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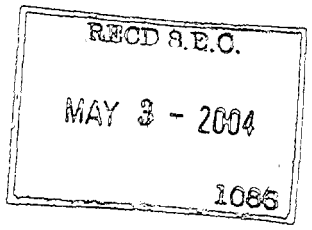
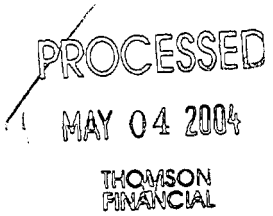


ADLR PROFILES 2003



ADOLOR CORPORATION: 2003 Annual Report

"In Business Development, we strive to identify product opportunities which can provide new treatment options for physicians in caring for their patients suffering from pain. In 2003, working closely with our R & D and Commercial groups, we in-licensed a sterile, easy-to-use, lidocaine patch that has the promise of reducing the pain associated with surgical incisions."

Gwen A. Melincoff
Vice President, Business Development

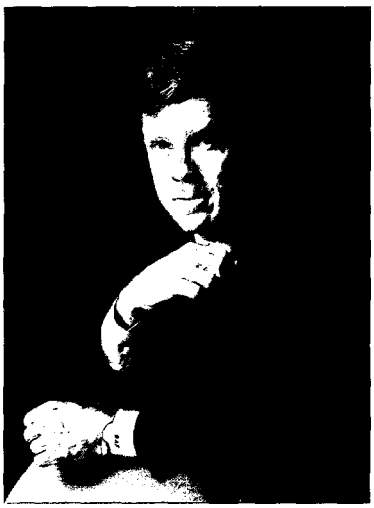
"IT IS WITH PRIDE THAT I SAY 2003 WAS A GREAT YEAR! THROUGH THE COMBINED EFFORTS AND DEDICATION OF OUR CLINICAL RESEARCH TEAM AND OUR ONGOING RELATIONSHIPS WITH PHYSICIANS IN THE SURGICAL COMMUNITY, WE REACHED OUR PROGRAM ENROLLMENT MILESTONES, AND NOW, ALL FOUR OF OUR PHASE 3 STUDIES OF ENTEREG™ (ALVIMOPAN) FOR POSTOPERATIVE ILEUS ARE COMPLETE.

ENTEREG™ IS AN EXCITING POTENTIAL THERAPEUTIC ADVANCEMENT. WE WILL WORK DILIGENTLY TO CONTINUE OUR GOAL-ACHIEVING MOMENTUM AS WE PREPARE TO SUBMIT THE NEW DRUG APPLICATION AND FURTHER EXPLORE CLINICAL APPLICATIONS FOR ENTEREG™ IN SURGICAL AS WELL AS NON-SURGICAL SETTINGS."

Bruce Wallin, M.D.
Vice President, Clinical Research and Development

"Project Management of the shared resources and creative perspectives of our multidisciplinary teams and those of our global partner, GlaxoSmithKline, created the opportunity to expand our research activities outside of the U.S. and established a close working relationship that enhances our ability to achieve our ambitious product development goals."

Carrie Frey
Vice President, Project Management



Dear Stockholders:

The annual report is the Company's "report card" to its stockholders for the year, and our report for 2003 profiles a year of hard work, accomplishment and evolution for Adolor. In last year's letter to you, I set out the following five priority goals for Adolor for 2003:

- Complete accrual in Entereg™ (alvimopan) clinical studies 308 and 313 and announce results from those two studies and from study 302. All three studies were designed to investigate the use of Entereg™ in the management of postoperative ileus (POI);
- Submit to the FDA a new drug application for Entereg™ in the management of postoperative ileus;
- Initiate Entereg™ clinical studies outside the United States;
- Advance our programs to discover and develop novel pain treatment products, including initiation of further clinical studies of our compounds directed at the kappa receptor; and
- Evaluate in-licensing opportunities and add to our product portfolio.

Taking each one of these goals in turn:

- In 2003 we completed accrual in studies 308 and 313 and we announced top-line results from study 313 as well as from studies 302 and 306. We announced top-line results from study 308 early in 2004. The completion of these four Phase 3 studies of Entereg™ is an important milestone in Adolor's evolution and the result of a significant effort by the study investigators, Adolor employees, and our collaborator, GlaxoSmithKline (Glaxo).

- We did not achieve our goal of submitting a new drug application, or NDA, for Entereg™ in 2003. We strive to achieve all of our goals within their targeted timeframe. In May of 2003, however, we made a decision to increase the number of subjects to be enrolled in both study 313 and study 308. This decision pushed back the completion of enrollment in both studies and re-set our target timeline for the submission of the NDA. We believe that the results from the expanded studies 313 and 308, in combination with the other Phase 3 studies, 302 and 306, are an important component of a package of information about the use of Entereg™ in postoperative ileus and support the submission of a new drug application to the FDA. Making the NDA submission is one of our key goals in 2004.

- Entereg™ is in clinical testing outside the United States. Glaxo initiated a Phase 3 clinical study evaluating Entereg™ in POI in Europe in 2003. Also in 2003, Glaxo initiated enrollment of subjects in Europe as part of their Phase 2b clinical trial program evaluating Entereg™ in patients who treat their chronic pain with opioid analgesics and who suffer from opioid bowel dysfunction.

- In April of 2003 we initiated further clinical testing of our kappa compounds. However, we terminated the studies early following an assessment of the data generated which indicated that the balance between therapeutic effect and safety did not warrant continuing the studies. We are continuing our discovery efforts to develop other kappa compounds, and we also have efforts underway exploring compounds targeted at the delta opioid receptor.

- We added to our product portfolio by in-licensing a sterile lidocaine patch for treating post surgery incisional pain. The acquisition of this analgesic patch adds a Phase 2 product candidate to our pipeline. This proprietary product candidate combines a well-known anesthetic with a unique, sterile delivery system. This is an investigational product candidate that, if approved, may be marketed to surgeons, a target physician group compatible with our plans for building a United States hospital-based sales force.

- In addition to the progress against the five priority goals highlighted above, we completed a successful financing in November of last year which provided net proceeds of $112 million from the sale of 6.9 million shares of our common stock.

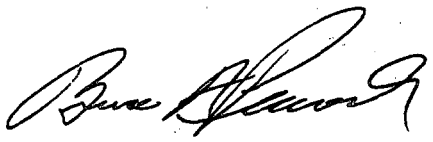
We also continued to develop our organizational capabilities with the addition of: David Christ, Ph.D., Vice President, Preclinical Development; Stephen Kutz, Ph.D., Senior Director, Safety Assessment; Kevin Robinson, Controller; Denise Kerton, Vice President, Human Resources, and Robert Jones, Vice President, Finance. In addition, we were also pleased to promote Amy Romero to Vice President, Marketing and David Stephon to Vice President, Quality Assurance. August of 2003 marked the retirement of Peter Schied who served as Adolor's first Chief Financial Officer and was instrumental in the Company's successful initial public offering and its progress and growth. Michael Dougherty now serves as the Company's Senior Vice President, Chief Operating Officer and Chief Financial Officer.

We welcomed Donald Nickelson, Vice Chairman of Harbour Group Industries, Inc., George Hager, Jr., Chairman and Chief Executive Officer of Genesis HealthCare Corporation, and Armando Anido, Senior Vice President, Sales and Marketing of MedImmune, to our Board of Directors. Each brings knowledge and commercial experience to the Board and they will be a valuable resource as the Company's operations evolve. Finally, what the Company was able to achieve in 2003 and throughout its history would not have been possible without the dedicated efforts of Ellen Feeney who retired in August as a member of the Board of Directors after 9 years of service. I thank her for her valuable insight, service and support.

In 2004 we will endeavor to build upon our progress in 2003. Our goals for 2004 include:

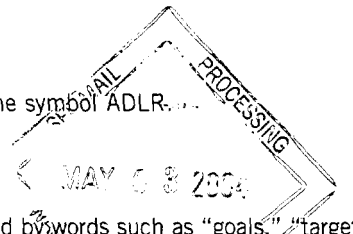
- Submitting to the FDA a new drug application for Entereg™ in POI;
- Initiating additional clinical studies of Entereg™ in a variety of other potential areas of utility;
- Supporting Glaxo in their clinical development efforts evaluating Entereg™ in POI in Europe as well as in their Phase 2 OBD and chronic constipation studies;
- Initiating Phase 2 clinical studies of our sterile lidocaine patch; and
- Identifying a compound from our discovery research efforts to be moved into development in 2005.

We will work diligently to achieve our goals and create value for our stockholders. Our mission at Adolor is to make a positive difference for patients, caregivers and the medical community by applying our knowledge and expertise in pain management. I thank you for your confidence and continued support.



