opportunities, we announced in December 2008 that we will not pursue further development of alvimopan to treat OBD.

### Discovery Research and In-licensing Efforts

Our pain research efforts initially focused on designing small molecules to target opioid receptors as a means of improving the benefit-to-risk profile of currently available opioid analgesics. While work continues on the selective targeting of opioid receptors, we also are seeking to use advancements in molecular biology and medicinal chemistry to design molecules that target other, non-opioid, pain receptors and other central nervous system targets. Through our internal discovery effort, we have several product candidates in preclinical development intended to address the treatment of moderate-to-severe pain.

We believe there may be opportunities to expand our product portfolio through the acquisition or in-licensing of products and/or product development candidates and intend to continue to explore and evaluate such opportunities.

*The following discussion is included to describe our financial position and results of operations as of December 31, 2008 and 2007 and for each of the years in the three-year period ended December 31, 2008. The financial statements and notes thereto contain detailed information that should be referred to in conjunction with this discussion.*

## LIQUIDITY AND CAPITAL RESOURCES

Cash, cash equivalents and short-term investments were approximately $131.9 million at December 31, 2008 and approximately $167.2 million at December 31, 2007, representing 91% and 94% of our total assets, respectively. We invest excess cash in U.S. Treasury obligations. Our working capital, which is calculated as current assets less current liabilities, was $112.3 million at December 31, 2008 compared to $147.5 million at December 31, 2007. The decrease in cash, cash equivalents and short-term investments and working capital was primarily from the use of cash to fund our operating activities.

The following is a summary of selected cash flow information for the years ended December 31, 2008, 2007 and 2006:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2008 | 2007 | 2006 |
| Net loss | $(30,122,260) | $(48,442,975) | $ (69,738,378) |
| Adjustments for non-cash operating items | (7,904,004) | 4,844,719 | 6,820,313 |
| Net cash operating loss | (38,026,264) | (43,598,256) | (62,918,065) |
| Net change in assets and liabilities | 3,815,612 | 25,548,879 | (924,740) |
| Net cash used in operating activities | $(34,210,652) | $(18,049,377) | $ (63,842,805) |
| Net cash provided by (used in) investing activities | $ 26,447,663 | $ 30,293,329 | $ (82,064,044) |
| Net cash provided by (used in) financing activities | $ (277,669) | $ 52,994 | $147,456,608 |

### Net Cash Used in Operating Activities

Net operating cash outflows of $34.2 million, $18.0 million and $63.8 million for the years ended December 31, 2008, 2007 and 2006, respectively, resulted primarily from research and development expenditures associated with our product candidates and selling, general and administrative expenses, offset by payments received under the Glaxo and Pfizer collaboration agreements. In 2008, we received $29.7 million under our collaboration agreements, including a $20.0 million milestone payment from Glaxo following FDA approval of ENTEREG for POI. In addition, we received $1.5 million of cash related to shipments of ENTEREG during 2008. In 2007, we received $38.2 million under our collaboration agreements, consisting primarily of $31.9 million received from Pfizer upon execution of the collaboration agreement relating to our *delta* opioid receptor agonists. In 2006, we received $8.5 million from Glaxo under the collaboration agreement relating to ENTEREG.

### Net Cash Provided By (Used In) Investing Activities

Net cash provided by (used in) investing activities relates to purchases and maturities/sales of investment securities, as well as capital expenditures for property and equipment. Capital expenditures are primarily for the purchase of laboratory equipment, furniture and fixtures, office equipment and leasehold improvements associated with our leased facility. We expect to fund a significant portion of our future operations through the maturities of investments in our portfolio, which consist of U.S. Treasury obligations.

Net cash provided by investing activities was $26.4 million for the year ended December 31, 2008 as compared to $30.3 million for the year ended December 31, 2007. The decrease in cash provided by investing activities in 2008 is primarily attributable to a decrease in cash provided from the net maturity/sale of available-for-sale securities in 2008.

Net cash provided by investing activities was $30.3 million for the year ended December 31, 2007 as compared to $82.1 million of net cash used in investing activities for the year ended December 31, 2006. The increase in cash provided from investing activities in 2007 is primarily attributable to a net investment in available-for-sale securities in 2006 resulting from the proceeds received from our equity offering in February 2006.

**Net Cash Provided By (Used In) Financing Activities**

Net cash provided by (used in) financing activities was not significant for the years ended December 31, 2008 and 2007. Net cash provided by financing activities for the year ended December 31, 2006 resulted primarily from the sale of 5,750,000 shares of common stock at $25.00 per share in February 2006. We received net proceeds from the offering of approximately $135.1 million. In addition, we received $12.4 million from the exercise of stock options in 2006.

**Contractual Commitments**

The following table summarizes our obligations to make future payments under current contracts:

| | Payments Due by Period | | | | |
|---|---|---|---|---|---|
| **Contractual obligations** | **Total** | **2009** | **2010 and 2011** | **2012 and 2013** | **2014 and thereafter** |
| Operating leases | $5,526,000 | $1,294,000 | $2,505,000 | $1,727,000 | $— |
| Purchase obligations | 2,552,000 | 1,352,000 | 1,200,000 | — | — |
| Total | $8,078,000 | $2,646,000 | $3,705,000 | $1,727,000 | $— |

Contractual commitments in the table above represent future cash obligations that are legally binding and enforceable under agreements with third parties. This table summarizes our significant contractual commitments as of December 31, 2008 and the effects such commitments are expected to have on our liquidity and cash flows in future periods.

Excluded from the table above are contingent liabilities associated with various agreements that we have entered into for services with third-party vendors, including agreements to conduct clinical trials, to manufacture product candidates and for consulting and other contracted services. These contingent liabilities require future performance by the third party in order for payment to be executed, and we accrue the costs of these agreements based on estimates of work completed to date. We estimate that approximately $19.2 million will be payable in future periods under the arrangements in place at December 31, 2008. Of this amount, approximately $5.6 million has been accrued for work estimated to have been completed as of December 31, 2008 and approximately $13.6 million relates to future performance under these arrangements.

In addition to the above, we have committed to make potential future milestone payments to third parties as part of our in-licensing agreements. Payments generally become due and payable only upon the achievement of certain developmental, regulatory and/or commercial milestones. Because the achievement of these milestones is neither probable nor reasonably estimable, we have not recorded a liability on our balance sheet for any such contingencies. As of December 31, 2008, the maximum potential milestone payments due under current contractual agreements are $22.0 million.

*Glaxo Collaboration Agreement*

Under the terms of the Glaxo agreement, we reimburse Glaxo for a portion of certain third-party expenses incurred by them relating to ENTEREG, pursuant to an agreed upon development plan and budget which is subject to annual review. We also incur certain third-party expenses ourselves relating to ENTEREG, pursuant to an agreed upon development plan and budget, a portion of which are reimbursable to us by Glaxo. We record these expenses as incurred.

*Pfizer Collaboration Agreement*

Under the terms of the Pfizer agreement, we reimburse Pfizer for a portion of certain third-party expenses incurred by them relating to our *delta* opioid agonists, pursuant to an agreed upon development plan and budget that is subject to annual review. We also incur certain third-party expenses ourselves relating to the *delta* opioid agonists, pursuant to an agreed upon development plan and budget, a portion of which is reimbursable to us by Pfizer. We record these expenses as incurred.

*License Agreement*

In November 1996, Roberts Laboratories, Inc. (Roberts) licensed from Eli Lilly and Company (Eli Lilly) certain intellectual property rights relating to ENTEREG. In June 1998, we entered into an option and license agreement with Roberts under which we sublicensed these rights from Roberts. In December 2000, Shire U.S. Inc. became the successor in interests to Roberts under our option and license agreement with Roberts. The Company has made license and milestone payments under this agreement totaling $2.5 million, including $0.9 million paid during 2008 as a result of the regulatory approval of ENTEREG. Our license to ENTEREG and our obligations to pay royalties to Shire and Eli Lilly expire on the later of either the date of the last to expire of the licensed Eli Lilly patents or November 5, 2011.

**Outlook**

We expect to use our cash, cash equivalents and investments for working capital and to fund our operations. Since inception, we have experienced significant operating losses and negative operating cash flow and have funded our operations primarily from the proceeds received from the sale of our equity securities, as well as from amounts received under collaboration agreements. Our accumulated deficit at December 31, 2008 was $455.1 million and we expect to continue to incur substantial losses for at least the next several years.

We may never generate significant product sales, achieve profitable operations or generate positive cash flows from operations and, even if profitable operations are achieved, they may not be sustained on a continuing basis or sufficient to support our current or projected levels of operations. At this time, we cannot accurately predict the effect of certain developments on our product sales, such as the degree of market acceptance, patent protection and exclusivity of ENTEREG, the impact of competition, the effectiveness of our sales and marketing efforts and the outcome of our current efforts to develop, receive approval for and successfully launch our other product candidates. However, we believe that our existing cash, cash equivalents and investments are adequate to fund our operations into 2011 based upon the level of research and development and marketing and administrative activities we believe will be necessary to achieve our strategic objectives. We may need to obtain funding for our future operational needs, and we cannot be certain that funding will be available on terms acceptable to us, or at all.

*ENTEREG*

Our ability to generate positive cash flow from operations depends, in large part, on our ability to successfully commercialize ENTEREG in the United States. To that end, we expect that sales and marketing expenses associated with the product will continue to increase during 2009. Prior to the FDA approval of ENTEREG, costs associated with the manufacture of alvimopan were expensed to research and development. As a result, at December 31, 2008, we have inventory related to alvimopan that carries a zero-cost and is not reflected on the December 31, 2008 balance sheet. Certain of this inventory is expected to be used in further research and development activities, with the remaining inventory available for commercial sale. To the extent that this inventory is sold, our cost of product sales will not reflect costs associated with such product manufacture, and our gross margins will be favorably impacted. We currently are unable to estimate the timing of the impact to future profitability resulting from the sell-through of any inventory manufactured after FDA approval of ENTEREG for POI.

*Research and Development*

Over the past few years, we have incurred significant expenditures related to conducting clinical studies to develop new pharmaceutical products. During 2009, we expect to continue to incur significant levels of both internal and external research and development expenditures related to our preclinical and clinical product candidates. We expect to begin or continue a number of clinical programs including, among others, a Phase 4 study of ENTEREG for the management of POI in patients undergoing radical cystectomy, additional Phase 1 and Phase 2a clinical trials of ADL5747 and ADL5859 and Phase 1 clinical trials for ADL7445. We also expect to continue to conduct research, preclinical studies and process development activities on other product candidates. It is likely that expenses related to these efforts will increase over time should these programs advance to later stages of development.

## RESULTS OF OPERATIONS

*This section should be read in conjunction with the discussion above under "Liquidity and Capital Resources."*

### Product Sales

Net product sales are derived solely from ENTEREG. ENTEREG was approved by the FDA in May 2008 and product shipments to hospitals began in June 2008. In accordance with SEC Staff Accounting Bulletin (SAB) No. 101, *Revenue Recognition in Financial Statements* (SAB 101), as amended by SAB No. 104, *Revenue Recognition,* and Statement of Financial Accounting Standards (SFAS) No. 48, *Revenue Recognition When Right of Return Exists*, we defer recognition of revenue associated with the first shipment of ENTEREG to each hospital customer as we are not yet able to reasonably estimate future returns. When an existing customer places a new order, we recognize product sales on the previous shipment for an amount equal to the lesser of (a) the previous shipment or (b) the new order. Hospital orders are processed through wholesalers; however, product is drop-shipped from Glaxo's warehouse directly to a registered hospital. Wholesalers remit payment to Glaxo and, on a monthly basis, Glaxo remits the net proceeds to us. We record product sales net of prompt payment discounts, returns and other discounts as reported to us by Glaxo. While we undertake certain procedures to review the reasonableness of this information, we cannot obtain absolute assurance over the accounting methods and controls over such information utilized by Glaxo.

Net shipments of ENTEREG through December 31, 2008 were $2.2 million. We recognized net product sales of $1.2 million on shipments to the approximately 185 hospitals that reordered ENTEREG during the year ended December 31, 2008. We have a customer deposit balance of $0.3 million at December 31, 2008. Customer deposits represent net shipments made for which payment has been received from Glaxo, but which have not yet been recognized as product sales revenue. The remaining $0.7 million difference represents product shipments for which payment has not yet been received from Glaxo and for which the conditions of revenue recognition have not been met.

No product sales were recognized prior to 2008.

### Contract Revenues

Contract revenues are derived from our collaboration agreements with Glaxo and Pfizer and include milestones, amortization of up-front license fees and cost reimbursement. Contract revenues were $48.2 million, $9.1 million and $15.1 million in the years ended December 31, 2008, 2007 and 2006, respectively. The increase in 2008 compared to 2007 was primarily the result of a $20.0 million milestone payment received from Glaxo following FDA approval of ENTEREG for POI and an increase of $18.0 million due to a full year of contract revenues under the Pfizer collaboration. In addition, Glaxo contract revenues increased by $1.1 million year-over-year as a result of increased expense reimbursement from Glaxo. The decrease in 2007 compared to 2006

was primarily the result of a $4.0 million reduction in expense reimbursement from Glaxo due to reduced expenses incurred by us relating to alvimopan programs, a reduction in co-promotion revenues of $2.4 million relating to the Arixtra co-promotion with Glaxo, which was terminated in December 2006, and a $0.9 million reduction in the amortization of the up-front license fee received from Glaxo resulting from extending the estimated end of the performance period from April 2014 to April 2016. These decreases were partially offset by an increase in amortization of upfront fees and cost reimbursements associated with the Pfizer collaboration of $1.3 million in 2007.

**Cost of Product Sales**

Cost of product sales was $0.2 million in the year ended December 31, 2008 and consisted primarily of royalty payments under certain alvimopan license agreements and FDA fees. Prior to the FDA approval of ENTEREG for POI, costs associated with the manufacture of alvimopan were expensed to research and development. Since the unit product shipments in 2008 were less than the quantity of product manufactured prior to FDA approval, no manufacturing costs were recorded in cost of product sales during the year ended December 31, 2008.

**Research and Development Expenses**

Our research and development expenses can be identified as internal or external expenses. External expenses include expenses incurred with clinical research organizations, contract manufacturers and other third-party vendors. Internal expenses include expenses such as personnel, laboratory and overhead expenses.

Research and development expenses were $52.7 million, $41.6 million and $56.7 million for the years ended December 31, 2008, 2007 and 2006, respectively, and consist of the following:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2008 | 2007 | 2006 |
| External research and development expenses: | | | |
| ENTEREG POI program | $ 5,040,590 | $ 5,115,904 | $ 9,441,130 |
| *Delta* agonist program | 10,499,302 | 7,834,043 | 2,493,115 |
| OBD program | 1,704,907 | 2,480,941 | 14,529,666 |
| Other programs | 9,971,473 | 3,408,043 | 5,127,495 |
| Total external research and development expenses | 27,216,272 | 18,838,931 | 31,591,406 |
| Total internal research and development expenses | 25,447,941 | 22,770,791 | 25,068,344 |
| Total research and development expenses | $52,664,213 | $41,609,722 | $56,659,750 |

We report all expenses gross within our statements of operations in accordance with Emerging Issues Task Force (EITF) Issue No. 99-19, *Reporting Revenue Gross as a Principal Versus Net as an Agent* (EITF 99-19), and, as such, the above table does not reflect any cost reimbursements from our collaboration partners. Total research and development expenses increased in 2008 as compared to 2007 due to the costs of Phase 2a clinical studies in our *delta* agonist program and increased activity in our preclinical programs, partially offset by lower expenses in our OBD program. Total research and development expenses decreased in 2007 as compared to 2006 due to a reduction in costs associated with our ENTEREG program in POI, our OBD development program and our other programs, partially offset by an increase in expenses related to our *delta* agonist program.

There are significant risks and uncertainties inherent in the preclinical and clinical studies associated with each of our research and development programs. These studies may yield varying results that could delay, limit or prevent the advancement of a program through the various stages of product development and significantly impact the costs to be incurred, and time involved, in bringing a program to completion. As a result, the cost to complete such programs, as well as the period in which net cash inflows from significant programs are expected to commence, are not reasonably estimable.

**Selling, General and Administrative Expenses**

Our selling, general and administrative expenses were $31.1 million, $24.0 million and $37.7 million for the years ended December 31, 2008, 2007 and 2006, respectively. The increase in 2008 compared to 2007 was primarily driven by sales and marketing expenses associated with the launch of ENTEREG. The expense decrease in 2007 compared to 2006 was principally related to decreased personnel expenses, including expense associated with the elimination of our sales force in December 2006, as well as lower marketing expenses.

**Interest Income**

Our interest income was $4.3 million, $7.9 million and $9.0 million for the years ended December 31, 2008, 2007 and 2006, respectively. The decreases year over year were due to lower average investment balances resulting from the use of cash in operating activities and an overall decline in interest rates during these periods.

**Other Income, Net**

Other income, net was $0.1 million, $0.1 million and $0.5 million for the years ended December 31, 2008, 2007 and 2006, respectively, and primarily represents cash received from the sale of certain Pennsylvania research and development tax credits.

**Income Taxes**

As of December 31, 2008, we had $345.1 million of Federal net operating loss carryforwards and $336.4 million of state net operating loss carryforwards, which are potentially available to offset future taxable income. The state net operating loss carryforwards began expiring during 2008 and the Federal net operating loss carryforwards will begin expiring in 2009, if not utilized. In addition, the utilization of the state net operating loss carryforwards is subject to annual limitation. At December 31, 2008, we also had $11.3 million of Federal and $0.8 million of state research and development tax credit carryforwards, which begin expiring in 2011, and are available to reduce Federal and state income taxes.

The Tax Reform Act of 1986 (the Act) provides for a limitation on the annual use of net operating loss and research and development tax credit carryforwards (following certain ownership changes, as defined by the Act) that could significantly limit our ability to utilize these carryforwards. We may have experienced various ownership changes, as defined by the Act, as a result of past financings. Additionally, because United States and certain state tax laws limit the time during which these carryforwards may be applied against future taxes, we may not be able to take full advantage of these attributes for Federal and state income tax purposes.

## CRITICAL ACCOUNTING POLICIES AND ESTIMATES

Management's Discussion and Analysis of Financial Condition and Results of Operations discusses our financial statements, which we have prepared in accordance with U.S. generally accepted accounting principles. In preparing our financial statements, we must make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. We develop and periodically change these estimates and assumptions based on historical experience and on various other factors that we believe are reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions.

Our significant accounting policies are described in Note 2 to our Financial Statements for the year ended December 31, 2008 included in Part II, Item 8 of this Annual Report on Form 10-K. In addition, the Securities and Exchange Commission defines critical accounting policies as those that are, in management's view, most important to the portrayal of the company's financial condition and results of operations and most demanding of

their judgment. Management considers the following policies to be critical to an understanding of our financial statements and the uncertainties associated with the complex judgments made by us that could impact our results of operations, financial position and cash flows.

**Revenue Recognition**

We recognize revenue in accordance with SAB 101, as amended by SAB 104, EITF Issue No. 00-21, *Revenue Arrangements with Multiple Deliverables* (EITF 00-21), and EITF 99-19.

*Product Sales, Net*

ENTEREG was approved by the FDA in May 2008 and product shipments to hospitals began in June 2008. In accordance with SAB 101, SAB 104 and SFAS No. 48, we defer recognition of revenue associated with the first shipment of ENTEREG to each hospital customer as we are not yet able to reasonably estimate future returns. When an existing customer places a new order, we recognize revenue on the previous shipment for an amount equal to the lesser of (a) the previous shipment or (b) the new order. Hospital orders are processed through wholesalers; however, ENTEREG is drop-shipped from Glaxo's warehouse directly to a hospital registered under the ENTEREG E.A.S.E. Program. This results in us being able to directly track actual hospital purchases. Once we have developed sufficient historical experience to estimate product returns, we intend to recognize net product sales upon the transfer of ownership and risk of loss for the product to the customer.

We record product sales net of prompt payment discounts, returns and other discounts as reported to us by Glaxo. When payment from Glaxo is received but the conditions for revenue recognition have not yet been met, we record a liability classified as customer deposits. As of December 31, 2008, we had recorded $0.3 million of customer deposits on our balance sheet related to payments received from Glaxo for which the conditions of revenue recognition had not been met.

*Contract Revenues*

Contract revenues, which include revenues from collaborative agreements, consist primarily of amortization of up-front fees, ongoing research and development funding and milestone and other payments under such agreements. Non-refundable up-front license fees are recognized as revenue if we have a contractual right to receive such payment, the contract price is fixed or determinable, the collection of the resulting receivable is reasonably assured and we have no further performance obligations under the license agreement. Multiple element arrangements, such as license and development arrangements, are analyzed to determine whether the deliverables, which often include a license and performance obligations, can be separated in accordance with EITF 00-21. We would recognize up-front license payments as revenue upon delivery of the license only if the license had standalone value and the fair value of the undelivered performance obligations could be determined. If the fair value of the undelivered performance obligations could be determined, such obligations would then be accounted for separately as performed. If the license is considered to either (i) not have standalone value or (ii) have standalone value but the fair value of any of the undelivered performance obligations could not be determined, the up-front license payment would be recognized as revenue ratably over the estimated period of when our performance obligations are to be performed. We estimate our performance period based on the specific terms of each collaborative agreement and subsequently adjust the performance periods, if appropriate, based upon available facts and circumstances. During the third quarter of 2008, the performance period of the Pfizer collaboration agreement was extended by six months to August 2010 based on the current status of the development programs. The effect of this change in estimate was a decrease to contract revenues of $1.2 million for the year ended December 31, 2008.

Our collaboration agreements also contain substantive milestone payments. Substantive milestone payments are considered to be performance payments that are recognized upon achievement of the milestone only if all of the following conditions are met: (i) the milestone payment is non-refundable; (ii) achievement of the milestone

involves a degree of risk and was not reasonably assured at the inception of the arrangement; (iii) substantive effort is involved in achieving the milestone; (iv) the amount of the milestone payment is reasonable in relation to the effort expended or the risk associated with achievement of the milestone; and (v) a reasonable amount of time passes between the up-front license payment and the first milestone payment as well as between each subsequent milestone payment. Determination as to whether a milestone meets the aforementioned conditions involves the judgment of management. If any of these conditions are not met, the resulting payment would not be considered a substantive milestone, and such payment would therefore be considered part of the consideration and be recognized as revenue as such performance obligations are performed in accordance with the policies described above.

Reimbursement of costs is recognized as revenue provided the provisions of EITF 99-19 are met, the amounts are determinable and collection of the related receivable is reasonably assured.

Amounts received prior to satisfying the above revenue recognition criteria for contract revenues are recorded as deferred revenue in the accompanying balance sheets. Amounts not expected to be recognized within one year of the balance sheet date are classified as long-term deferred revenue. The estimate of the classification of deferred revenue as short-term or long-term is based upon management's estimate of its performance period based on the specific terms of each collaborative agreement. These estimates may change in the future and such changes to estimates would be accounted for prospectively and would result in a change in the amount of revenue recognized in future periods.

**Research and Development Expenses**

We have entered into contracts with third parties to conduct certain research and development activities including preclinical, clinical and manufacturing activities. We accrue expenses related to such contracts based upon an estimate of the amounts due for work completed under the contracts. Factors considered in preparing such estimates include the number of subjects enrolled in studies and other criteria relating to the progress of efforts by our vendors.

**Valuation of Equipment and Leasehold Improvements**

Our equipment and leasehold improvements have been recorded at cost and are being depreciated on a straight-line basis over the estimated useful life of those assets. We periodically assess our equipment and leasehold improvements for impairment in accordance with SFAS No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets.* We review long-lived assets, specifically equipment and leasehold improvements, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. If indicators of impairment exist, impairment loss would be tested for if estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition is less than its carrying amount. The impairment charge, if any, is determined based on the excess of the carrying value of the asset over its fair value, with fair value determined based on an estimate of discounted future cash flows or other appropriate measures of fair value. Since inception, we have not recorded any impairment charges.

**Equity-based Compensation**

Beginning January 1, 2006, we have accounted for our employee stock option grants under the provisions of SFAS No. 123R, *Share-Based Payment.* SFAS No. 123R requires the recognition of the fair value of equity-based compensation in the statement of operations. The fair value of our stock option awards is estimated using a Black-Scholes option valuation model. The Black-Scholes option-pricing model requires several inputs, one of which is volatility. Our estimate of volatility is based upon the historical volatility experienced in our stock price. To the extent volatility of our stock price increases in the future, our estimates of the fair value of stock options granted in the future could increase, thereby increasing stock-based compensation expense in future periods. The

expected life of our stock options represents the period of time that option awards are expected to be outstanding giving consideration to vesting schedules and our historical exercise patterns, which we believe are relevant indicators of future exercise patterns. The fair value of equity-based awards is amortized over the vesting period of the award using the straight-line method. For equity-based awards with performance conditions, we recognize compensation cost if and when we conclude that it is probable that the performance condition will be achieved. As a result of our stock options vesting on a monthly basis, we do not estimate a forfeiture rate.

**Income Taxes**

We provide for income taxes in accordance with SFAS No. 109, *Accounting for Income Taxes*, which requires that income taxes are accounted for under the asset and liability method. Deferred income tax assets and liabilities are determined based on differences between the financial statement reporting and tax bases of assets and liabilities and net operating loss and credit carryforwards, and are measured using the enacted tax rates and laws that will be in effect when such items are expected to reverse. Deferred income tax assets are reduced, as necessary, by a valuation allowance when management determines it is more likely than not that some or all of the tax benefits will not be realized. The effect on deferred income tax assets and liabilities of a change in tax rates is recognized in the period that such tax rate changes are enacted.

**Recently Issued Accounting Pronouncements**

In September 2006, the Financial Accounting Standards Board (FASB) issued SFAS No. 157, *Fair Value Measurements*. SFAS No. 157 clarifies the definition of fair value, establishes a framework for measuring fair value and expands disclosures on fair value measurements. SFAS No. 157 is effective for financial statements issued for fiscal years beginning after November 15, 2007 and interim periods within those fiscal years; however, the FASB did provide a one year deferral for the implementation of SFAS No. 157 for certain non-financial assets and liabilities. We adopted the provisions of SFAS No. 157 during the first quarter of 2008. See Note 3 of the Financial Statements included in Part II, Item 8 of this Annual Report on Form 10-K.