Bruce A. Peacock
President and Chief Executive Officer

STOCKHOLDER INFORMATION



ADOLOR COMMON STOCK LISTING

Common Stock is traded on the NASDAQ National Market ® under the symbol ADLR.

FORWARD LOOKING STATEMENT

Forward-looking statements made in this Annual Report can be identified by words such as "goals," "targets," "plans," "expectations" and others. Our forward-looking statements 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. Further information about these and other relevant risks and uncertainties may be found in Adolor's filings with the Securities and Exchange Commission, available in its EDGAR database at http://www.sec.gov and from Adolor. Given the uncertainties affecting pharmaceutical companies in the development stage, you are cautioned not to place undue reliance on any such forward-looking statements, any of which may turn out to be wrong due to inaccurate assumptions, unknown risks, uncertainties or other factors. Adolor undertakes no obligation to publicly update or revise the statements made herein or the risks factors that may relate thereto.

FORM 10-K

A copy of Adolor's Annual Report on Form 10-K for fiscal year ended December 31, 2003 is included with this Annual Report. A copy of Adolor's Annual Report on Form 10-K, filed with the Securities and Exchange Commission, is available without charge. Please contact: Adolor Corporation, Investor Relations, 700 Pennsylvania Drive, Exton, PA 19341.

ANNUAL STOCKHOLDERS MEETING

The annual meeting of stockholders will be held at 9:00 a.m. on Thursday, May 13, 2004, at the Inn at Chester Springs Conference Center, Exton PA.

REGISTRAR AND TRANSFER AGENT

StockTrans
44 West Lancaster Avenue
Ardmore, PA 19003

COMPANY COUNSEL

Dechert LLP
Philadelphia, PA

AUDITORS

KPMG LLP
Philadelphia, PA

INVESTOR RELATIONS

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

OFFICERS

Bruce A. Peacock
President and Chief Executive Officer

Michael R. Dougherty
Senior Vice President, Chief Operating Officer and Chief Financial Officer

David Jackson, M.D.
Senior Vice President, Research and Development

Martha E. Manning, Esquire
Senior Vice President, General Counsel and Secretary

David D. Christ, Ph.D.
Vice President, Preclinical Development

Wei Du, Ph.D.
Vice President, Biometrics

Carrie Frey
Vice President, Project Management

Deanne Garver, Ph.D.
Vice President, Discovery Research

Linda Y. Harver, J.D.
Vice President, Regulatory Affairs

Robert B. Jones
Vice President, Finance

Denise B. Kerton
Vice President, Human Resources

Gwen A. Melincoff
Vice President, Business Development

Amy Romero
Vice President, Marketing

William K. Schmidt, Ph.D.
Vice President, Scientific Affairs

David M. Stephon
Vice President, Quality Assurance

Bruce Wallin, M.D.
Vice President, Clinical Research and Development

CORPORATE HEADQUARTERS

Adolor Corporation
700 Pennsylvania Drive
Exton, PA 19341

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

BOARD OF DIRECTORS

Back row left to right: Robert Nelsen, David Madden, Bruce A. Peacock, George V. Hager, Jr.
Middle row left to right: Donald E. Nickelson, Armando Anido
Seated left to right: Claude Nash, Ph.D., Paul Goddard, Ph.D.

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 Fiscal Year Ended December 31, 2003

OR

☐ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

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: None

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

(Title of class)	(Name of each exchange on which registered)
Common Stock, $0.0001 par value	NASDAQ National Market
Series A Junior Participating Preferred Stock Purchase Rights	Not applicable

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 an accelerated filer (as defined in Rule 12b-2 of the Act). Yes ☑ No ☐

The approximate aggregate market value of Common Stock held by non-affiliates of the registrant was $640,451,152 as of November 12, 2003, the most recent date at which common stock of the Company was issued to the public. (For purposes of determining this amount only, the registrant has defined affiliates as including (a) the executive officers of the registrant as of November 12, 2003, (b) all directors of the registrant as of November 12, 2003 and (c) each stockholder that informed the registrant that as of November 12, 2003 it was the beneficial owner of 10% or more of the outstanding common stock of the registrant.)

The number of shares of the registrant's Common Stock outstanding as of February 27, 2004 was 38,796,226 shares.

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, 2003 are incorporated by reference into Part III of this Report.

ADOLOR CORPORATION

FORM 10-K

December 31, 2003

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PART I

ITEM 1. BUSINESS

Forward-Looking Statements

Various statements made in this Annual Report on Form 10-K are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements include those which express plan, anticipation, intent, contingency, goals, targets or future development and/or otherwise are not statements of historical fact. We have based these forward-looking statements on our current expectations and projections about future events and they are subject to risks and uncertainties known and unknown which could cause actual results and developments to differ materially from those expressed or implied in such statements. These forward-looking statements include statements about the following:

- our product development efforts, including results from clinical trials;
- anticipated dates of clinical trial initiation, completion and announcement of trial results;
- anticipated trial results and regulatory filing dates for our product candidates;
- the status and anticipated timing of regulatory approval, if any, for our product candidates;
- analysis and interpretation of data by regulatory authorities;
- anticipated operating losses and capital expenditures;
- our intentions regarding the establishment of collaborations;
- anticipated efforts of our collaborators;
- estimates of the market opportunity and the commercialization plans for our product candidates, including our plans for the development of a sales force;
- our intention to rely on third parties for manufacturing;
- our ability to raise additional capital; and
- our ability to acquire or in-license products or product candidates.

In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "could," "would," "expect," "plan," "anticipate," "believe," "estimate," "target," "goal," "continue," or the negative of such terms or other similar expressions. Factors that might cause or contribute to differences include, but are not limited to, those discussed elsewhere in this Report in sections entitled "Business" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," (including a subsection thereof entitled "Certain Risks Related to our Business") and discussed in our other Securities and Exchange Commission (SEC) filings.

We urge you to carefully review and consider the disclosures found in these filings, all of which are available in the SEC EDGAR database at www.sec.gov. Given the uncertainties affecting pharmaceutical companies in the development stage, you are cautioned not to place undue reliance on any such forward-looking statements, any of which may turn out to be wrong due to inaccurate assumptions, unknown risks, uncertainties or other factors. We undertake no obligation to (and expressly disclaim any such obligation to) publicly update or revise the statements made herein or the risk factors that may relate thereto whether as a result of new information, future events or otherwise.

The following discussions should be read in conjunction with our audited Consolidated Financial Statements and related Notes thereto included elsewhere in this Report and the sections of this Report entitled "Management's Discussion and Analysis of Financial Condition and Results of Operation," (including a subsection thereof entitled "Certain Risks Related to our Business").

Our Company

We are a biopharmaceutical corporation formed in 1993 specializing in the discovery, development and commercialization of prescription pain management products. Entereg™ (alvimopan), our lead product candidate, is being developed to manage postoperative ileus ("POI"), the gastrointestinal ("GI") side effect which can affect millions of patients following many types of surgery. Entereg™ is currently being evaluated as an oral dosage form in patients undergoing certain types of major abdominal surgery. Entereg™ is also being developed to manage the opioid bowel dysfunction ("OBD") which can negatively impact the quality of life for millions of patients using opioid analgesic products, such as morphine, for treating pain. While there are products which are used to attempt to treat certain of the symptoms of POI and OBD, currently, there are no products that are approved by the U.S. Food and Drug Administration ("FDA") for these indications. Entereg™ is also being evaluated as a treatment for chronic constipation. We are collaborating with GlaxoSmithKline ("Glaxo") for the global development and commercialization of Entereg™. Our next product candidate is a sterile lidocaine patch in clinical development for treating postoperative incisional pain. We also have a number of discovery research programs focused on the identification of novel compounds for the treatment of pain.

Entereg™ (alvimopan)

Opioid analgesics produce pain relief by blocking pain signals through stimulation of opioid receptors located on the surface of nerves that transmit pain signals. Because there are opioid receptors present in the GI tract, opioid analgesics can disrupt normal GI function that allows for the passage, absorption and expulsion of ingested solid materials through the GI tract and, consequently, can cause patients to experience significant discomfort and pain. Entereg™ is a small molecule, peripherally-acting mu opioid receptor antagonist designed to block the adverse side effects of opioid analgesics on the GI tract without blocking their beneficial analgesic effects.

In April 2002, we entered into a collaboration agreement with Glaxo for the exclusive worldwide development and commercialization of Entereg™ for certain indications. The companies have agreed to co-develop Entereg™ for a number of acute and chronic indications, which would potentially involve the use of Entereg™ in in-patient and out-patient settings. We have overall responsibility for development activities for acute-care indications such as POI, and Glaxo has overall responsibility for development activities for chronic care indications such as OBD. In the United States, we and Glaxo intend to co-promote Entereg™ and share commercial returns, if any, pursuant to contractually agreed percentages. Outside the United States, Glaxo will be responsible for the development and commercialization of Entereg™, and we will receive royalties on sales revenues, if any. Under the terms of the collaboration agreement, Glaxo paid us a non-refundable and non-creditable signing fee of $50.0 million during the quarter ended June 30, 2002, and we may receive milestone payments of up to $220.0 million over the term of the agreement based upon the successful achievement, if any, of certain clinical and regulatory objectives.

POI Clinical Development Program

Our Entereg™ POI Phase III clinical program included four studies which have been completed. Three of these studies (POI 14CL302, POI 14CL308 and POI 14CL313) were double-blind, placebo-controlled multi-center studies each designed to enroll patients scheduled to undergo certain types of major abdominal surgery

and receiving opioids for pain relief. Under the protocols, patients were randomized into three arms to receive placebo, 6 mg or 12 mg doses of Entereg™. The primary endpoint in these three efficacy studies was time to recovery of GI function, a composite measure of the time to recovery of both upper and lower GI function, as defined by time to tolerability of solid foods and time to first flatus or first bowel movement, whichever occurred last. The fourth POI clinical study in our Phase III program, POI 14CL306, was a double-blind, placebo-controlled multi-center observational safety study under which patients were randomized to receive either Entereg™ 12 mg (413 patients) or placebo (106 patients). The four Phase III clinical trials enrolled over 2,100 patients in total. We are targeting submitting a New Drug Application ("NDA") for Entereg™ late in the first half of 2004. The FDA has designated Entereg™ as a Fast Track product for the management of POI. The Fast Track Programs of the FDA are designed to facilitate the development and expedite the review of new drugs that are intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs.

Study 302. In April 2003, we announced top-line results of our first POI Phase III clinical study, POI 14CL302. Study 302 enrolled 451 patients, and was designed to include large bowel resection patients and radical hysterectomy patients, as well as simple hysterectomy patients (22% of enrolled patients). A statistically significant difference was achieved in the primary endpoint of the study, time to recovery of GI function, in patients in the Entereg™ 6 mg treatment group compared to patients in the placebo group (Cox proportional hazard model, hazard ratio = 1.44; P<0.01). A difference in favor of the Entereg™ 6 mg treatment group versus placebo was observed for all secondary endpoints, including time to hospital discharge order written. A positive trend was observed in the primary endpoint of the study for the Entereg™ 12 mg treatment group; however, the difference from placebo was not statistically significant (Cox proportional hazard model, hazard ratio = 1.23; P = 0.059). The most frequently observed adverse events in both the placebo and treatment groups were nausea, vomiting and abdominal dystension.

The hazard ratio measures the degree of difference between the study drug group and the placebo group. A hazard ratio of 1 would indicate no difference between the study drug group and the placebo group in achieving the endpoint. A hazard ratio of 1.5 means that, on the average during the course of the data collection period, the subjects receiving test drug are 50% more likely to achieve the endpoint. Statistical analyses estimate the probability that a positive effect is actually produced by the drug. This probability is expressed as a "P value" which refers to the likelihood that the difference measured between the drug group and the placebo group occurred just "by chance". For example, when a P value is reported as p<0.05, the probability that the drug produced an effect "by chance" is less than 5%.

Study 313. In September 2003, we announced top-line results of our second POI Phase III clinical study, POI 14CL313. Study 313 enrolled 510 patients and was designed to include large bowel resection patients, small bowel resection patients and radical hysterectomy patients, and exclude simple hysterectomy patients. A statistically significant difference was achieved in the primary endpoint of the study, time to recovery of GI function, in both the Entereg™ 6 mg and 12 mg treatment groups compared to the placebo group (Cox proportional hazard model; for 6 mg group, hazard ratio = 1.28; P < 0.05; for 12 mg group, hazard ratio = 1.54; P < 0.01). A difference in favor of Entereg™ was observed for all of the secondary endpoints in both the 6 mg and 12 mg treatment groups, including time to hospital discharge order written. The most frequently observed adverse events in both the placebo and treatment groups were nausea, vomiting and hypotension.

Study 308. In January 2004, we announced top-line results of our fourth POI Phase III clinical study, POI 14CL308. Study 308 enrolled 666 patients, and was designed to include large bowel resection patients, small bowel resection patients and radical hysterectomy patients, as well as simple hysterectomy patients (14% of enrolled patients). A positive trend was observed in the primary endpoint of the study when each of the Entereg™ 6 mg and 12 mg treatment groups were compared to placebo group (Cox proportional hazard model: for 6 mg group, hazard ratio = 1.20, P=0.08; for 12 mg group, hazard ratio = 1.24, P=0.038). Due to the multiple dose comparison to a single placebo group a P-value of less than 0.025 would be required in the 12 mg dose group to be considered statistically significant. A difference in favor of Entereg™ was observed for all of the secondary endpoints in both the 6 mg and 12 mg treatment groups. The most frequently observed adverse events in both the placebo and treatment groups were nausea, vomiting and pruritis.

Study 306. In October 2003, we announced top-line results of our third POI Phase III clinical study, POI 14CL306, which enrolled 519 patients. This study was designed to assess safety as its primary objective, and to

assess efficacy as a secondary objective and to enroll only patients scheduled to undergo simple hysterectomy procedures. Study 306 was the first study where dosing continued on an out-patient basis after patients were discharged from the hospital. Entereg was generally well tolerated in this observational safety study with 93% of patients completing treatment in the Entereg™ 12 mg treatment group and 92% of patients completing treatment in the placebo group. The most frequently observed adverse events in both the placebo and treatment groups were nausea, vomiting and constipation.

OBD and Chronic Constipation Clinical Development Program

In November 2002, we announced top-line results of Study 304 of Entereg™ in opioid bowel dysfunction patients. This outpatient study enrolled 168 patients who were chronic users of opioids, such as morphine and codeine, primarily for pain relief, and whose bowel function had been impaired as a result of opioid treatment. The patients received once daily dosing for 21 days of either a 0.5 mg or 1 mg dose of Entereg™ or placebo. The primary endpoint of the study was the proportion of patients having a bowel movement within 8 hours after each dose of study medication during the 21-day treatment period. On average, the proportion of patients who had at least one bowel movement within 8 hours of each dose during the 21-day treatment period was 43% for the Entereg™ 0.5 mg group, 55% for the Entereg™ 1 mg group and 29% for the placebo group. In this study Entereg™ was generally well tolerated; the most frequently occurring adverse events versus placebo included diarrhea, abdominal cramps, nausea and vomiting.

Based on the results of this study, our development and commercialization partner for Entereg™, Glaxo, is currently conducting additional Phase II clinical trials investigating longer duration of patient exposure and different dosing strategies in both cancer and non-cancer pain patients.

Glaxo is also conducting early stage studies evaluating Entereg™ in chronic constipation.

Sterile Patch Program (ADL 8-7223)

In July 2003, we entered into an agreement with EpiCept Corporation ("EpiCept") under which we licensed exclusive rights to develop and commercialize in North America a sterile lidocaine patch which is being developed for the management of postoperative incisional pain. A clinical study of this sterile lidocaine patch was previously conducted by EpiCept in Germany and enrolled 215 hospitalized patients undergoing hernia repair. Patients were randomized to receive a patch containing one of two doses of lidocaine or a placebo patch. The surgeons placed the sterile patch over the sutured incision at the end of the procedure and recorded pain scores from 2 to 48 hours. A 27% reduction in post-incisional pain was observed in patients receiving the higher dose lidocaine patch vs. patients receiving a placebo patch. We are targeting further evaluation of this product in Phase II clinical trials in 2004.

Discovery

We maintain an internal discovery research effort directed toward the development of compounds designed to elicit potential analgesic effects by targeting peripheral and central opioid receptors, including the delta, kappa and mu receptors. Additionally, we are exploring the development of an analgesic product candidate that would be a combination of Entereg™ and an opioid that would be intended to produce the pain relief of an opioid while reducing side effects, such as constipation, nausea and vomiting.

Competitive Environment

We operate in a highly regulated and competitive environment. 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.

Commercialization

We have 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 are currently negotiating commercial supply agreements with certain of these third party manufacturers. We presently do not maintain our own manufacturing facilities.

We have a small marketing organization to support our development efforts. We plan to build a sales force in the United States and expand our marketing organization to co-promote Entereg™ along with Glaxo in hospital-care settings, if regulatory approval is received. We intend to rely on Glaxo for sales and marketing of Entereg™ outside the United States. As we develop additional product candidates we may enter into strategic marketing or copromotion agreements with, and grant additional licenses to, pharmaceutical companies to gain access to additional markets both domestically and internationally.