In February 2007, the FASB issued SFAS No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities*. SFAS No. 159 permits entities to measure many financial instruments and certain other items at fair value at specified election dates. Under SFAS No. 159, any unrealized holding gains and losses on items for which the fair value option has been elected are reported in earnings at each subsequent reporting date. If elected, the fair value option (1) may be applied instrument-by-instrument, with a few exceptions, such as investments otherwise accounted for by the equity method; (2) is irrevocable (unless a new election date occurs); and (3) is applied only to entire instruments and not to portions of instruments. SFAS No. 159 is effective for fiscal years beginning after November 15, 2007. We did not elect to adopt the fair value option for eligible financial instruments under SFAS No. 159.

In June 2007, the FASB ratified the consensus reached in EITF Issue No. 07-3, *Accounting for Nonrefundable Advance Payments for Goods or Services Received for Use in Future Research and Development Activities* (EITF 07-3). EITF 07-3 requires that non-refundable advance payments for future research and development activities should be deferred and recognized as an expense as goods are delivered or the related services are performed. EITF 07-3 is effective for fiscal years beginning after December 15, 2007. The adoption of EITF 07-3 did not have a material impact on our results of operations and financial position.

In December 2007, the FASB issued EITF Issue No. 07-1, *Accounting for Collaborative Arrangements* (EITF 07-1), which applies to collaborative arrangements that are conducted by the participants without the creation of a separate legal entity for the arrangements and clarifies, among other things, how to determine whether a collaborative agreement is within the scope of this issue. EITF 07-1 is effective for financial statements issued for fiscal years beginning after December 15, 2008. We do not expect the adoption of EITF 07-1 to have a material impact on our results of operations and financial position.

## ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Our investment assets consist of U.S. Treasury obligations. The market value of such investments fluctuates with current market interest rates. In general, as rates increase, the market value of a debt instrument would be expected to decrease. The opposite is also true. To minimize such market risk, we have in the past held and, to the extent possible, will continue in the future to hold, such debt instruments to maturity at which time the debt instrument will be redeemed at its stated, or face, value. Due to the short duration and nature of these instruments, we do not believe that we have a material exposure to interest rate risk related to our investment portfolio. The investment portfolio at December 31, 2008 totaled $124.4 million, and the weighted-average yield-to-maturity was approximately 1.8% with maturities of investments ranging up to 12 months.

## ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

### INDEX TO FINANCIAL STATEMENTS

## REPORT OF MANAGEMENT

### Management's Report on Financial Statements

Our management is responsible for the preparation, integrity and fair presentation of information in our financial statements, including estimates and judgments. The financial statements presented in this Annual Report on Form 10-K have been prepared in accordance with accounting principles generally accepted in the United States. Our management believes the financial statements and other financial information included in this Annual Report on Form 10-K fairly present, in all material respects, our financial condition, results of operations and cash flows as of and for the periods presented in this Annual Report on Form 10-K. The financial statements have been audited by KPMG LLP, an independent registered public accounting firm, as stated in their report, which is included herein.

### Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Our internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States.

Our internal control over financial reporting includes those policies and procedures that:

- pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect our transactions and dispositions of our assets;
- provide reasonable assurance that our transactions are recorded as necessary to permit preparation of our financial statements in accordance with accounting principles generally accepted in the United States and that our receipts and expenditures are being made only in accordance with authorization of our management and our directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting can provide only reasonable assurance and may not prevent or detect misstatements. Also, projections of any evaluation of the effectiveness of such controls in future periods are subject to the risk that the controls may become inadequate because of changes in conditions or that the degree of compliance with the policies and procedures may deteriorate.

Our management conducted an assessment of the effectiveness of internal control over financial reporting based on the framework in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on this assessment, our management concluded that, as of December 31, 2008, our internal control over financial reporting was effective to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States.

The effectiveness of our internal control over financial reporting has been audited by KPMG LLP, an independent registered public accounting firm, as stated in their report which is included herein.

## REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders
Adolor Corporation:

We have audited the accompanying balance sheets of Adolor Corporation as of December 31, 2008 and 2007, and the related statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2008. In connection with our audits of the financial statements, we also have audited the financial statement schedule, Schedule II—Valuation and Qualifying Accounts. We also have audited Adolor Corporation's internal control over financial reporting as of December 31, 2008, based on criteria established in *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Adolor Corporation's management is responsible for these financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on these financial statements and financial statement schedule and an opinion on the Company's internal control over financial reporting based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement and whether effective internal control over financial reporting was maintained in all material respects. Our audits of the financial statements included examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Adolor Corporation as of December 31, 2008 and 2007, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2008, in conformity with U.S. generally accepted accounting principles. Also in our opinion, the related financial statement schedule, when considered in relation to the basic financial statements taken as a whole, presents fairly, in all material respects, the information

set forth therein. Also in our opinion, Adolor Corporation maintained, in all material respects, effective internal control over financial reporting as of December 31, 2008, based on criteria established in *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission.

/s/ KPMG LLP

Philadelphia, Pennsylvania
February 25, 2009

## ADOLOR CORPORATION

## BALANCE SHEETS

| | December 31, 2008 | December 31, 2007 |
|---|---|---|
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 7,535,146 | $ 15,575,804 |
| Short-term investments | 124,375,060 | 151,613,695 |
| Accounts receivable | 3,588,935 | 1,592,009 |
| Prepaid expenses and other current assets | 4,348,209 | 3,953,809 |
| Total current assets | 139,847,350 | 172,735,317 |
| Equipment and leasehold improvements, net | 4,466,803 | 5,776,410 |
| Other assets | 112,414 | 164,925 |
| Total assets | $ 144,426,567 | $ 178,676,652 |
| **Liabilities and Stockholders' Equity** | | |
| Current liabilities: | | |
| Accounts payable | $ 2,310,330 | $ 874,994 |
| Accrued expenses | 10,941,059 | 6,703,970 |
| Customer deposits | 274,425 | — |
| Deferred licensing fees and rent—current | 14,071,511 | 17,612,990 |
| Total current liabilities | 27,597,325 | 25,191,954 |
| Deferred licensing fees and rent—non-current | 28,207,240 | 41,098,260 |
| Other liabilities | 3,440 | 32,960 |
| Total liabilities | 55,808,005 | 66,323,174 |
| Commitments and contingencies (Notes 9 and 10) | | |
| Stockholders' equity: | | |
| Series A Junior Participating preferred stock, $0.01 par value; 35,000 shares authorized; none issued and outstanding | — | — |
| Preferred stock, $0.01 par value; 1,000,000 shares authorized; none issued and outstanding | — | — |
| Common stock, $.0001 par value; 99,000,000 shares authorized; 46,333,735 and 46,027,003 shares issued and outstanding at December 31, 2008 and 2007, respectively | 4,633 | 4,603 |
| Additional paid-in capital | 543,009,215 | 536,893,567 |
| Unrealized gain on available for sale securities | 671,457 | 399,791 |
| Accumulated deficit | (455,066,743) | (424,944,483) |
| Total stockholders' equity | 88,618,562 | 112,353,478 |
| Total liabilities and stockholders' equity | $ 144,426,567 | $ 178,676,652 |

The accompanying notes are an integral part of the financial statements.

## ADOLOR CORPORATION

## STATEMENTS OF OPERATIONS

| | Year ended December 31, | | |
|---|---|---|---|
| | 2008 | 2007 | 2006 |
| Revenues: | | | |
| Product sales, net | $ 1,247,271 | $ — | $ — |
| Contract revenues | 48,208,224 | 9,119,991 | 15,087,411 |
| Total revenues, net | 49,455,495 | 9,119,991 | 15,087,411 |
| Operating expenses incurred: | | | |
| Cost of product sales | 203,972 | — | — |
| Research and development | 52,664,213 | 41,609,722 | 56,659,750 |
| Selling, general and administrative | 31,114,718 | 23,970,339 | 37,689,565 |
| Total operating expenses | 83,982,903 | 65,580,061 | 94,349,315 |
| Loss from operations | (34,527,408) | (56,460,070) | (79,261,904) |
| Interest income | 4,314,658 | 7,890,494 | 8,991,261 |
| Other income, net | 90,490 | 126,601 | 532,265 |
| Net loss | $(30,122,260) | $(48,442,975) | $(69,738,378) |
| Basic and diluted net loss per share | $ (0.65) | $ (1.05) | $ (1.56) |
| Shares used in computing basic and diluted net loss per share | 46,158,458 | 45,932,981 | 44,731,350 |

The accompanying notes are an integral part of the financial statements.

## ADOLOR CORPORATION

## STATEMENTS OF COMPREHENSIVE LOSS

| | Year ended December 31, | | |
|---|---|---|---|
| | 2008 | 2007 | 2006 |
| Net loss | $(30,122,260) | $(48,442,975) | $(69,738,378) |
| Other comprehensive income: | | | |
| Unrealized gains on available for sale securities | 271,666 | 404,354 | 292,897 |
| Comprehensive loss | $(29,850,594) | $(48,038,621) | $(69,445,481) |

The accompanying notes are an integral part of the financial statements.

## ADOLOR CORPORATION

## STATEMENTS OF STOCKHOLDERS' EQUITY

| | Common stock | | Additional paid-in capital | Deferred compensation | Unrealized gain (loss) on available for sale securities | Accumulated deficit | Total stockholders' equity |
|---|---|---|---|---|---|---|---|
| | Number of shares | Amount | | | | | |
| Balance, January 1, 2006 | 39,106,362 | $3,911 | $373,751,232 | $(1,263) | $(297,460) | $(306,763,130) | $ 66,693,290 |
| Net proceeds from issuance of newly registered shares of common stock | 5,750,000 | 575 | 135,054,860 | — | — | — | 135,055,435 |
| Compensation expense under SFAS No. 123R | — | — | 8,671,724 | — | — | — | 8,671,724 |
| Reclassification of stock options issued to consultants | — | — | (300,428) | — | — | — | (300,428) |
| Reclassification of stock options exercised by consultants | — | — | 103,652 | — | — | — | 103,652 |
| Payments on notes granted to employees for stock options | — | — | 35,809 | — | — | — | 35,809 |
| Interest receivable converted to principal on employee notes | — | — | (766) | — | — | — | (766) |
| Exercise of stock options | 1,063,181 | 106 | 12,366,024 | — | — | — | 12,366,130 |
| Restricted stock issued | 80,000 | — | — | — | — | — | — |
| Unrealized gain on investments | — | — | — | — | 292,897 | — | 292,897 |
| Amortization of deferred compensation | — | — | — | 1,263 | — | — | 1,263 |
| Net loss | — | — | — | — | — | (69,738,378) | (69,738,378) |
| Balance, December 31, 2006 | 45,999,543 | 4,592 | 529,682,107 | — | (4,563) | (376,501,508) | 153,180,628 |
| Compensation expense under SFAS No. 123R | 16,487 | 10 | 7,158,474 | — | — | — | 7,158,484 |
| Payments on notes granted to employees for stock options | — | — | 6,681 | — | — | — | 6,681 |
| Exercise of stock options | 10,973 | 1 | 46,305 | — | — | — | 46,306 |
| Unrealized gain on investments | — | — | — | — | 404,354 | — | 404,354 |
| Net loss | — | — | — | — | — | (48,442,975) | (48,442,975) |
| Balance, December 31, 2007 | 46,027,003 | 4,603 | 536,893,567 | — | 399,791 | (424,944,483) | 112,353,478 |
| Vesting of deferred stock | 343,109 | 34 | (34) | — | — | — | — |
| Stock issued to directors | 10,881 | 1 | (1) | — | — | — | — |
| Forfeiture of restricted stock | (5,000) | — | — | — | — | — | — |
| Purchase and retirement of deferred stock | (81,326) | (8) | (425,230) | — | — | — | (425,238) |
| Compensation expense under SFAS No. 123R | — | — | 6,393,347 | — | — | — | 6,393,347 |
| Exercise of stock options | 39,068 | 3 | 147,566 | — | — | — | 147,569 |
| Unrealized gain on investments | — | — | — | — | 271,666 | — | 271,666 |
| Net loss | — | — | — | — | — | (30,122,260) | (30,122,260) |
| Balance, December 31, 2008 | 46,333,735 | $4,633 | $543,009,215 | $ — | $ 671,457 | $(455,066,743) | $ 88,618,562 |

The accompanying notes are an integral part of the financial statements.