Our Strategy

Our goal is to build a profitable pharmaceutical company specializing in the discovery, development and commercialization of prescription pain management products. We plan to pursue this objective by implementing the following strategies:

Focusing our Discovery Efforts On Opioid Receptors in Pain Management. We focus our discovery efforts principally on clinical conditions that can be treated by either stimulating or blocking opioid receptors. These conditions include postoperative ileus and chronic opioid bowel dysfunction, as well as various pain conditions, including inflammatory pain, itch and visceral pain. We have biological and chemical expertise to support drug discovery, including expertise in opioid receptors in analgesic pathways, cloned human opioid, orphan and chimeric receptors and the chemical synthesis of compounds that do not readily cross the blood-brain barrier.

Implementing a Strategy that will Combine Marketing and Product Development and Marketing Alliances with our internal Product Development and Marketing Efforts. We have built certain capabilities in discovery, development and commercialization in advancing our product candidates. In addition, we have established and will continue selectively to establish collaborations with pharmaceutical companies and leading academic institutions to enhance our internal capabilities.

Implementing an In-Licensing/Acquisition Strategy. We believe there are opportunities to expand our product portfolios by the acquisition or in-licensing of products and/or product development candidates to complement our internal development efforts. We intend to explore in-licensing or acquisition of products or product candidates or technology, as well as acquisition of companies.

Background On Opioid Analgesia

Pain Transmission Signals. When tissues such as the skin, muscles and joints become inflamed or are injured, pain receptors in those tissues are activated, and electrical pain signals are transmitted from the injured tissues through nerve fibers into the spinal cord. Within the spinal cord, the electrical pain signals are received by a second set of nerve fibers that continue the transmission of the signal up the spinal cord and into the brain. Within the brain, additional nerve fibers transmit the electrical signals to the "pain centers" of the brain where these signals are perceived as pain. Pain receptors are also present in internal, or visceral, organs such as the intestines, uterus, cervix and bladder. These pain receptors also send pain signals via similar pathways to the brain when these organs are inflamed or distended.

Opioid Receptors Block Pain Transmission Signals. Opioid receptors located on the surface of nerves that transmit pain signals block transmission of pain when activated by drugs specific for those receptors. There are three types of opioid receptors, *mu*, *kappa* and *delta*, each of which produces analgesia when activated. Virtually all marketed opioid analgesic drugs interact with *mu* opioid receptors in the brain and spinal cord. When these central nervous system *mu* opioid receptors are activated with opioid analgesics such as morphine, the perception of pain is reduced. However, activating these opioid receptors in the brain with morphine-like opioid analgesics often results in serious side effects such as sedation, decreased respiratory function and addiction. Because of the

potential to cause addiction, 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.

Our Approach To Pain Management

Peripheral Opioid Analgesia. Scientists have shown that opioid receptors are present on nerve endings in the skin, joints, eyes and visceral organs. Activation of these opioid receptors, which are outside of the central nervous system, with opioid analgesics reduces pain related to injury or inflammation by decreasing pain signal transmission from the peripheral nerves into the spinal cord. Proof-of-concept studies in animals and humans have shown that small doses of morphine, applied locally to inflamed tissues such as skin, joints and eyes are effective in reducing pain.

These findings have created the opportunity for us to potentially develop an entirely new class of analgesics that may selectively stimulate opioid receptors in inflamed tissues but not stimulate opioid receptors in the central nervous system thereby avoiding the central nervous system side effects of opioids. These pain medications are called peripheral analgesics. In preclinical studies, our peripheral *mu* opioid analgesics demonstrated positive results and our peripheral *kappa* opioid analgesics demonstrated positive results in blocking the visceral pain originating from internal organs such as the bowel and cervix. Because our peripheral analgesics are designed to have limited ability to cross the blood-brain barrier at therapeutic doses, they have the potential not to cause addiction or other adverse central nervous system side effects, such as sedation or decreased respiratory function or addiction. As a result, we expect that these analgesics may not be subject to United States Drug Enforcement Administration regulation under the Controlled Substances Act.

Peripheral Opioid Receptors in the GI Tract. Just as there are opioid receptors on peripheral nerves that regulate the transmission of pain signals into the spinal cord, there are also opioid receptors in the gastrointestinal tract that regulate functions such as motility and water secretion and absorption. Stimulation of these gastrointestinal *mu* opioid receptors by morphine or other opioid analgesics causes constipation associated with opioid bowel dysfunction. Scientists have shown that blocking these receptors with opioid receptor antagonist drugs during administration of morphine or other opioid analgesics may prevent or reverse the effects of opioid bowel dysfunction. However, currently marketed opioid receptor antagonist drugs also cross the blood-brain barrier and enter the brain where they can block the primary pain relieving effects of opioid analgesics such as morphine. These findings have created the opportunity to develop a new class of opioid antagonists which, when taken with opioid analgesics, are designed to block the side effects of the opioid analgesics on the GI tract but not the desired analgesic activity of opioid drugs because they are designed not to cross the blood-brain barrier.

Glaxo Collaboration

In April 2002, we entered into a collaboration agreement with Glaxo for the exclusive worldwide development and commercialization of Entereg™ for certain indications. Under the terms of the collaboration agreement, Glaxo paid us a non-refundable and non-creditable signing fee of $50.0 million during the quarter ended June 30, 2002. We may receive milestone payments of up to $220.0 million over the term of the agreement upon the successful achievement, if any, of certain clinical and regulatory objectives. The milestone payments relate to substantive achievements in the development lifecycle and it is anticipated that these will be recognized as revenue if and when the milestones are achieved.

We and Glaxo have agreed to develop Entereg™ for a number of acute and chronic indications which would potentially involve the use of Entereg™ in in-patient and out-patient settings. In the United States, we have the right to co-develop and co-promote Entereg™ with Glaxo, and share development expenses and commercial returns, if any, pursuant to contractually agreed percentages. We have overall responsibility for development activities for acute care indications such as POI, and Glaxo has overall responsibility for development activities for chronic care indications such as OBD. Outside the United States, Glaxo will be responsible for the development and commercialization of Entereg™ for all indications, and we will receive royalties on sales revenues, if any.

The term of the collaboration agreement varies depending on the indication and the territory. 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, if any. Generally the term for the OBD indication in the United States is fifteen years from the first commercial sale of Entereg™ in that indication, if any. In the rest of the world, the term is generally fifteen years from the first commercial sale of Entereg™, if any, on a country-by-country and indication-by-indication basis.

Glaxo has certain rights to terminate the collaboration agreement. Glaxo also has the right to terminate its rights and obligations with respect to the acute-care indications, or its rights and obligations for the chronic-care indications. Glaxo 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. Glaxo's rights to terminate the acute-care indications or the chronic-care indications are generally triggered by failure to achieve certain milestones within certain timeframes, adverse product developments or adverse regulatory events. If Glaxo terminates the collaboration agreement, we may not be able to find a new collaborator to replace Glaxo, and our business will be adversely affected.

License Agreements

In November 1996, Roberts Laboratories Inc. ("Roberts") licensed from 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 licensed from Roberts the rights Roberts had licensed from Eli Lilly for Entereg™. Under our Option and License Agreement we have paid $600,000 to Roberts. Under our Option and License Agreement we are obligated to pay milestone payments to Roberts and Eli Lilly upon the achievement of certain clinical and regulatory milestones that in the aggregate may total up to $1.9 million. We are also responsible for the costs to develop Entereg™. In addition, if Entereg™ receives regulatory approval, we are obligated to pay royalties to Roberts and Eli Lilly on commercial sales of Entereg™. Under the terms of our arrangements, the license to Entereg™ expires on the later of either the life of the last to expire of the licensed Eli Lilly patents or fifteen years from November 5, 1996, following which we will have a fully paid up license.

In August 2002, we expanded our intellectual property rights related to Entereg™ by entering into a separate exclusive license agreement with Eli Lilly under which we obtained an exclusive license to six issued U.S. patents and related foreign equivalents and know-how relating to peripherally selective opioid antagonists. We paid Eli Lilly $4.0 million upon signing the agreement and are 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, we agreed to pay Eli Lilly a $4.0 million payment upon acceptance by a regulatory authority of the first application for marketing authorization for Entereg™.

We are a party to various license agreements that give us rights to use technologies and biological materials in our research and development processes. We may not be able to maintain such rights on commercially reasonable terms, if at all. Failure by us or our licensors to maintain such rights could harm our business.

Intellectual Property

We seek United States and international patent protection for important and strategic components of our technology. 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 commercial 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.