## ADOLOR CORPORATION

## STATEMENTS OF CASH FLOWS

| | Year ended December 31, | | |
|---|---|---|---|
| | 2008 | 2007 | 2006 |
| Net cash flows from operating activities: | | | |
| Net loss | $ (30,122,260) | $ (48,442,975) | $ (69,738,378) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | | |
| Stock-based compensation expense | 6,363,827 | 7,112,957 | 8,554,691 |
| Deferred licensing fees and rent | (16,432,499) | (4,627,556) | (4,329,164) |
| Depreciation and amortization expense | 2,164,668 | 2,359,318 | 2,594,786 |
| Changes in assets and liabilities: | | | |
| Accounts receivable | (1,996,926) | 1,687,365 | (64,540) |
| Prepaid expenses and other current assets | (394,400) | 537,141 | (2,038,759) |
| Other assets | 52,511 | 77,828 | 54,250 |
| Accounts payable | 1,435,336 | (1,787,707) | (690,595) |
| Accrued expenses | 4,444,666 | (6,839,094) | 1,814,904 |
| Customer deposits | 274,425 | — | — |
| Deferred licensing fees | — | 31,873,346 | — |
| Net cash used in operating activities | (34,210,652) | (18,049,377) | (63,842,805) |
| Net cash flows from investing activities: | | | |
| Purchases of equipment and leasehold improvements, net of disposals | (1,062,638) | (780,481) | (1,419,810) |
| Purchases of short-term investments | (154,476,699) | (161,926,190) | (342,644,234) |
| Maturities/sales of short-term investments | 181,987,000 | 193,000,000 | 262,000,000 |
| Net cash provided by (used in) investing activities | 26,447,663 | 30,293,329 | (82,064,044) |
| Net cash flows from financing activities: | | | |
| Net proceeds from exercise of stock options | 147,569 | 46,313 | 12,366,130 |
| Payment of withholding taxes related to deferred stock | (425,238) | — | — |
| Proceeds received on notes receivable | — | 6,681 | 35,809 |
| Interest receivable converted to principal on notes | — | — | (766) |
| Net proceeds from issuance of common stock | — | — | 135,055,435 |
| Net cash provided by (used in) financing activities | (277,669) | 52,994 | 147,456,608 |
| Net increase (decrease) in cash and cash equivalents | (8,040,658) | 12,296,946 | 1,549,759 |
| Cash and cash equivalents at beginning of period | 15,575,804 | 3,278,858 | 1,729,099 |
| Cash and cash equivalents at end of period | $ 7,535,146 | $ 15,575,804 | $ 3,278,858 |
| Supplemental disclosure of cash flow information: | | | |
| Cash received from sale of Pennsylvania research and development tax credits | $ 93,656 | $ 142,938 | $ 551,158 |
| Supplemental disclosure of non-cash financing activities: | | | |
| Unrealized gains on available for sale securities, net | $ 271,666 | $ 404,354 | $ 292,897 |
| Change in accrued expenses related to purchases of equipment | $ (207,577) | $ 387,240 | $ — |

The accompanying notes are an integral part of the financial statements.

## 1. ORGANIZATION AND BUSINESS ACTIVITIES

Adolor Corporation (the Company) is a biopharmaceutical company focused on the discovery, development and commercialization of novel prescription pain management products. On May 20, 2008, the U.S. Food and Drug Administration (FDA) approved the Company's first product, ENTEREG® (alvimopan), for the management of postoperative ileus following bowel resection surgery (POI). POI causes significant discomfort for patients and results in increased expense to healthcare providers. ENTEREG is specifically indicated to accelerate the time to upper and lower gastrointestinal recovery following partial large or small bowel resection surgery with primary anastomosis. In collaboration with Glaxo Group Limited (Glaxo), the Company launched ENTEREG in the United States in mid-2008.

The Company also has a number of product candidates in various stages of clinical and preclinical development. It is collaborating with Pfizer Inc. (Pfizer) for the development and commercialization of two *delta* opioid receptor agonist compounds, ADL5859 and ADL5747 (Pfizer compounds PF-04856880 and PF-04856881, respectively), for the treatment of pain. The Company recently completed three Phase 2a clinical trials of the initial formulation of ADL5859 and, based on the results of these trials, Pfizer and the Company are re-formulating ADL5859 before resuming clinical testing in 2009. The Company recently completed Phase 1 clinical testing of ADL5747 and has not observed any dose-limiting toxicity or serious adverse events with this compound. In addition to its *delta* compounds, the Company is developing ADL7445 to treat opioid bowel dysfunction (OBD), a condition that often results from chronic use of opioid analgesics to treat persistent pain conditions. ADL7445 is in preclinical development and the Company intends to submit an Investigational New Drug Application in the third quarter of 2009. The Company's other product candidates are in preclinical development for treating moderate-to-severe pain and other central nervous system conditions.

The Company was considered to be a development stage enterprise, as defined in Statement of Financial Accounting Standards (SFAS) No. 7, *Accounting and Reporting by Development Stage Enterprises*, through June 30, 2008. With the commencement of product sales in the quarter ended September 30, 2008, the Company is no longer considered to be a development stage enterprise.

## 2. BASIS OF ACCOUNTING AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

### Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses and related disclosure of assets and liabilities. The estimates made are principally in the areas of revenue recognition, research and development accruals and stock option expenses. Management bases its estimates on historical experience and various assumptions that are believed to be reasonable under the circumstances. Actual results may differ from those estimates.

### Concentration of Risk

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash equivalents, short-term investments and receivables. The Company invests its excess cash in accordance with a policy objective that seeks both liquidity and safety of principal. The policy limits investments to instruments issued by the U.S. government and commercial institutions with strong investment grade credit ratings and places restrictions on maturity terms and concentrations by type and issuer.

For the year ended December 31, 2008, which is the first period with commercial sales, three wholesale customers accounted for 93% of the Company's total gross shipments. Through its distribution services agreement with Glaxo, the Company and Glaxo have established credit rating guidelines relative to sales of ENTEREG to customers.

For the years ended December 31, 2008, 2007 and 2006, 97%, 100% and 100%, respectively, of the Company's revenues resulted from its collaboration agreements with Glaxo and Pfizer. Any failure by the Company's collaborators to perform their obligations or any decision by its collaborators to terminate these agreements under the terms provided for in their respective agreements could negatively impact the Company's ability to successfully develop, obtain regulatory approvals for and commercialize its products and product candidates, which would likely materially impact its financial condition and results of operations. In addition, any termination of the Company's collaboration agreements will terminate the funding it receives under the relevant collaboration agreement and may materially and adversely impact the Company's ability to fund further development efforts.

The Company depends on Piramal Healthcare (Canada) Limited (formerly Torcan Chemical Ltd.) as the sole approved supplier under its New Drug Application (NDA) of the active pharmaceutical ingredient in ENTEREG. The Company also depends on Pharmaceutics International, Inc. to manufacture ENTEREG finished capsules. The Company seeks to maintain inventories of finished products to protect against supply disruptions. Any future change in manufacturers or manufacturing process would require regulatory approval.

**Fair Value of Financial Instruments**

The carrying amounts of the Company's financial instruments, which include cash and cash equivalents, short-term investments, accounts receivable and accounts payable, approximate their fair values due to the short-term maturities of these instruments.

**Cash and Cash Equivalents**

The Company considers all highly liquid investments with a maturity of three months or less when purchased to be cash equivalents. The Company has $7.3 million in short-term money market accounts as of December 31, 2008.

**Short-term Investments**

The Company's entire portfolio of short-term investments is currently classified as available for sale and is stated at fair value as determined by quoted market values. Investments are comprised of U.S. Treasury obligations. All investments are short-term and are classified as current assets. Changes in net unrealized gains and losses are included as a separate component of stockholders' equity and comprehensive loss. For purposes of determining realized gains and losses, the cost of short-term investments sold is based upon specific identification. The Company has not experienced any other-than-temporary losses.

**Inventory**

As of December 31, 2008, the Company did not carry any inventory on its balance sheet. All manufacturing expenses related to ENTEREG, the Company's only FDA-approved product, were incurred prior to FDA approval and, therefore, were recorded as research and development expense on the Company's statement of operations. Future costs to manufacture ENTEREG will be capitalized as inventory and recorded to cost of product sales on the statement of operations as the related product is sold.

**Equipment and Leasehold Improvements**

Purchases of equipment (consisting of computer, office and laboratory equipment), furniture and fixtures and leasehold improvements are recorded at cost. Depreciation and amortization is calculated using the straight-

line method over the estimated useful lives of the assets, generally three to seven years, or the lease term, whichever is shorter. Expenditures for repairs and maintenance are charged to expense as incurred. When assets are retired or otherwise disposed, the assets and related allowances for depreciation and amortization are eliminated from the accounts and any resulting gain or loss is reflected in operating expenses.

**Valuation of Equipment and Leasehold Improvements**

The Company periodically assesses its equipment and leasehold improvement assets for impairment in accordance with SFAS No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets*. The Company reviews long-lived assets, specifically equipment and leasehold improvements, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. If indicators of impairment exist, impairment loss would be tested for if the estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition is less than its carrying amount. The impairment charge, if any, is determined based on the excess of the carrying value of the asset over its fair value, with fair value determined based on an estimate of discounted future cash flows or other appropriate measures of fair value. Since inception, the Company has not recorded any impairment charges.

**Revenue Recognition**

The Company recognizes revenue in accordance with Securities and Exchange Commission Staff Accounting Bulletin (SAB) No. 101, *Revenue Recognition in Financial Statements* (SAB 101), as amended by SAB No. 104, *Revenue Recognition* (SAB 104), Emerging Issues Task Force (EITF) Issue No. 00-21, *Revenue Arrangements with Multiple Deliverables*, and EITF Issue No. 99-19, *Reporting Revenue Gross as a Principal versus Net as an Agent.*

*Product Sales, Net*

ENTEREG was approved by the FDA in May 2008 and product shipments to hospitals began in June 2008. In accordance with SAB 101, SAB 104 and SFAS No. 48, *Revenue Recognition When Right of Return Exists*, the Company defers recognition of revenue associated with the first shipment of ENTEREG to each hospital customer as it is not yet able to reasonably estimate future returns. When an existing customer places a new order, the Company recognizes revenue on the previous shipment for an amount equal to the lesser of (a) the previous shipment or (b) the new order. Hospital orders are processed through wholesalers; however, ENTEREG is drop-shipped from Glaxo's warehouse directly to a hospital registered under the Entereg Access Support and Education (E.A.S.E.™) Program. This results in the Company being able to directly track actual hospital purchases. Once the Company has developed sufficient historical experience to estimate product returns, it intends to recognize net product sales upon the transfer of ownership and risk of loss for the product to the customer.

The Company records product sales net of prompt payment discounts, returns and other discounts as reported to it by Glaxo. When payment from Glaxo is received but the conditions for revenue recognition have not yet been met, the Company will record a liability classified as customer deposits. As of December 31, 2008, the Company had recorded $0.3 million of customer deposits on its balance sheet related to payments received from Glaxo for which the conditions of revenue recognition had not been met.

*Contract Revenues*

Contract revenues, which include revenues from collaborative agreements, consist primarily of amortization of up-front fees, ongoing research and development funding and milestone and other payments under such agreements. Non-refundable up-front license fees are recognized as revenue if the Company has a contractual

right to receive such payment, the contract price is fixed or determinable, the collection of the resulting receivable is reasonably assured and the Company has no further performance obligations under the license agreement. Multiple element arrangements, such as license and development arrangements, are analyzed to determine whether the deliverables, which often include a license and performance obligations, can be separated in accordance with EITF Issue No. 00-21. The Company would recognize up-front license payments as revenue upon delivery of the license only if the license had standalone value and the fair value of the undelivered performance obligations could be determined. If the fair value of the undelivered performance obligations could be determined, such obligations would then be accounted for separately as performed. If the license is considered to either (i) not have standalone value or (ii) have standalone value but the fair value of any of the undelivered performance obligations could not be determined, the up-front license payment would be recognized as revenue ratably over the estimated period of when the Company's performance obligations are to be performed. The Company estimates its performance period based on the specific terms of each collaborative agreement and subsequently adjusts the performance periods, if appropriate, based upon available facts and circumstances.

The Company's collaboration agreements also contain substantive milestone payments. Substantive milestone payments are considered to be performance payments that are recognized upon achievement of the milestone only if all of the following conditions are met: (i) the milestone payment is non-refundable; (ii) achievement of the milestone involves a degree of risk and was not reasonably assured at the inception of the arrangement; (iii) substantive effort is involved in achieving the milestone; (iv) the amount of the milestone payment is reasonable in relation to the effort expended or the risk associated with achievement of the milestone; and (v) a reasonable amount of time passes between the up-front license payment and the first milestone payment as well as between each subsequent milestone payment. Determination as to whether a milestone meets the aforementioned conditions involves the judgment of management. If any of these conditions are not met, the resulting payment would not be considered a substantive milestone, and such payment would therefore be considered part of the consideration and be recognized as revenue as such performance obligations are performed in accordance with the policies described above.

Reimbursement of costs is recognized as revenue provided the provisions of EITF Issue No. 99-19 are met, the amounts are determinable and collection of the related receivable is reasonably assured.

Amounts received prior to satisfying the above revenue recognition criteria for contract revenues are recorded as deferred revenue in the accompanying balance sheets. Amounts not expected to be recognized within one year of the balance sheet date are classified as long-term deferred revenue. The estimate of the classification of deferred revenue as short-term or long-term is based upon management's estimate of its performance period based on the specific terms of each collaborative agreement. These estimates may change in the future and such changes to estimates would be accounted for prospectively and would result in a change in the amount of revenue recognized in future periods.

**Research and Development Expenses**

Research and product development expenses are charged to expense as incurred. Research and development expenses include, among other costs, salaries and other personnel-related costs, costs to conduct clinical trials, costs to manufacture drug candidates and clinical supplies and laboratory supplies costs.

**Advertising Costs**

Advertising costs are charged to expense as incurred and are included in selling, general and administrative expense within the statements of operations.

**Comprehensive Loss**

Comprehensive loss is comprised of the Company's net loss and certain changes in stockholders' equity that are excluded from the statement of operations. The Company includes unrealized gains and losses on certain marketable securities in other comprehensive loss.

**Accounting for Income Taxes**

The Company provides for income taxes in accordance with SFAS No. 109, *Accounting for Income Taxes*, which requires that income taxes are accounted for under the asset and liability method. Deferred income tax assets and liabilities are determined based on differences between the financial statement reporting and tax bases of assets and liabilities and net operating loss and credit carryforwards, and are measured using the enacted tax rates and laws that will be in effect when such items are expected to reverse. Deferred income tax assets are reduced, as necessary, by a valuation allowance when management determines it is more likely than not that some or all of the tax benefits will not be realized. The effect on deferred income tax assets and liabilities of a change in tax rates is recognized in the period that such tax rate changes are enacted.