We have rights to patents related to Entereg™ which expire between 2011 and 2019 and include a U.S. patent claiming composition of matter which expires in 2011, which may be eligible for patent term extension. If

we are granted a patent term extension for an Entereg™ patent, such patent term extension may only provide limited proprietary protection during the period of extension. We also have U.S. patents claiming the use of Entereg™ in postoperative ileus and the combination of Entereg™ plus an opioid agonist, both of these patents expire in 2019. These expiration dates are all based on the presumption that the applicable maintenance fees are paid and the patents, if challenged, are not held to be invalid. We have licensed rights to patents and patent applications relating to the sterile lidocaine patch. There is no assurance that any patents we have licensed will provide any meaningful proprietary protection for the sterile lidocaine patch.

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

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

In addition, patent law relating to the scope of claims in the technology 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.

Enactment of legislation implementing the General Agreement on Tariffs and Trade has resulted in certain changes to United States patent laws that became effective on June 8, 1995. Most notably, the term of patent protection for patent applications filed on or after June 8, 1995 is no longer a period of 17 years from the date of issuance. The new term of United States patents will commence on the date of issuance and terminate 20 years from the earliest effective filing date of the application. Because the time from filing to issuance of biotechnology patent applications is often more than three years, a 20-year term from the effective date of filing may result in a substantially shortened period of patent protection which may harm our patent position.

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.

Government Regulation

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 approvals 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 products will receive FDA approval.

The drug approval process:

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 Investigational New Drug application (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;
- submission to the FDA of a New Drug Application (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 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 I: The drug is initially introduced into healthy human subjects or patients and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In addition, it is sometimes possible to assess efficacy in Phase I trials for analgesia.
- Phase II: This phase involves studies in a limited patient population to identify possible adverse effects and safety risks, to determine the efficacy of the product for specific targeted diseases and to determine optimal dosage and tolerance.
- Phase III: When Phase II evaluations demonstrate that a dosage range of the product is effective and has an acceptable safety profile, Phase III trials are undertaken to further evaluate dosage, clinical efficacy and to further test for safety in an expanded patient population at geographically dispersed clinical study sites.

Other regulatory requirements

The FDA mandates that drugs be manufactured in conformity with cGMP regulations and at facilities approved to manufacture such drugs. In addition, if approval is granted, FDA requirements for labeling, advertising, record keeping and adverse experience reporting will apply. Failure to comply with these requirements could result, among other things, in suspension of marketing approval, recalls, injunctions or civil or criminal sanctions.

In addition, if our products are approved for marketing by FDA, we will be required to comply with several other types of state and federal laws applicable to pharmaceutical marketing. These laws include antikickback statutes and false claims statutes. Additionally, we may also be subject to regulations under other federal, state, and local laws, including the Occupational Safety and Health Act, the Environmental Protection Act, the Clean Air Act, national restrictions on technology transfer, import, export, and customs regulations.

Whether or not FDA approval has been obtained, approvals of comparable governmental regulatory authorities in foreign countries must be obtained prior to the commencement of clinical trials and subsequent sales and marketing efforts in those countries. The approval procedure varies in complexity from country to country, and the time required may be longer or shorter than that required for FDA approval.

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, if any, applicable to a product is its actual or potential abuse profile. A pharmaceutical product may be "scheduled" 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 to cause addiction, drugs that are able to activate *mu* opiod receptors in the brain (morphine-like opioid analgesics) are regulated, or scheduled, under the Controlled Substances Act. Any of our products that contain one of our product candidates in combination with narcotic analgesics will be subject to such regulation.

Available Information

We make available free of charge on or through our internet website at www.adolor.com, our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to these reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

Employees

As of December 31, 2003, we had 126 full-time employees and 2 part-time employees, including 27 employees with Ph.D. or M.D. degrees. Eighty-eight of our employees are engaged in research and development activities. Most of our senior management and professional employees have had prior experience in pharmaceutical or biotechnology companies. None of our employees are covered by collective bargaining agreements. We believe that our relations with our employees are good.

ITEM 2. PROPERTIES

In June 2003, we consolidated operations in a building in Exton, Pennsylvania under a ten-year lease expiring in July 2013. The building has approximately 80,000 square feet of space. We have built out and occupy approximately 30,000 square feet of office space and approximately 25,000 square feet of laboratory space. The remaining approximately 25,000 square feet of space is unfinished and is available for potential future expansion. During 2003, we occupied additional space under three lease agreements. Two of these leases have expired and the third will expire in October 2004.

ITEM 3. LEGAL PROCEEDINGS

From time to time we are party to various legal proceedings in the normal course of our business. We do not believe that resolution of any of these claims will have a material negative effect on our financial condition, results of operation or liquidity.

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 fiscal year ended December 31, 2003.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY AND RELATED STOCKHOLDER MATTERS

(a) Our common stock is traded on The Nasdaq National Market under the symbol "ADLR". The initial public offering of our stock occurred on November 13, 2000 at an initial price of $15.00 per share. The price range per share reflected in the table below is the highest and lowest bid price for our stock as reported by The Nasdaq National Market during each quarter of the two most recent years that our common stock has been publicly traded.

	High	Low
2002		
First Quarter	$18.50	$11.04
Second Quarter	15.29	9.83
Third Quarter	14.64	9.09
Fourth Quarter	15.43	12.68
2003		
First Quarter	$14.32	$ 9.53
Second Quarter	20.50	9.61
Third Quarter	20.17	11.90
Fourth Quarter	21.71	17.11

In our initial public offering (the "Offering"), we sold 6,000,000 shares of common stock on November 14, 2000. Upon the exercise of the underwriter's over-allotment option, we sold an additional 900,000 shares of common stock. The effective date of the registration statement on Form S-1 for the 6,900,000 shares of common stock sold in our initial public offering was November 13, 2000 and the file number is 333-96333. The proceeds of the offering were approximately $95,376,000, net of offering costs.

As of December 31, 2002, we had used all of the Offering proceeds and applied them for general corporate purposes, including the continued development of existing product candidates, manufacturing, commercialization expenditures, research and development for additional product opportunities, hiring of sales, marketing, development, research and administrative personnel and expansion of our facilities.

In May 2001, we sold 3,000,000 shares of common stock to certain institutional investors. The proceeds of the offering were approximately $58,962,000, net of offering costs.

In November 2003 we sold 6,000,000 shares of our common stock. Upon the exercise of the underwriter's over-allotment option, we sold an additional 900,000 shares of common stock. The effective date of the registration statement on Form S-3 for the 6,900,000 shares of common stock sold in the shelf registration was October 27, 2003 and the file number is 333-107998. The proceeds of the offering were approximately $111,585,000, net of offering costs.

(b) *Holders*. As of February 27, 2004, there were approximately 179 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.

(c) *Dividends*. 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 any earnings for use in the operation of our business and to fund future growth.

ITEM 6. SELECTED FINANCIAL DATA

The following selected financial data should be read in conjunction with our consolidated financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included elsewhere in this Report. The consolidated statements of operations data except as otherwise indicated below for the five years ended December 31, 2003, and our consolidated balance sheet data as of December 31, 2003 and 2002, are derived from our audited consolidated financial statements which are included elsewhere in this Report. The consolidated statements of operations data for the years ended December 31, 2000 and 1999 and the consolidated balance sheet data as of December 31, 2001, 2000 and 1999 are derived from audited financial statements not included in this Report. Historical results are not necessarily indicative of the results to be expected in the future.

Please see Note 2 to our consolidated financial statements for an explanation of the method used to calculate the net loss allocable to common stockholders, net loss per share and the number of shares used in the computation of per share amounts.