**Segment Information**

The Company is operated as one business and is managed by a single management team that reports to the chief executive officer. The Company does not operate separate lines of business or separate business entities with respect to any of its product candidates. Accordingly, the Company does not prepare discrete financial information with respect to separate product areas or by location, and does not have separately reportable segments.

**Net Loss Per Common Share**

The Company accounts for and discloses net loss per common share in accordance with SFAS No. 128, *Earnings per Share*. Basic net loss per common share is computed by dividing net loss by the weighted average number of common shares outstanding. Diluted net loss per common share is computed by dividing net loss by the weighted average number of common shares and dilutive potential common share equivalents then outstanding. Potential common shares consist of shares issuable upon the exercise of stock options and unvested deferred and restricted stock awards calculated using the treasury stock method. Because the inclusion of potential common stock would be anti-dilutive for all periods presented as a result of the net losses, diluted net loss per share is the same as basic net loss per share.

The following table sets forth the potential common stock excluded from the calculation of net loss per share because its inclusion would be anti-dilutive:

| | December 31, | | |
|---|---|---|---|
| | 2008 | 2007 | 2006 |
| Options to purchase common stock | 5,520,472 | 5,326,368 | 4,242,085 |
| Unvested deferred and restricted common stock | 62,500 | 347,046 | 80,000 |

**Stock-Based Compensation**

The Company follows the provisions of SFAS No. 123R, *Share-Based Payment*, which the Company adopted as of January 1, 2006 using the modified prospective basis transition method. SFAS No. 123R requires companies to recognize stock-based awards granted to employees and directors as compensation expense using

the fair value method. Under the fair value recognition provisions of SFAS No. 123R, stock-based compensation cost is measured at the grant date based on the fair value of the award and is generally recognized as expense on a straight-line basis over the service period, which represents the vesting period. For equity-based awards with performance conditions, the Company recognizes compensation cost if and when it concludes that it is probable that the performance condition will be achieved. The Company calculates the fair value of its stock options using the Black-Scholes option pricing model and the fair value of its deferred and restricted stock is based upon the market value of the underlying common stock on the date of the grant. As a result of the Company's stock options vesting on a monthly basis, it does not estimate a forfeiture rate.

Certain of the Company's share-based payment arrangements are outside the scope of SFAS No. 123R and are subject to EITF Issue No. 00-19, *Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock*, which requires vested stock options held by certain non-employee consultants to be accounted for as liability awards. The fair value of these awards is remeasured at each financial statement date until the awards are settled or expire.

**Recent Accounting Pronouncements**

In September 2006, the Financial Accounting Standards Board (FASB) issued SFAS No. 157, *Fair Value Measurements*. SFAS No. 157 clarifies the definition of fair value, establishes a framework for measuring fair value and expands disclosures on fair value measurements. SFAS No. 157 is effective for financial statements issued for fiscal years beginning after November 15, 2007 and interim periods within those fiscal years; however, the FASB did provide a one year deferral for the implementation of SFAS No. 157 for certain non-financial assets and liabilities. The Company adopted the provisions of SFAS No. 157 during the first quarter of 2008. The adoption of SFAS No. 157 did not have any impact on the Company's results of operations and financial position.

In February 2007, the FASB issued SFAS No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities*. SFAS No. 159 permits entities to measure many financial instruments and certain other items at fair value at specified election dates. Under SFAS No. 159, any unrealized holding gains and losses on items for which the fair value option has been elected are reported in earnings at each subsequent reporting date. If elected, the fair value option: (1) may be applied instrument-by-instrument, with a few exceptions, such as investments otherwise accounted for by the equity method; (2) is irrevocable (unless a new election date occurs); and (3) is applied only to entire instruments and not to portions of instruments. SFAS No. 159 is effective for fiscal years beginning after November 15, 2007. The Company did not elect to adopt the fair value option for eligible financial instruments under SFAS No. 159.

In June 2007, the FASB ratified the consensus reached in EITF Issue No. 07-3, *Accounting for Nonrefundable Advance Payments for Goods or Services Received for Use in Future Research and Development Activities*. EITF Issue No. 07-3 requires that non-refundable advance payments for future research and development activities should be deferred and recognized as an expense as goods are delivered or the related services are performed. EITF Issue No. 07-3 is effective for fiscal years beginning after December 15, 2007. The adoption of EITF Issue No. 07-3 did not have a material impact on the Company's results of operations and financial position.

In December 2007, the FASB issued EITF Issue No. 07-1, *Accounting for Collaborative Arrangements*, which applies to collaborative arrangements that are conducted by the participants without the creation of a separate legal entity for the arrangements and clarifies, among other things, how to determine whether a collaborative agreement is within the scope of this issue. EITF Issue No. 07-1 is effective for financial statements issued for fiscal years beginning after December 15, 2008. The Company does not expect the adoption of EITF Issue No. 07-1 to have a material impact on its results of operations and financial position.

## 3. SHORT-TERM INVESTMENTS

Short-term investments consist of investment-grade, fixed-income securities with original maturities of greater than three months. All investments are classified as available for sale and are considered current assets as the contractual maturities of the Company's short-term investments are all less than one year.

The following summarizes the short-term investments at December 31, 2008 and 2007:

| | Cost | Gross Unrealized Gains | Gross Unrealized Losses | Fair Value |
|---|---|---|---|---|
| U.S. Government obligations at December 31, 2008 | $123,703,603 | $671,457 | $ — | $124,375,060 |
| U.S. Government obligations at December 31, 2007 | $151,213,904 | $419,412 | $(19,621) | $151,613,695 |

SFAS No. 157 establishes a valuation hierarchy for disclosure of the inputs to valuations used to measure fair value. This hierarchy prioritizes the inputs into three broad levels. Level 1 inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities. Level 2 inputs include quoted prices for identical or similar assets and liabilities that are not active, quoted prices for similar assets and liabilities in active markets or inputs that are observable for the asset or liability, either directly or indirectly through market corroboration, for substantially the full term of the financial instrument. Level 3 inputs are unobservable inputs based on management's own assumptions used to measure assets and liabilities at fair value. The classification of a financial asset or liability within the hierarchy is determined based on the lowest level input that is significant to the fair value measurement.

The following table provides the Company's assets and liabilities carried at fair value measured on a recurring basis as of December 31, 2008:

| | | Fair Value Measurements at December 31, 2008 using | | |
|---|---|---|---|---|
| | Total Carrying Value as of December 31, 2008 | Quoted Prices in Active Markets (Level 1) | Significant Other Observable Inputs (Level 2) | Significant Unobservable Inputs (Level 3) |
| Short-term investments | $124,375,060 | $124,375,060 | $— | $— |

## 4. CONTRACT REVENUES

Contract revenues consist of the following:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2008 | 2007 | 2006 |
| Milestone revenue | $20,000,000 | $ — | $ — |
| Amortization of deferred license fees | 16,269,972 | 4,465,029 | 4,166,636 |
| Cost reimbursement under collaborative agreements | 11,938,252 | 4,654,962 | 8,533,750 |
| Co-promotion revenue | — | — | 2,387,025 |
| Total contract revenues | $48,208,224 | $9,119,991 | $15,087,411 |

In April 2002, the Company entered into a collaboration agreement with Glaxo for the exclusive worldwide development and commercialization of ENTEREG for certain indications. Under the terms of the agreement, Glaxo paid the Company a non-refundable and non-creditable signing fee of $50.0 million. The $50.0 million signing fee was recorded as deferred licensing fees and is being recognized as revenue on a straight-line basis over the estimated performance period under the collaboration agreement, which extends to March 2016. Revenue related thereto of approximately $3.3 million, $3.3 million and $4.2 million was recognized in each of the years ended December 31, 2008, 2007 and 2006, respectively. During the year ended December 31, 2008, the Company recorded $20.0 million in milestone revenue under the Glaxo collaboration agreement following FDA approval of ENTEREG in May 2008. Glaxo has the right to terminate the collaboration agreement, subject to the terms of specified notice provisions contained in the agreement. In September 2008, Glaxo terminated the agreement with respect to, among other things, the OBD indication. Glaxo retained its rights with respect to the POI indication.

External expenses for research and development and marketing activities incurred in the United States by each party are reimbursed pursuant to contractually agreed percentages. Reimbursement amounts owed to the Company by Glaxo are recorded gross in the statements of operations as contract revenues. The Company recorded collaboration agreement cost reimbursements from Glaxo of approximately $5.6 million, $4.5 million and $8.5 million, respectively, in the years ended December 31, 2008, 2007 and 2006 under this arrangement. As of December 31, 2008 and 2007, approximately $2.4 million and $1.6 million, respectively, were receivable from Glaxo for reimbursement of expenses incurred by the Company pursuant to the collaboration agreement.

In December 2007, the Company entered into a collaboration agreement with Pfizer for the exclusive worldwide development and commercialization of ADL5859 and ADL5747. Under the terms of the agreement, Pfizer paid the Company an up-front payment of $30.0 million and reimbursed $1.9 million of Phase 2a development costs incurred by the Company prior to entering into the collaboration agreement. The $31.9 million up-front fee was recorded as deferred licensing fees and is being recognized as revenue on a straight-line basis over the estimated performance period under the collaboration agreement. During the third quarter of 2008, the performance period was extended by six months to August 2010 based on the current status of the development programs. The effect of this change in estimate was an increase to net loss of $1.2 million, or $0.03 per share, for the year ended December 31, 2008. The Company recorded amortization of deferred license fees under the collaboration agreement with Pfizer of $13.0 million and $1.2 million in the years ended December 31, 2008 and 2007, respectively.

External expenses for research and development and marketing activities incurred in the United States by each party are reimbursed pursuant to contractually agreed percentages. Reimbursement amounts owed to the Company by Pfizer are recorded gross on the statements of operations as contract revenues. The Company recorded collaboration cost reimbursement from Pfizer of $6.3 million and $0.1 million in the years ended December 31, 2008 and 2007, respectively. As of December 31, 2008 and 2007, $1.2 million and $30,000, respectively, were receivable from Pfizer for reimbursement of expenses incurred by the Company pursuant to the collaboration agreement.

In 2005, the Company established a hospital-focused sales force under a co-promotion agreement with Glaxo to co-promote Glaxo's anti-thrombotic agent, Arixtra. Under the terms of the co-promotion agreement, Glaxo provided payments to the Company at a contractual rate for the Company's sales representatives deployed to promote Arixtra. The Company recognized co-promotion revenue of $2.4 million in the year ended December 31, 2006. The co-promotion agreement with Glaxo terminated effective December 31, 2006 and the Company eliminated the sales force in December 2006 (see Note 12).

## 5. EQUIPMENT AND LEASEHOLD IMPROVEMENTS

Equipment and leasehold improvements consist of the following:

| | December 31, | |
|---|---|---|
| | 2008 | 2007 |
| Laboratory, computer and office equipment | $ 12,539,858 | $ 11,979,336 |
| Furniture, fixtures and leasehold improvements | 7,531,074 | 7,366,679 |
| | 20,070,932 | 19,346,015 |
| Less accumulated depreciation and amortization | (15,604,129) | (13,569,605) |
| | $ 4,466,803 | $ 5,776,410 |

Depreciation and amortization expense related to equipment and leasehold improvements was $2.2 million, $2.4 million and $2.6 million for the years ended December 31, 2008, 2007 and 2006, respectively.

## 6. ACCRUED EXPENSES

Accrued expenses consist of the following:

| | December 31, | |
|---|---|---|
| | 2008 | 2007 |
| Clinical development costs | $ 315,169 | $ 156,045 |
| Manufacturing costs | 2,404,698 | 735,092 |
| Sales and marketing costs | 1,195,942 | 127,043 |
| Consulting and other costs | 2,670,894 | 2,322,122 |
| Collaboration agreement expenses | 1,148,154 | 71,932 |
| Professional fees | 336,871 | 587,367 |
| Personnel related costs | 2,869,331 | 2,689,807 |
| Restructuring costs (Note 12) | — | 14,562 |
| | $10,941,059 | $6,703,970 |

## 7. COMMON STOCK AND SHARE-BASED PAYMENTS

*Common Stock Sale*

In 2006, the Company sold 5,750,000 shares of common stock at $25.00 per share. The proceeds of the offering were approximately $135.1 million, net of offering costs.

*Shareholder Rights Plan*

The Company's Board of Directors adopted a Shareholder Rights Plan (the Plan) in February 2001. Under the Plan, preferred stock purchase rights (each, a Right) were distributed as a dividend at the rate of one Right for each share of common stock outstanding as of the close of business on February 20, 2001, and automatically attach to shares issued thereafter. Each Right entitles the holder to purchase one ten-thousandth of a share of newly created Series A Junior Participating preferred stock of the Company at an exercise price of $155.00 (the Exercise Price) per Right. In general, the Rights will be exercisable if a person or group (Acquiring Person) becomes the beneficial owner of 15% or more of the outstanding common stock of the Company or announces a

tender offer for 15% or more of the common stock of the Company. When the Rights become exercisable, a holder, other than the Acquiring Person, will have the right to receive, upon exercise, common stock having a value equal to two times the Exercise Price of the Right. The Board of Directors will in general be entitled to redeem the Rights for $.0001 per Right at any time prior to the occurrence of the stock acquisition events described above. If not redeemed, the Rights will expire on February 19, 2011.

*Standstill Arrangements*

The Glaxo collaboration agreement generally provides that during its term, Glaxo will not, directly or indirectly, alone or in concert with others: (i) acquire, or agree to acquire any shares of the Company's common stock or any securities exercisable for or convertible into the Company's common stock; (ii) make, or in any way participate in, any solicitation of proxies to vote the Company's common stock; or (iii) acquire or agree to acquire any of the Company's tangible or intangible assets not offered for sale by the Company. However, Glaxo may, under certain circumstances, acquire equity securities of the Company set forth in the agreement, including following the initiation by a third party of an unsolicited tender offer to purchase the Company or in connection with stock splits or recapitalizations or on exercise of pre-emptive rights afforded to the Company's stockholders generally.

The Pfizer license and collaboration agreement generally provides that for a period lasting until the earlier of (a) a number of years as defined in the agreement and (b) a period of time following the effective date of termination, Pfizer will not directly or indirectly, and will not encourage others to: (i) acquire, or agree to acquire securities of the Company; (ii) make, or in any way participate in, any solicitation of proxies to vote the Company's common stock; or (iii) acquire or agree to acquire any of the assets, tangible or intangible, of the Company. The agreement sets forth certain circumstances under which Pfizer may acquire securities of the Company or be released from the standstill arrangement.

*Equity Compensation Plans*

The Company has established equity compensation plans for its employees and directors and certain other individuals. The equity plans are administered by the Compensation Committee of the Company's Board of Directors. The Company's 1994 Amended and Restated Equity Compensation Plan, as amended (the 1994 Plan), and 2003 Amended and Restated Stock-Based Incentive Compensation Plan (the 2003 Plan), together known as the Plans, allow for the granting of incentive and nonqualified stock options to employees, directors, consultants and contractors. In addition, the 2003 Plan also allows for the granting of deferred and restricted stock awards. In aggregate, 12,950,000 shares of the Company's common stock are authorized to be issued under the Plans. As of December 31, 2008, there were 270,004 and 2,756,728 shares available for future grants under the 1994 Plan and the 2003 Plan, respectively, and the Company has reserved approximately 8,600,000 shares of common stock for the exercise of stock options.

Under the provisions of SFAS No. 123R and EITF Issue No. 00-19, the following aggregate stock-based compensation expense resulting from stock options, restricted stock awards and deferred stock awards was included in the Company's statements of operations:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2008 | 2007 | 2006 |
| Selling, general and administrative | $3,397,555 | $3,780,745 | $5,784,623 |
| Research and development | 2,966,272 | 3,332,212 | 2,768,805 |
| Total stock-based compensation expense | $6,363,827 | $7,112,957 | $8,553,428 |

There were no recognized tax benefits related to stock compensation during the years ended December 31, 2008, 2007 or 2006, as any benefit was offset by the Company's full valuation allowance on its net deferred tax asset. In addition, the Company has not recognized any windfall tax benefit as the resulting deduction has not been realized via a reduction of income taxes payable.

*Stock Options*

Stock options generally vest over four years from the date of grant and stock options are exercisable generally for a period of ten years from the date of grant. Upon the exercise of stock options, new shares of the Company's common stock are issued. The Company uses the Black-Scholes option pricing model to calculate the fair value of stock options on the date of grant and option awards are generally granted with an exercise price equal to the closing market price of the Company's stock at the date of grant. Expected volatility for the expected life of the option is based upon historical volatility and the expected life of the stock options represents the period of time that option awards are expected to be outstanding giving consideration to vesting schedules and the Company's historical exercise patterns. The risk-free interest rate is calculated using the U.S. Treasury yield curves in effect at the time of grant, for the period equal to the expected term of the options. The Company has not paid any dividends in the past and does not plan to pay any dividends in the foreseeable future. The fair value of stock options granted to employees was estimated using the following weighted-average assumptions for the years ended December 31, 2008, 2007 and 2006:

| | 2008 | 2007 | 2006 |
|---|---|---|---|
| Expected dividend yield | — | — | — |
| Expected stock price volatility | 81.2% | 76.6% | 67.5% |
| Risk-free interest rate | 3.11% | 4.73% | 4.52% |
| Expected life (in years) | 5.0 | 5.0 | 6.0 |

The following table summarizes the aggregate stock option activity for the year ended December 31, 2008:

| | Options | Weighted Average Exercise Price | Weighted Average Remaining Contractual Life (years) | Aggregate Intrinsic Value |
|---|---|---|---|---|
| Outstanding at January 1, 2008 | 5,326,368 | $10.96 | | |
| Granted | 1,687,860 | 4.37 | | |
| Exercised | (39,068) | 3.78 | | |
| Forfeited | (596,890) | 6.74 | | |
| Expired | (857,798) | 12.33 | | |
| Outstanding at December 31, 2008 | 5,520,472 | $ 9.24 | 7.2 | $1,608 |
| Exercisable at December 31, 2008 | 3,380,874 | $11.42 | 6.1 | $1,608 |

Intrinsic value in the above table was calculated as the difference between the Company's closing stock price on the last trading day of 2008 and the exercise price, multiplied by the number of options. For any of the Company's outstanding stock options with an exercise price equal to or greater than the Company's closing stock price on December 31, 2008, the intrinsic value was considered to be zero.

As of December 31, 2008, total unrecognized compensation cost related to outstanding stock options was approximately $7.8 million, which will be amortized over the weighted average remaining service period of 2.4 years. There were 1,252 in-the-money options exercisable as of December 31, 2008. For the years ended

December 31, 2008, 2007 and 2006, the Company received net proceeds of $0.1 million, $46,000 and $12.4 million, respectively, from the exercise of stock options.

The weighted-average grant date fair value of the options issued during the years ended December 31, 2008, 2007 and 2006 was $2.90, $3.61 and $9.31 per share, respectively. The intrinsic value of stock options exercised for the years ended December 31, 2008, 2007 and 2006 was $43,000, $20,000 and $12.6 million, respectively.

A summary of options outstanding and exercisable by price range at December 31, 2008, is as follows:

| | Options Outstanding | | | Options Exercisable | |
|---|---|---|---|---|---|
| Range of exercise prices | Number of Options | Weighted Average Remaining Option Life | Weighted Average Exercise Price (per share) | Number of Shares | Weighted Average Exercise Price (per share) |
| $ 0.38— 2.79 | 144,711 | 5.6 | $ 2.17 | 71,558 | $ 2.32 |
| $ 2.80— 5.59 | 2,129,544 | 8.7 | $ 4.10 | 804,010 | $ 3.98 |
| $ 5.60— 8.39 | 1,079,474 | 8.2 | $ 7.51 | 484,480 | $ 7.76 |
| $ 8.40—11.19 | 397,908 | 6.0 | $ 9.51 | 381,603 | $ 9.51 |
| $11.20—13.99 | 384,112 | 4.5 | $12.92 | 382,547 | $12.92 |
| $14.00—16.79 | 729,241 | 5.4 | $15.04 | 633,587 | $15.09 |
| $16.80—19.59 | 97,216 | 4.2 | $18.52 | 97,216 | $18.52 |
| $19.60—22.39 | 383,516 | 4.3 | $21.25 | 383,516 | $21.25 |
| $22.40—25.19 | 142,750 | 7.5 | $23.54 | 115,567 | $23.46 |
| $25.20—27.99 | 32,000 | 7.4 | $26.40 | 26,790 | $26.22 |
| | 5,520,472 | | $ 9.24 | 3,380,874 | $11.42 |

*Deferred and Restricted Stock Awards*

Deferred and restricted stock awards generally vest when a performance condition is satisfied or ratably over terms ranging from immediately to four years from the date of grant. The Company granted 179,169, 342,056 and 80,000 deferred and restricted stock awards to employees during the years ended December 31, 2008, 2007 and 2006, respectively. Of these grants, 380,609 deferred and restricted stock awards vested upon FDA approval of ENTEREG during the second quarter of 2008. In connection with the vesting of deferred and restricted stock awards during the year ended December 31, 2008, approximately 81,000 shares, with an aggregate fair value of $0.4 million, were withheld and retired in satisfaction of minimum tax withholding obligations. The following table summarizes deferred and restricted stock awards for the year ended December 31, 2008:

| | Number of Shares | Weighted Average Grant Date Fair Value (Per Share) | Aggregate Intrinsic Value |
|---|---|---|---|
| Nonvested at January 1, 2008 | 347,046 | $6.39 | |
| Granted | 179,169 | $4.43 | |
| Vested | (380,609) | $5.47 | |
| Forfeited | (83,106) | $5.75 | |
| Nonvested at December 31, 2008 | 62,500 | $7.20 | $— |

As of December 31, 2008, total unrecognized compensation cost related to unvested deferred and restricted stock awards was $0.5 million, which will be expensed based upon the achievement, if any, of certain performance conditions. The weighted-average grant date fair value of deferred and restricted stock issued during the years ended December 31, 2008, 2007 and 2006 was $4.43, $5.61 and $9.23 per share, respectively. The estimated fair value of deferred and restricted stock awards that vested during the years ended December 31, 2008 and 2007 was $2.1 million and $0.1 million, respectively. There were no deferred or restricted stock awards that vested for the year ended December 31, 2006.

In January 2009, the Company granted 622,561 stock options and 301,043 deferred stock awards to employees.

Certain of the Company's share-based payment arrangements are outside the scope of SFAS No. 123R and are subject to EITF Issue No. 00-19, which requires vested stock options held by certain non-employee consultants to be accounted for as liability awards. The fair value of these awards is remeasured at each financial statement date until the awards are settled or expire. During the years ended December 31, 2008, 2007 and 2006, approximately $29,500, $45,500 and $0.1 million of income was recorded based on the remeasurement of these options, respectively. As of December 31, 2008, stock options to acquire 24,000 shares of common stock held by non-employee consultants remained unexercised and a liability of approximately $3,400 is included in other liabilities in the accompanying balance sheet.

## 8. INCOME TAXES

No federal and state taxes are payable as of December 31, 2008 and 2007.

As of December 31, 2008, the Company had $345.1 million of Federal and $336.4 million of state net operating loss carryforwards potentially available to offset future taxable income. The Federal and state net operating loss carryforwards will expire as follows:

| | Federal | State |
|---|---|---|
| 2009 | $ 33,000 | $ — |
| 2010 | 482,000 | — |
| 2011 | 1,079,000 | — |
| 2012 | 1,867,000 | — |
| 2013 | — | — |
| 2014 | — | — |
| 2015 | — | — |
| Thereafter | 341,648,000 | 336,419,000 |
| | $345,109,000 | $336,419,000 |

Federal and state net operating loss carryforwards described above do not reflect a portion of the benefit related to certain stock option exercises as prescribed by SFAS No. 123R. At December 31, 2008, the Company also has $11.3 million of Federal and $0.8 million of state research and development tax credit carryforwards, which begin expiring in 2011, and are available to reduce Federal and state income taxes.

The Tax Reform Act of 1986 (the Act) provides for a limitation on the annual use of net operating loss and research and development tax credit carryforwards following certain ownership changes (as defined by the Act). Because the Company may have experienced various ownership changes, as defined by the Act, as a result of past financings and its initial public offering, the Company's ability to utilize the above mentioned Federal and state net operating loss and credit carryforwards in any given year may be limited. Federal tax law limits the time

during which carryforwards may be applied against future taxes and Pennsylvania tax law limits the utilization of state net operating loss carryforwards to $3.0 million annually.

Significant components of the Company's deferred tax assets and liabilities are shown below. At December 31, 2008, a valuation allowance of $189.7 million has been recognized to offset the deferred tax asset. A valuation allowance to reduce the deferred tax asset is required if, based on the weight of the evidence, it is more likely than not that some, or all, of the deferred tax assets will not be realized. Realization of the Company's deferred tax asset is dependent upon generating future taxable income and given the uncertainty of future profitability, management has determined that a valuation allowance is necessary. The change in the deferred tax asset valuation allowance in 2008 and 2007 was $12.8 million and $19.9 million, respectively, and such change reduced the statutory Federal tax benefit at a rate of 35% to no tax benefit or provision in the statement of operations.

| | 2008 | 2007 |
|---|---|---|
| Deferred tax assets: | | |
| Net operating losses | $ 142,633,000 | $ 122,463,000 |
| Capitalized research and development costs | 11,849,000 | 16,134,000 |
| Tax credit carryforwards | 11,797,000 | 10,180,000 |
| Deferred revenue | 17,600,000 | 24,416,000 |
| Accrued expenses and other | 6,081,000 | 3,870,000 |
| Total deferred tax assets | 189,960,000 | 177,063,000 |
| Less valuation allowance | (189,682,000) | (176,897,000) |
| Net deferred tax assets | 278,000 | 166,000 |
| Deferred tax liability | (278,000) | (166,000) |
| Net deferred tax | $ — | $ — |

In addition, other income, net of $0.1 million, $0.1 million and $0.5 million for the years ended December 31, 2008, 2007 and 2006 represents cash received from the sale of certain Pennsylvania research and development tax credits.

## 9. COMMITMENTS

Future minimum lease payments under non-cancelable operating leases for equipment and office and laboratory space are as follows:

| Year Ending December 31, | |
|---|---|
| 2009 | $1,294,000 |
| 2010 | 1,257,000 |
| 2011 | 1,248,000 |
| 2012 | 1,219,000 |
| 2013 | 508,000 |
| 2014 and beyond | — |
| | $5,526,000 |

Rent expense was $1.0 million for each of the years ended December 31, 2008, 2007 and 2006. In December 2002, the Company signed a ten-year lease agreement for office and laboratory space. The lease includes a renewal option for two consecutive additional five-year periods and the Company has a purchase option exercisable at the

fifth and tenth year of the lease term. The Company recognizes rent expense on a straight-line basis over the life of the lease, and as a result, rent escalation expense is accrued on the balance sheet.