	Years Ended December 31,				
	2003	2002	2001	2000	1999
	(In thousands, except per share data)				
Consolidated Statements of Operations					
Contract revenues	$ 20,727	$ 28,409	$ 1,387	$ 44	$ 11
Operating expenses incurred during the development stage:					
Research and development	56,654	71,705	36,005	15,884	7,398
Marketing, general and administrative	17,648	21,693	15,229	7,626	3,698
Total operating expenses	74,302	93,398	51,234	23,510	11,096
Net other income	2,369	4,465	7,440	2,228	404
Net loss	(51,206)	(60,524)	(42,407)	(21,238)	(10,681)
Undeclared dividends attributable to mandatorily redeemable convertible preferred stock	—	—	—	48,906	—
Beneficial conversion feature on mandatorily redeemable convertible preferred stock	—	—	—	4,103	2,430
Net loss allocable to common stockholders	$ (51,206)	$ (60,524)	$ (42,407)	$ (74,247)	$ (13,111)
Basic and diluted net loss per share allocable to common stockholders	$ (1.57)	$ (1.94)	$ (1.42)	$ (13.99)	$ (12.55)
Shares used in computing basic and diluted net loss per share allocable to common stockholders	32,586	31,252	29,801	5,307	1,045

	As of December 31,				
	2003	2002	2001	2000	1999
	(In thousands)				
Consolidated Balance Sheet Data					
Cash, cash equivalents and short-term investments	$ 210,174	$ 153,985	$156,444	$131,630	$ 5,264
Working capital	195,531	140,290	149,708	128,671	3,069
Total assets	224,664	168,271	164,182	135,610	6,258
Total long-term debt	—	—	—	215	—
Mandatorily redeemable convertible preferred stock	—	—	—	—	33,000
Deficit accumulated during the development stage	(206,380)	(155,174)	(94,649)	(52,242)	(31,004)
Total stockholders' equity (deficit)	165,279	100,728	152,781	129,040	(29,590)

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

Overview

We are a development stage biopharmaceutical corporation that was formed in 1993. We specialize in the discovery, development and commercialization of prescription pain management products. We have a number of small molecule product candidates that are in various stages of development ranging from preclinical studies to Phase III clinical trials. Our lead product candidate, Entereg™ (alvimopan), is designed to selectively block the unwanted effects of opioid analgesics on the gastrointestinal tract. Our other product candidates are being designed as analgesics to treat moderate-to-severe pain conditions.

We have invested a significant portion of our time and financial resources since our inception in the development of Entereg™, and our potential to achieve revenues from product sales and generate positive cash flows in the foreseeable future is dependent upon successfully commercializing Entereg™ . We have completed four Phase III clinical studies of Entereg™ for the management of postoperative ileus, and our target is to file a New Drug Application for Entereg™ late in the first half of 2004. Results from these clinical studies have not yet been reviewed by the FDA in an application for approval. FDA approval is contingent on many factors, including review and approval of our application with respect to the manufacture of our products. Even if Entereg™ is approved by the FDA, we will not be successful unless Entereg™ gains market acceptance. We do not expect to generate positive cash flows from operations for at least the next several years, if at all.

Entereg™ is being evaluated in acute and chronic indications. Our Entereg™ POI Phase III program included four studies which have been completed. Three of these studies (POI 14CL302, POI 14CL308 and POI 14CL313) were double-blind, placebo-controlled multi-center studies each designed to enroll patients scheduled to undergo certain types of major abdominal surgery and receiving opiods for pain relief. Under the protocols, patients were randomized into three arms to receive placebo, 6 mg or 12 mg doses of Entereg™. The primary endpoint in these three efficacy studies was time to recovery of GI function, a composite measure of the time to recovery of both upper and lower GI function, as defined by time to tolerability of solid foods and time to first flatus or first bowel movement, whichever occurred last. The fourth POI clinical study in our Phase III program, POI 14CL306, was a double-blind, placebo-controlled multi-center observational study under which patients were randomized to receive either Entereg™ 12 mg (413 patients) or placebo (106 patients). The four Phase III clinical trials enrolled over 2,100 patients in total. We are targeting submitting an NDA for Entereg™ late in the first half of 2004. The FDA has designated Entereg™ as a Fast Track product for the management of POI. The Fast Track Programs of the FDA are designed to facilitate the development and expedite the review of new drugs that are intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs.

In April 2003, we announced top-line results of our first POI Phase III clinical study, POI 14CL302. Study POI 14CL302 enrolled 451 patients and was designed to include large bowel resection patients and radical hysterectomy patients, as well as simple hysterectomy patients (22% of enrolled patients). A statistically significant difference was achieved in the primary endpoint of the study, time to recovery of GI function, in patients in the Entereg™ 6 mg treatment group compared to patients in the placebo group (Cox proportional hazard model, hazard ratio = 1.44; $P<0.01$). A difference in favor of the Entereg™ 6 mg treatment group versus placebo was observed for all secondary endpoints, including time to hospital discharge order written. A positive trend was observed in the primary endpoint of the study for the Entereg™ 12 mg treatment group; however, the difference from placebo was not statistically significant (Cox proportional hazard model, hazard ratio = 1.23; $P = 0.059$). The most frequently observed adverse events of both the placebo and treatment groups were nausea, vomiting and abdominal dystension.

The hazard ratio measures the degree of difference between the study drug group and the placebo group. A hazard ratio of 1 would indicate no difference between the study drug group and the placebo group in achieving the endpoint. A hazard ratio of 1.5 means that, on the average during the course of the data collection period, the subjects receiving test drug are 50% more likely to achieve the endpoint. Statistical analyses estimate the probability that a positive effect is actually produced by the drug. This probability is expressed as a "P value" which refers to the likelihood that the difference measured between the drug group and the placebo group

occurred just "by chance." For example, when a P value is reported as P<0.05, the probability that the drug produced an effect "by chance" is less than 5%.

In September 2003, we announced top-line results of our second POI Phase III clinical study, POI 14CL313. Study POI 14CL313 enrolled 510 patients and was designed to include large bowel resection patients, small bowel resection patients and radical hysterectomy patients, and exclude simple hysterectomy patients. A statistically significant difference was achieved in the primary endpoint of the study, time to recovery of gastrointestinal function, in both the Entereg™ 6 mg and 12 mg treatment groups compared to the placebo group (Cox proportional hazard model; for 6 mg group, hazard ratio = 1.28; P < 0.05; for 12 mg group, hazard ratio = 1.54; P < 0.01). A difference in favor of Entereg™ was observed for all of the secondary endpoints in both the 6 mg and 12 mg treatment groups, including time to hospital discharge order written. The most frequently observed adverse events in both the placebo and treatment groups were nausea, vomiting and hypotension.

In October 2003, we announced top-line results of our third POI Phase III clinical study, POI 14CL306, which enrolled 519 patients. This study was designed to assess safety as its primary endpoint, and to assess efficacy as a secondary endpoint and to only enroll patients scheduled to undergo simple hysterectomy procedures. Study POI 14CL306 was the first study where dosing continued on an out-patient basis after patients were discharged from the hospital. Entereg™ was generally well tolerated in this observational safety study with 93% of patients completing treatment in the Entereg™ 12 mg treatment group and 92% of patients completing treatment in the placebo group. The most frequently observed adverse events in both the placebo and treatment groups were nausea, vomiting and constipation.

In January 2004, we announced top-line results of our fourth POI Phase III clinical study, POI 14CL308. Study POI 14CL308 enrolled 666 patients, and was designed to include large bowel resection patients, small bowel resection patients and radical hysterectomy patients, as well as simple hysterectomy patients (14% of enrolled patients). A positive trend was observed in the primary endpoint of the study when each of the Entereg™ 6 mg and 12 mg treatment groups were compared to the placebo group (Cox proportional hazard model; for 6 mg group, hazard ratio = 1.20, P=0.08; for 12 mg group, hazard ratio = 1.24, P=0.038). Due to the multiple dose comparison to a single placebo group a P-value of less than 0.025 would be required in the 12 mg dose group to be considered statistically significant. A difference in favor of Entereg™ was observed for all of the secondary endpoints in both the 6 mg and 12 mg treatment groups. The most frequently observed adverse events in both the placebo and treatment groups were nausea, vomiting and pruritis.

The results of studies POI 14CL302, POI 14CL313, POI 14CL306 and POI 14CL308 have not been submitted in an application for regulatory approval, or reviewed in such an application, by the FDA or any other regulatory agency.

In April 2002, we entered into a collaboration agreement with Glaxo for the exclusive worldwide development and commercialization of Entereg™ for certain indications. The companies have agreed to co-develop Entereg™ for a number of indications, both acute and chronic, which would potentially involve the use of Entereg™ in in-patient and out-patient settings. Under the terms of the collaboration agreement, Glaxo paid us a non-refundable and non-creditable signing fee of $50.0 million during the quarter ended June 30, 2002 and we may receive milestone payments of up to $220.0 million over the term of the agreement upon the successful achievement, if any, of certain clinical and regulatory objectives.

We have also completed several clinical trials studying the use of Entereg™ for the reversal of the severe constipating effects associated with chronic use of opioids. Overall responsibility for the development of Entereg™ in chronic indications is now carried on by Glaxo. Glaxo is also conducting early stage studies evaluating Entereg™ in chronic constipation.

We believe there are opportunities to expand our product portfolio by the acquisition or in-licensing of products and/or product development candidates, and intend to explore and evaluate such opportunities.

In July 2003, we entered into an agreement with EpiCept, under which we obtained exclusive rights to develop and commercialize in North America a sterile lidocaine patch which is being developed for the

management of postoperative incisional pain. We made a $2.5 million payment to EpiCept upon execution of the agreement and may make up to $20.0 million in additional development milestone payments if certain clinical and regulatory achievements are reached.

We also have other compounds that are being designed to elicit potential analgesic effects by targeting peripheral and central opioid receptors, including the delta, kappa and mu receptors. Additionally, we are exploring the development of an analgesic product candidate that would be a combination of Entereg™ and an opioid that would be intended to produce the pain relief of an opioid while reducing side effects, such as constipation, nausea and vomiting.

We have 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 are currently negotiating commercial supply agreements with certain of these third party manufacturers. We presently do not maintain our own manufacturing facilities.

We have a small marketing organization to support our development efforts. We plan to build a sales force in the United States and expand our marketing organization to co-promote Entereg™ along with Glaxo in hospital-care settings, if regulatory approval is received. We intend to rely on Glaxo for sales and marketing of Entereg™ outside the United States. As we develop additional product candidates we may enter into strategic marketing or co-promotion agreements with, and grant additional licenses to, pharmaceutical companies to gain access to additional markets both domestically and internationally.

We have not generated any product sales revenues and have not achieved profitable operations. Our deficit accumulated during the development stage through December 31, 2003 aggregated approximately $206.4 million, and we expect to continue to incur substantial losses in future periods. A significant portion of our revenue recognized in 2003 and 2002 was from reimbursement of expenses from Glaxo under our collaboration agreement and we expect such revenues to decrease in future periods as we expect the related reimbursable expenses to decrease. We are highly dependent on the success of our research, development and licensing efforts and, ultimately, upon regulatory approval and market acceptance of our proposed future products. We may never become profitable and even if we become profitable, we may not be able to sustain profitability on a continuing basis.

We reported an operating cash outflow of $50.2 million for the year ended December 31, 2003 and we do not expect to generate a positive cash flow from operations for the next several years, if ever. Prior to exhausting our current cash and short term investments, we will need to raise additional funds to finance our operating activities. There are no assurances that we will be successful in obtaining an adequate level of financing for the long-term development and commercialization of our product candidates.

Collaboration Agreement with Glaxo

In April 2002, we entered into a collaboration agreement with Glaxo for the exclusive worldwide development and commercialization of Entereg™ for certain indications. Under the terms of the collaboration agreement, Glaxo paid us a non-refundable and non-creditable signing fee of $50.0 million during the quarter ended June 30, 2002. The $50.0 million signing fee is reflected in deferred licensing fees and is expected to be recognized on a straight-line basis through April 2014, the estimated performance period under the collaboration agreement. We recognized revenue of $4,166,675 and $2,951,394, respectively, in the years ended December 31, 2003 and 2002 related thereto. We may receive milestone payments of up to $220.0 million over the term of the agreement upon the successful achievement, if any, of certain clinical and regulatory objectives. The milestone payments relate to substantive achievements in the development lifecycle and it is anticipated that these will be recognized as revenue if and when the milestones are achieved.

We and Glaxo have agreed to develop Entereg™ for a number of acute and chronic indications which would potentially involve the use of Entereg™ in in-patient and out-patient settings. In the United States, we and Glaxo intend to co-develop and intend to co-promote Entereg™ and share development expenses and commercial returns, if any, pursuant to contractually agreed percentages. We have overall responsibility for development

activities for acute care indications such as POI, and Glaxo has overall responsibility for development activities for chronic care indications such as OBD. Outside the United States, Glaxo will be responsible for the development and commercialization of Entereg™ for all indications, and we will receive royalties on sales revenues, if any.

Glaxo has certain rights to terminate the collaboration agreement. Glaxo also has the right to terminate its rights and obligations with respect to the acute-care indications, or its rights and obligations for the chronic-care indications. Glaxo 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. Glaxo's rights to terminate the acute-care indications or the chronic-care indications are generally triggered by failure to achieve certain milestones within certain timeframes, adverse product developments or adverse regulatory events. If Glaxo terminates the collaboration agreement, we may not be able to find a new collaborator to replace Glaxo, and our business will be adversely affected.

External expenses for research and development and marketing activities incurred by each company in the United States are reimbursed by the other party pursuant to contractually agreed percentages. Contract reimbursement amounts owed to us by Glaxo are recorded gross on our consolidated statements of operations as contract reimbursement revenue. Amounts reimbursable to Glaxo by us are recorded as research and development or marketing expense, as appropriate, on our consolidated statements of operations.

We recorded contract reimbursement revenue of $16,141,916 and $24,246,332 respectively, in the years ended December 31, 2003 and 2002 under the Glaxo arrangement. These revenues represent reimbursement of expenses incurred by us primarily in our POI development program. Additionally, we incurred research and development and marketing expenses of $3,644,165 and $204,650, respectively, in the years ended December 31, 2003 and 2002, representing reimbursement by us to Glaxo of expenses incurred by Glaxo primarily in the OBD development program. We expect contract reimbursement revenues to continue to decline in future periods because we expect the costs of the POI development program to decrease. We also expect that we will incur increasing expenses in future periods in connection with the OBD development program, including payments to Glaxo to reimburse them for our proportionate share of expenses they incur.

Critical Accounting Policies and Estimates

The preparation of our consolidated financial statements in conformity with accounting principles generally accepted in the United States requires management to adopt critical accounting policies and to make estimates and assumptions that affect the amounts reported in our consolidated financial statements and accompanying notes. The principal items in our consolidated financial statements reflecting critical accounting policies or requiring significant estimates and judgments are as follows:

Stock Compensation—We apply Accounting Principal Board Opinion No. 25, "Accounting for Stock Issued to Employees," ("APB 25"), and related interpretations, in accounting for stock options granted to employees. Under APB 25, compensation cost related to stock options is computed based on the intrinsic value of the stock option at the date of grant, reflected by the difference between the exercise price and the fair market value of our Common Stock. Since our November 2000 public offering we have generally granted options to employees with exercise prices equal to fair market value on the date of grant, and for such option grants we do not record compensation expense. Under Statement of Financial Accounting Standards ("SFAS") No. 123, "Accounting for Stock-Based Compensation", compensation cost related to stock options granted to employees and non-employees is computed based on the value of the stock options at the date of grant using an option valuation methodology, typically the Black-Scholes model. SFAS No. 123 can be applied either by recording the Black-Scholes model value of the options as compensation expense or by continuing to record the APB 25 value and by disclosing SFAS No. 123 compensation costs on a pro-forma basis. Had we adopted the Black-Scholes model value provisions of SFAS No. 123, our loss in 2003, 2002, and 2001 would have been increased by approximately $5.3 million, $2.1 million, and $1.0 million, respectively.

In December 2002, the Financial Accounting Standards Board ("FASB") issued Statement No. 148, "Accounting for Stock-Based Compensation – Transition and Disclosure". This statement amends FASB

Statement No. 123, to provide alternative methods of transition for a voluntary change to the fair value based method of accounting for stock-based employee compensation. In addition, this statement amended the disclosure requirements of SFAS No. 123 to require prominent disclosures in both annual and interim financial statements about the method of accounting for stock-based employee compensation and the effect of the method used on reported results. The disclosure requirements of Statement No. 148, which were effective for financial statements issued after December 15, 2002, have been incorporated herein.

Collaborative Agreement Revenues—We record deferred revenue for amounts received upfront under collaboration agreements in which we have continuing involvement, and we recognize such deferred amounts as revenue ratably over the estimated contract performance period. Such revenue recognition may be accelerated in the event of contract termination prior to completion of the expected performance period. Under the terms of the collaboration agreement with Glaxo we received a non-refundable and non-creditable upfront fee of $50.0 million and, in 2003, approximately $4.2 million of the $50.0 million up-front fee was recognized as revenue. We expect to recognize approximately $4.2 million per year as revenue through 2014, the estimated contract performance period.

Milestone fees are recorded as revenue when the milestone event is achieved.

Amounts reimbursable for costs incurred pursuant to the terms of collaboration agreements are recognized as revenue in the period in which the reimbursable costs are incurred. Such revenues are based on estimates of the reimbursable amount and are subject to verification by the collaborators. The $3.1 million of accounts receivable from Glaxo at December 31, 2003 is related to estimated reimbursable expenses for the fourth quarter of 2003, and is subject to verification by Glaxo.

Research and Development Expenses—We have entered into contracts with third parties to conduct certain research and development activities including pre-clinical, clinical and manufacturing development 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, materials produced by our manufacturers and other criteria relating to the progress of efforts by our vendors.

Liquidity and Capital Resources

We have experienced negative operating annual cash flows since our inception and have funded our operations primarily from the proceeds received from the sale of our equity securities, as well as contract revenues. Cash, cash equivalents and short-term investments were approximately $210.2 million at December 31, 2003, and approximately $154.0 million at December 31, 2002, representing 93.6% and 91.5% of our total assets, respectively. We invest excess cash in investment-grade fixed income securities, including United States Treasury obligations and corporate securities.