*Other Commitments*

The Company has committed to make future minimum payments to third parties for the manufacture of ENTEREG and for contracted sales force services. These obligations are legally binding and enforceable under agreements with third parties, and as of December 31, 2008, these minimum purchase commitments totaled $2.6 million.

The Company also has contingent liabilities associated with various agreements that it has entered into for services with third-party vendors, including agreements to conduct clinical trials, to manufacture product candidates and for consulting and other contracted services. These contingent liabilities require future performance by the third party in order for payment to be executed, and the Company accrues the costs of these agreements based on estimates of work completed to date. The Company estimates that $19.2 million will be payable in future periods under the arrangements in place at December 31, 2008. Of this amount, $5.6 million has been accrued for work estimated to have been completed as of December 31, 2008 and $13.6 million relates to future performance under these arrangements.

In addition to the above, the Company has committed to make potential future milestone payments to third parties as part of its in-licensing agreements. Payments generally become due and payable only upon the achievement of certain developmental, regulatory and/or commercial milestones. Because the achievement of these milestones is neither probable nor reasonably estimable, the Company has not recorded a liability on its balance sheet for any such contingencies. As of December 31, 2008, the maximum potential milestone payments due under current contractual agreements are $22.0 million.

*Glaxo Collaboration Agreement*

Under the terms of the Glaxo agreement, the Company is obligated to partially reimburse Glaxo for third-party expenses incurred by Glaxo in the development of ENTEREG for certain indications in the United States, pursuant to an agreed upon development plan and budget. The Company also incurs certain expenses in the development of ENTEREG, pursuant to an agreed upon development plan and budget, for certain other indications in the United States, a portion of which are reimbursable to the Company by Glaxo. The Company records these expenses as incurred.

In addition, the Company and Glaxo have a profit-sharing arrangement under which the Company reimburses Glaxo for 55% of profits, which are calculated as net sales of ENTEREG less certain agreed-upon costs, subject to certain adjustments. The Company records these profit-sharing expenses as incurred.

*Pfizer Collaboration Agreement*

Under the terms of the Pfizer agreement, the Company is obligated to partially reimburse Pfizer for third-party expenses incurred by Pfizer in the development of certain *delta* agonist compounds in support of regulatory filings in the United States, pursuant to an agreed upon development plan and budget. The Company also incurs expenses in the development of certain *delta* agonist compounds, pursuant to an agreed upon development plan and budget, a portion of which are reimbursable to the Company by Pfizer. The Company records these expenses as incurred.

*License Agreements*

With regard to the Company's commercial product, ENTEREG, the Company has commitments to Roberts Laboratories, Inc. (Roberts) and Eli Lilly and Company (Eli Lilly). In November 1996, Roberts licensed from Eli Lilly certain intellectual property rights relating to ENTEREG. In June 1998, the Company entered into an Option and License Agreement with Roberts under which the Company sublicensed these rights from Roberts. In December 2000, Shire U.S. Inc. became the successor in interests to Roberts under the Company's option and license agreement with Roberts. The Company has made license and milestone payments under this agreement totaling $2.5 million, including $0.9 million paid during 2008 as a result of the regulatory approval of ENTEREG. In addition to the license and milestone payments, the Company is obligated under the agreement to pay royalties on commercial sales of ENTEREG. For the year ended December 31, 2008, the Company incurred $0.1 million of royalty expense related to sales of ENTEREG. The Company's license to ENTEREG and its obligations to pay royalties to Shire and Eli Lilly expire on the later of either the date of the last to expire of the licensed Eli Lilly patents or November 5, 2011.

In August 2002, the Company entered into a separate exclusive license agreement with Eli Lilly under which the Company obtained an exclusive license to six issued U.S. patents and related foreign equivalents and know-how relating to peripherally selective opioid antagonists. The Company paid Eli Lilly $4.0 million upon signing the agreement and is subject to additional clinical and regulatory milestone payments and royalty payments to Eli Lilly on sales, if any, of new products utilizing the licensed technology. Under this license agreement, the Company also paid Eli Lilly $4.0 million upon acceptance for review of the Company's ENTEREG NDA by the FDA, which payment was made in the third quarter of 2004. However, there are no ongoing royalties on commercial sales of ENTEREG due to Eli Lilly under this agreement.

The Company charges to expense research and development milestone payments that are required to be made upon the occurrence of future events prior to receipt of applicable regulatory approval.

## 10. LEGAL PROCEEDINGS

On April 21, 2004, a lawsuit was filed in the U.S. District Court for the Eastern District of Pennsylvania against the Company, one of its directors and certain of its officers seeking unspecified damages on behalf of a putative class of persons who purchased Adolor common stock between September 23, 2003 and January 14, 2004. The complaint alleges violations of Section 10(b) and Section 20(a) of the Securities Exchange Act of 1934, in connection with the announcement of the results of certain studies in the Company's Phase 3 clinical trials for alvimopan, which allegedly had the effect of artificially inflating the price of the Company's common stock. This suit has been consolidated with three subsequent actions asserting similar claims under the caption *In re Adolor Corporation Securities Litigation*, No. 2:04-cv-01728. On December 29, 2004, the District Court issued an order appointing the Greater Pennsylvania Carpenters' Pension Fund as Lead Plaintiff. The appointed Lead Plaintiff filed a consolidated amended complaint on February 28, 2005. That complaint purported to extend the class period, so as to bring claims on behalf of a putative class of Adolor shareholders who purchased stock between September 23, 2003 and December 22, 2004. The complaint also adds as defendants the Company's Board of Directors asserting claims against them and the other defendants for violation of Section 11 and Section 15 of the Securities Act of 1933 in connection with the Company's public offering of stock in November 2003. Together with the management and director defendants, the Company moved to dismiss the complaint on April 29, 2005. The plaintiffs responded to the motion to dismiss on June 28, 2005, and the Company's reply was filed on August 12, 2005.

On August 2, 2004, two shareholder derivative lawsuits were filed in the U.S. District Court for the Eastern District of Pennsylvania, purportedly on behalf of the Company, against its directors and certain of its officers seeking unspecified damages for various alleged breaches of fiduciary duty and waste. The allegations are similar to those set forth in the class action complaints, involving the announcement of the results of certain studies in

the Company's Phase 3 clinical trials for alvimopan. On November 12, 2004, the derivative plaintiff filed an amended complaint. On December 13, 2004, the Company filed a motion challenging the standing of the derivative plaintiff to file the derivative litigation on its behalf. On December 13, 2004, the Company's directors and officers moved to dismiss the complaint for the failure to state a claim. Plaintiffs responded to these motions on January 27, 2005 and the Company filed reply briefs on February 18, 2005.

The Company believes that the allegations in each of these matters are without merit and intends to vigorously defend against the litigation. The Company has not accrued any amount in its financial statements as of December 31, 2008 for these matters, and the Company awaits the decision of the District Court in each matter.

## 11. 401(k) PROFIT SHARING PLAN

The Company maintains a 401(k) Profit Sharing Plan (the 401(k) Plan) available to all employees meeting certain eligibility criteria. The 401(k) Plan permits participants to contribute up to 100% of their salary, not to exceed the limits established by the Internal Revenue Code. All contributions made by participants into the participant's account vest immediately. In 2008, 2007 and 2006, the Company made contributions to the 401(k) Plan of $0.2 million, $0.2 million and $0.3 million, respectively. The Company's common stock is not, and never has been, an investment option for 401(k) Plan participants.

## 12. RESTRUCTURING CHARGE

On December 14, 2006, the Company announced that it had disbanded its sales force of approximately 35 people and made other selected reductions to the Company's work force. This reduction was due to the November 2006 FDA approvable letter and subsequent delay to possible market entry for the Company's lead product, ENTEREG.

The reduction in the Company's work force resulted in a severance charge of $2.5 million, of which none was paid in 2006. Substantially all of the accrued severance balance at December 31, 2006 of $2.5 million was paid in 2007, with the remaining amount paid in 2008. The severance charge is included in research and development and selling, general and administrative expense in the statements of operations for the year ended December 31, 2006.

## 13. UNAUDITED QUARTERLY INFORMATION

The table below summarizes the unaudited results of operations for each quarter of 2008 and 2007:

| | Quarter Ended | | | |
|---|---|---|---|---|
| | March 31 | June 30 | September 30 | December 31 |
| | (In thousands, except per share amounts) | | | |
| Fiscal 2008 | | | | |
| Revenue | $ 6,211 | $ 26,964 | $ 7,870 | $ 8,410 |
| Income (loss) from operations | $(10,758) | $ 6,477 | $(14,166) | $(16,080) |
| Net income (loss) | $ (9,055) | $ 7,485 | $(13,255) | $(15,297) |
| Basic and diluted net income (loss) per share | $ (0.20) | $ 0.16 | $ (0.29) | $ (0.33) |
| Fiscal 2007 | | | | |
| Revenue | $ 1,821 | $ 1,806 | $ 1,820 | $ 3,673 |
| Loss from operations | $(15,569) | $(13,655) | $(15,420) | $(11,816) |
| Net loss | $(13,208) | $(11,595) | $(13,539) | $(10,101) |
| Basic and diluted net loss per share | $ (0.29) | $ (0.25) | $ (0.29) | $ (0.22) |

## 14. SUBSEQUENT EVENTS

On January 30, 2009, the Company and Glaxo entered into Amendment No. 4 to Collaboration Agreement, as previously amended. Under Amendment No. 4, the Company and Glaxo, effective as of January 1, 2009, modified certain provisions of the collaboration agreement (i) to reflect the current plan jointly developed by the parties relating to the sale and promotion of ENTEREG and (ii) to modify certain payment provisions of the collaboration agreement, principally including the acceleration of payments owed by Glaxo to the Company. These payments are expected to total approximately $9.0 million and are expected to be received by the Company in the first half of 2009.

## ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

## ITEM 9A. CONTROLS AND PROCEDURES

### (a) Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our President and Chief Executive Officer and our Senior Vice President, Finance and Chief Financial Officer (the principal financial and accounting officer), evaluated the effectiveness of our disclosure controls and procedures as of the end of the period covered by this Annual Report on Form 10-K. Based on that evaluation, the President and Chief Executive Officer and the Senior Vice President, Finance and Chief Financial Officer concluded that our disclosure controls and procedures as of the end of the period covered by this Annual Report on Form 10-K have been designed and are functioning effectively to provide reasonable assurance that the information required to be disclosed by us in reports filed under the Securities Exchange Act of 1934 is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. We believe that a control system, no matter how well designed and operated, cannot provide absolute assurance that the objectives of the control system are met, and no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within a company have been detected.

### (b) Management's Annual Report on Internal Control over Financial Reporting

Management's Report on Internal Control over Financial Reporting is included in Part II, Item 8 of this Annual Report on Form 10-K and incorporated into this Item 9A by reference.

### (c) Attestation Report of the Registered Public Accounting Firm

The effectiveness of our internal control over financial reporting as of December 31, 2008 has been audited by KPMG LLP, an independent registered public accounting firm, as stated in their report included in Part II, Item 8 of this Annual Report on Form 10-K and incorporated into this Item 9A by reference.

### (d) Changes in Internal Control over Financial Reporting

There have been no changes in our internal control over financial reporting during our most recent fiscal quarter that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

## ITEM 9B. OTHER INFORMATION

None.

## PART III

## ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

### Directors

The information required by this Item 10 with respect to our Directors is incorporated herein by reference to the information contained under the caption "Proposal 1—Election of Directors" in our definitive proxy statement related to the 2009 annual meeting of stockholders, to be filed within 120 days after the end of the year covered by this Annual Report on Form 10-K.

### Executive Officers

The information concerning our executive officers required by this Item 10 is provided under the caption "Executive Officers of the Registrant" in Part I, Item 4 of this Annual Report on Form 10-K.

### Section 16(a) Beneficial Ownership Reporting Compliance

The information required by this Item 10 concerning Section 16(a) beneficial ownership reporting compliance by our directors and executive officers is incorporated herein by reference to the information contained under the caption "Section 16(a) Beneficial Ownership Reporting Compliance" in our definitive proxy statement related to the 2009 annual meeting of stockholders, to be filed within 120 days after the end of the year covered by this Annual Report on Form 10-K.

### Code of Ethics

The information required by this Item 10 concerning our code of ethics is incorporated herein by reference to the information contained under the caption "Governance of the Company—Does the Company have a 'Code of Ethics'?" in our definitive proxy statement related to the 2009 annual meeting of stockholders, to be filed within 120 days after the end of the year covered by this Annual Report on Form 10-K.

## ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item 11 is incorporated herein by reference to the information contained in our definitive proxy statement related to the 2009 annual meeting of stockholders, to be filed within 120 days after the end of the year covered by this Annual Report on Form 10-K.

## ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this Item 12 is incorporated herein by reference to the information contained in our definitive proxy statement related to the 2009 annual meeting of stockholders, to be filed within 120 days after the end of the year covered by this Annual Report on Form 10-K.

## ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this Item 13 is incorporated herein by reference to the information contained in our definitive proxy statement related to the 2009 annual meeting of stockholders, to be filed within 120 days after the end of the year covered by this Annual Report on Form 10-K.

## ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this Item 14 is incorporated herein by reference to the information contained in our definitive proxy statement related to the 2009 annual meeting of stockholders, to be filed within 120 days after the end of the year covered by this Annual Report on Form 10-K.

## PART IV

### ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

### (a) DOCUMENTS FILED AS PART OF THIS REPORT

The following is a list of our financial statements and supplementary data included in this Annual Report on Form 10-K under Item 8 of Part II hereof:

**1. FINANCIAL STATEMENTS AND SUPPLEMENTAL DATA**

Report of Management.

Report of Independent Registered Public Accounting Firm.

Balance Sheets as of December 31, 2008 and 2007.

Statements of Operations for the years ended December 31, 2008, 2007 and 2006.

Statements of Comprehensive Loss for the years ended December 31, 2008, 2007 and 2006.

Statements of Stockholders' Equity for the years ended December 31, 2008, 2007 and 2006.

Statements of Cash Flows for the years ended December 31, 2008, 2007 and 2006.

Notes to Financial Statements.

**2. FINANCIAL STATEMENT SCHEDULE**

Schedule II—Valuation and Qualifying Accounts.

Schedules, other than those listed above, are omitted because they are not applicable or are not required, or because the required information is included in the financial statements or notes thereto.

**(b) Exhibits**

The following is a list of exhibits filed as part of this Annual Report on Form 10-K. When so indicated by footnote, exhibits that were previously filed are incorporated by reference. For exhibits incorporated by reference, the location of the exhibit in the previous filing is indicated.

| Exhibit Number | Description |
|---|---|
| 3.1 | Amended and Restated Certificate of Incorporation of Adolor, filed as Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q filed on May 17, 2001. |
| 3.2 | Amended and Restated Bylaws of the Company as amended December 13, 2007, filed as Exhibit 3.2 to the Company's Current Report on Form 8-K filed on December 14, 2007. |
| 3.3 | Amended and Restated Bylaws of the Company, dated February 24, 2009, filed as Exhibit 3.1 to the Company's Current Report on Form 8-K filed on February 24, 2009. |
| 4.1 | Rights Agreement, dated as of February 20, 2001, between Adolor and StockTrans, Inc., as Rights Agent, filed as Exhibit 4.1 to the Company's Current Report on Form 8-K filed on February 23, 2001, which included as Exhibit B thereto the Form of Rights Certificate, filed as Exhibit 1.1 to the Company's Registration Statement on Form 8-A, dated February 22, 2001. |
| 4.2 | Form of Common Stock Certificate, filed as Exhibit 4.14 to Amendment No. 3 to the Company's Registration Statement on Form S-1 filed on March 21, 2000. |
| †10.1 | Amended and Restated 1994 Equity Compensation Plan, filed as Exhibit 10.1 to the Company's Annual Report on Form 10-K filed on February 29, 2008. |
| †10.2 | Adolor Corporation Amended and Restated 2003 Stock-Based Incentive Compensation Plan, filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed on May 27, 2008. |
| †10.3 | Incentive Compensation Plan, filed as Exhibit 10.31 to the Company's Annual Report on Form 10-K filed on February 27, 2007. |
| †10.4 | Adolor Corporation Incentive Compensation Plan, as amended and restated April 9, 2008, filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed on April 11, 2008. |
| †10.5 | Amended and Restated Adolor Corporation Incentive Compensation Plan, effective as of January 2009, filed as Exhibit 10.2 to the Company's Current Report on Form 8-K filed on January 12, 2009. |
| †10.6 | Adolor Corporation Executive Severance Pay Program, filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on November 1, 2002. |
| †10.7 | Letter Agreement between the Company and Michael R. Dougherty, dated October 24, 2002, filed as Exhibit 10.15 to the Company's Annual Report on Form 10-K filed on March 18, 2003. |
| †10.8 | Amendment dated January 26, 2004 to Letter Agreement between the Company and Michael R. Dougherty, dated October 24, 2002, filed as Exhibit 10.6 to the Company's Annual Report on Form 10-K filed on March 4, 2004. |
| †10.9 | Letter Agreement between the Company and Michael R. Dougherty dated December 14, 2006 amending letter agreement dated October 24, 2002, as amended January 26, 2004, filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed on December 14, 2006. |
| †10.10 | Amendment dated February 21, 2008 to Letter Agreement between the Company and Michael R. Dougherty dated October 24, 2002, as amended January 26, 2004, as further amended December 14, 2006, filed as Exhibit 10.20 to the Company's Annual Report on Form 10-K filed on February 29, 2008. |
| *†10.11 | Amendment dated December 31, 2008 to Letter Agreement between the Company and Michael R. Dougherty dated October 24, 2002, as amended January 26, 2004, as further amended December 14, 2006, as further amended February 21, 2008. |

| Exhibit Number | Description |
|---|---|
| †10.12 | Letter Agreement between the Company and Eliseo Orestes Salinas, MD, MSc dated February 28, 2008, filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed on April 15, 2008. |
| *†10.13 | Amendment dated December 31, 2008 to Letter Agreement between the Company and Eliseo Orestes Salinas, MD, MSc dated February 28, 2008. |
| †10.14 | Letter Agreement between the Company and Stephen Webster, M.B.A. dated June 13, 2008, filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed on June 13, 2008. |
| †10.15 | Letter Agreement between the Company and John M. Limongelli, Esq., dated August 15, 2008, filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed on September 15, 2008. |
| †10.16 | Letter Agreement between the Company and Thomas Hess dated September 16, 2005, filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed on October 31, 2005. |
| †10.17 | Letter Agreement between the Company and Martha E. Manning, dated June 30, 2002, filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on August 13, 2002. |
| †10.18 | Letter Agreement between the Company and David Jackson, dated June 3, 2008, filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed on June 5, 2008. |
| †10.19 | Stock Award Letter Agreement between the Company and Michael R. Dougherty dated December 14, 2006, filed as Exhibit 10.2 to the Company's Current Report on Form 8-K filed on December 14, 2006. |
| †10.20 | Performance Stock Option Award between the Company and Michael R. Dougherty dated January 8, 2008, filed as Exhibit 10.22 to the Company's Annual Report on Form 10-K filed February 29, 2008. |
| *†10.21 | Summary of Oral Agreement for Payment of Services between Adolor Corporation and its Board of Directors. |
| †10.22 | Form of Stock Option Agreement for members of the Board of Directors of Adolor Corporation filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on July 31, 2006. |
| †10.23 | Form of Stock Option Agreement, filed as Exhibit 10.26 to the Company's Annual Report on Form 10-K filed on March 1, 2005. |
| †10.24 | Form of Deferred Stock Award, filed as Exhibit 10.30 to the Company's Annual Report on Form 10-K filed on February 27, 2007. |
| †10.25 | Form of Performance Deferred Stock Award (January 2008), filed as Exhibit 10.29 to the Company's Annual Report on Form 10-K filed on February 29, 2008. |
| †10.26 | Form of Performance-Based Deferred Stock Award dated January 6, 2009, filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed on January 6, 2009. |
| 10.40 | Option and License Agreement between Adolor and Roberts Laboratories, Inc., dated June 10, 1998, filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed on September 3, 2008. (1) |
| 10.41 | Collaboration Agreement dated as of April 14, 2002, by and between the Company and Glaxo Group Limited, filed as Exhibit 10.1 to the Company's Current Report on Form 8-K/A filed on December 22, 2005. (1) |
| 10.42 | Amendment No. 1, dated as of June 22, 2004, to the Collaboration Agreement by and between Glaxo Group Limited and the Company, filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on August 4, 2004. |

| Exhibit Number | Description |
|---|---|
| 10.43 | Amendment No. 2, dated December 22, 2004, to Collaboration Agreement by and between Glaxo Group Limited and the Company, filed as Exhibit 10.1 to the Company's Current Report on Form 8-K/A filed on February 25, 2005. (1) |
| 10.44 | Amendment No. 3, dated as of July 23, 2008, to Collaboration Agreement by and between Glaxo Group Limited and the Company, filed as Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q filed on October 28, 2008. (1) |
| 10.45 | Notice of Termination For GI Products Received from Glaxo Group Limited dated August 29, 2008, filed as Exhibit 10.5 to the Company's Quarterly Report on Form 10-Q filed on October 28, 2008. |
| 10.46 | Distribution Services Agreement between SmithKline Beecham Corporation and the Company, dated June 29, 2004, filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on August 4, 2004. (1) |
| 10.47 | API Compound Supply Agreement between the Company and Torcan Chemical Ltd., dated July 13, 2004, filed as Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed on August 4, 2004. (1) |
| 10.48 | API Compound Supply Agreement Between the Company and Girindus AG, dated July 6, 2004, filed as Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q filed on August 4, 2004. (1) |
| 10.49 | Drug Product Supply Agreement between the Company and Pharmaceutics International, Inc., dated July 1, 2004, filed as Exhibit 10.5 to the Company's Quarterly Report on Form 10-Q filed on August 4, 2004. (1) |
| 10.50 | License Agreement between Adolor Corporation and Eli Lilly and Company, dated August 8, 2002, filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on November 1, 2002. (1) |
| 10.51 | License and Collaboration Agreement between the Company and Pfizer Inc. dated December 4, 2007, filed as Exhibit 10.14 to the Company's Annual Report on Form 10-K filed on February 29, 2008. (1) |
| 10.52 | Amended and Restated Build to Suit Lease between the Company and 700 Pennsylvania Drive Associates, dated February 27, 2003, filed as Exhibit 10.4 to the Company's Annual Report on Form 10-K filed on March 18, 2003. |
| *23.1 | Consent of KPMG LLP. |
| *31.1 | Certification Pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. |
| *31.2 | Certification Pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. |
| *32.1 | Certification Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. |
| *32.2 | Certification Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. |

* Filed herewith.

† Compensation plans and arrangements for executives and others.

(1) Portions of the Exhibit have been omitted and have been filed separately pursuant to an application for confidential treatment granted by the Securities and Exchange Commission.

## ADOLOR CORPORATION

## SCHEDULE II—VALUATION AND QUALIFYING ACCOUNTS

| Year Ended December 31, | Balance at Beginning of the Year | Additions (Deductions) (1) | Other Additions (Deductions) (2) | Balance at End of the Year |
|---|---|---|---|---|
| Reserve for income tax valuation allowance: | | | | |
| 2008 | $176,897,000 | $12,785,000 | $— | $189,682,000 |
| 2007 | 157,007,000 | 19,890,000 | — | 176,897,000 |
| 2006 | 128,083,000 | 28,924,000 | — | 157,007,000 |

(1) Amounts represent increases to the valuation allowance.

(2) Amounts represent utilization and adjustments of balance sheet reserve accounts.

## SIGNATURES

**Pursuant to the requirements of Section 13 or 15(d) of the Security Exchange Act of 1934, the Registrant has duly caused this Annual Report to be signed on its behalf by the undersigned, thereunto duly authorized.**

Date: February 26, 2009

ADOLOR CORPORATION

By: /s/ MICHAEL R. DOUGHERTY
Name: Michael R. Dougherty
Title: *President, Chief Executive Officer and Director*

**Pursuant to the requirements of the Securities Exchange Act of 1934, this Annual Report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.**

| Signature | Title | Date |
|---|---|---|
| /s/ MICHAEL R. DOUGHERTY<br>**Michael R. Dougherty** | President, Chief Executive Officer and Director (Principal Executive Officer) | February 26, 2009 |
| /s/ STEPHEN W. WEBSTER<br>**Stephen W. Webster** | Senior Vice President, Finance and Chief Financial Officer (Principal Financial and Accounting Officer) | February 26, 2009 |
| /s/ ARMANDO ANIDO<br>**Armando Anido** | Director | February 26, 2009 |
| /s/ GEORGES GEMAYEL<br>**Georges Gemayel** | Director | February 26, 2009 |
| /s/ PAUL GODDARD<br>**Paul Goddard** | Director | February 26, 2009 |
| /s/ GEORGE V. HAGER, JR.<br>**George V. Hager, Jr.** | Director | February 26, 2009 |
| /s/ DAVID M. MADDEN<br>**David M. Madden** | Director | February 26, 2009 |
| /s/ GUIDO MAGNI<br>**Guido Magni** | Director | February 26, 2009 |
| /s/ CLAUDE H. NASH<br>**Claude H. Nash** | Director | February 26, 2009 |
| /s/ DONALD E. NICKELSON<br>**Donald E. Nickelson** | Director | February 26, 2009 |

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In 2008, Adolor joined an elite group of life science companies who have achieved approval of their first product from the U.S. Food and Drug Administration. ENTEREG® (alvimopan) belongs to a new class of medicines, peripherally-acting mu opioid receptor antagonists, and is indicated to accelerate the time to upper and lower gastrointestinal (GI) recovery following partial large or small bowel resection surgery with primary anastomosis. ENTEREG is available for short-term use in hospitals registered under the ENTEREG Access Support and Education (E.A.S.E.™) Program. In extensive clinical studies, ENTEREG accelerated GI recovery by up to one day without compromising analgesia and reduced time to hospital discharge order written. For more information on this innovative therapy — including full prescribing and safety information for ENTEREG — please visit www.entereg.com.

Adolor®

*Discovery-driven. Pain-focused. Patient-centered.*

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Exton, Pennsylvania 19341

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484.595.1520 f

www.adolor.com