We believe that our current financial resources and sources of liquidity are adequate to fund operations into 2007 based upon our expectations of the level of research and development, marketing and administrative activities necessary to achieve our strategic objectives.

The following is a summary of selected cash flow information for the twelve months ended December 31, 2003 and 2002:

	Twelve Months Ended December 31,	
	2003	2002
Net loss	$(51,206,219)	$(60,524,470)
Adjustments for non-cash operating items	4,624,708	8,803,506
Net cash operating loss	(46,581,511)	(51,720,964)
Net change in assets and liabilities	(3,579,014)	49,899,007
Net cash used in operating activities	(50,160,525)	(1,821,957)
Net cash used in investing activities	(94,283,146)	(12,856,529)
Net cash provided by financing activities	113,115,504	1,328,356

Net Cash Used In Operating Activities

Our operating cash outflows for 2003 and 2002 have resulted primarily from research and development expenditures associated with our product candidates, including clinical development and manufacturing development costs for Entereg™, and for the compensation of our employees. These outflows were reduced by cost reimbursement amounts received from Glaxo, and in 2002 by the $50.0 million upfront payment received from Glaxo.

Operating Cash Flow Requirements Outlook

We expect to continue to use cash resources to fund operating losses. We expect that our revenue for contract reimbursement under our collaboration agreement with Glaxo will decline in future periods as compared to 2003 as expenses related to the POI clinical development program decrease. We expect that other operating expenses will increase in future periods as a result of manufacturing scale-up efforts and in preparation for potential commercialization of our product candidates. We expect that as Glaxo incurs increasing expenses under our collaboration related to the OBD program in the United States, we will incur substantial expenses relating to our reimbursements owed to Glaxo. Further, we may in-license or acquire product candidates which will require additional cash outlays.

Contractual Commitments

Lease Payments

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

Year ending December 31,	
2004	$ 1,365,000
2005	1,268,000
2006	1,218,000
2007	1,215,000
2008	1,215,000
2009 & beyond	4,861,000
	$11,142,000

Glaxo Collaboration Agreement

Under the terms of the Glaxo agreement, we will partially reimburse Glaxo for third party expenses incurred by them in the development of Entereg™ for certain indications in the United States, pursuant to an agreed upon development plan and budget which is subject to annual review. We also expect to incur 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 us by Glaxo. We expect to record these expenses as incurred.

Other Service Agreements

We have entered into various agreements for services with third party vendors, including agreements to conduct clinical trials, to manufacture product candidates, and for consulting and other contracted services. We accrue the costs of these agreements based on estimates of work completed to date. We estimate that approximately $15.0 million will be payable in future periods under arrangements in place at December 31, 2003. Of this amount, approximately $10.3 million has been accrued for work estimated to have been completed as of December 31, 2003 and approximately $4.7 million relates to future performance under these arrangements.

License and Research Agreements

With regard to our product, Entereg™, we have commitments to Roberts and Eli Lilly. In November 1996, Roberts licensed from 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 licensed from Roberts the rights Roberts had licensed from Eli Lilly for Entereg™. As of December 31, 2003, we have paid $600,000 to Roberts. Under our Option and License Agreement we are obligated to pay milestone payments to Roberts and Eli Lilly upon the achievement of certain clinical and regulatory milestones that in the aggregate may total up to $1.9 million. We are also responsible for the costs to develop Entereg™. In addition, if Entereg™ receives regulatory approval, we are obligated to pay royalties to Roberts and Eli Lilly on commercial sales of Entereg™. Under the terms of our arrangements, the license to Entereg™ expires on the later of either the life of the last to expire of the licensed Eli Lilly patents or fifteen years from November 5, 1996, following which we will have a fully paid up license.

In August 2002, we entered into a separate exclusive license agreement with Eli Lilly under which we obtained an exclusive license to six issued U.S. patents, related foreign equivalents and know-how relating to peripherally selective opioid antagonists. We paid Eli Lilly $4.0 million upon signing the agreement and are 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, we also agreed to pay Eli Lilly a $4.0 million dollar payment upon acceptance by a regulatory authority of the first application for marketing authorization for Entereg™.

In July 2003, we entered into an agreement with EpiCept under which we licensed exclusive rights to develop and commercialize in North America a sterile lidocaine patch which is being developed for the management of postoperative incisional pain. We made a $2.5 million payment to EpiCept upon execution of the agreement and may make up to $20.0 million in additional development milestone payments if certain clinical and regulatory achievements are reached. The $2.5 million payment was recorded as research and development expense in 2003 as the underlying technology licensed has not reached technological feasibility and has no alternative uses.

Net Cash Used In Investing Activities

Net cash used in investing activities for the years ended December 31, 2003 and 2002 relates primarily to investments made in investment securities. Capital expenditures in 2003 and 2002 were primarily for leasehold improvements associated with our newly leased facility, purchases of laboratory equipment, furniture and fixtures and office equipment.

Investing Requirements Outlook

We expect to continue to require investments in information technology, laboratory and office equipment to support our research and development activities, and potential commercialization activities. Operations are expected to be funded through the maturity of investments in our portfolio.

Net Cash Provided by Financing Activities

In November 2003 we completed the sale of 6.9 million shares of our common stock, which yielded proceeds of $111.6 million, net of offering costs. During 2003 and 2002, we received $0.9 million and $0.9 million, respectively, from stock option exercises.

Financing Requirements Outlook

We do not expect to generate positive cash flows from operations for at least the next several years, if at all. We expect to continue to use our cash, cash equivalents and short-term investments to fund operating and investing activities. We believe that our existing cash, cash equivalents and short-term investments of

approximately $210.2 million as of December 31, 2003 will be sufficient to meet our currently estimated operating and investing requirements into 2007. Prior to exhausting our current cash reserve, we will need to raise additional funds to finance our operating activities. If we do not raise additional cash, we may be required to curtail or limit certain marketing support and research and development activities. A curtailment of certain activities would delay or possibly prevent development of certain of our products. We may seek to obtain additional funds through equity or debt financings or strategic alliances with third parties. These financings could result in substantial dilution to the holders of our common stock. Any such required financing may not be available in amounts or on terms acceptable to us.

Results of Operations

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

Revenues. Revenues decreased in 2003 as compared to 2002 primarily due to a reduction in expenses incurred by us which are reimburseable by Glaxo under the collaboration agreement, partially offset by the recording in 2003 of a full year's amortization of the Glaxo signing fee. Revenues increased in 2002 as compared to 2001 primarily due to the execution of the Glaxo collaboration in 2002, which resulted in significant cost reimbursement and license fee revenue.

Research and Development Expenses. Our research and development expenses consist primarily of salaries and other personnel-related expense, costs of clinical trials, costs to manufacture product candidates, technology licensing costs, laboratory supply costs and facility related costs. Research and development expenses decreased to approximately $56.7 million for the year ended December 31, 2003 from approximately $71.7 million for the year ended December 31, 2002 due principally to a decrease of approximately $14.6 million in expenditures associated with clinical testing of Entereg™, as well as a decrease in technology license fees of approximately $1.5 million, offset partially by an increase of approximately $1.0 million for personnel-related expenses and laboratory supply and facility related expenses.

Research and development expenses increased to approximately $71.7 million for the year ended December 31, 2002 from approximately $36.0 million for the year ended December 31, 2001 primarily due to an increase of $29.0 in expenses associated with the clinical testing of Entereg™, as well as higher personnel costs and a license fee payment of $4.0 million to Eli Lilly and Company.

Our research and development expenses can be identified as internal or external expenses. Internal expenses include expenses such as personnel, laboratory, and overhead related expenses. These expenses totaled $21.6 million, $21.1 million, and $17.5 million in the years ended December 31, 2003, 2002, and 2001 respectively, and are largely related to our Entereg™ development efforts. External expenses include expenses incurred with clinical research organizations, contract manufacturers, and other third party vendors and can be allocated to significant research and development programs as follows:

	Years Ended December 31,		
	2003	2002	2001
Entereg™ Program	$29,628,072	$44,222,837	$15,192,238
Sterile Patch Program	2,785,863	—	—
Other Programs	2,728,202	6,351,956	3,330,395
Total	$35,142,137	$50,574,793	$18,522,633

Due to the significant risks and uncertainties inherent in the preclinical and clinical studies associated with each of our research and development programs, 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. Preclinical and clinical studies may yield varying results that could delay, limit or prevent a program's advancement through the various stages of product development, and significantly impact the costs to be incurred, and time involved, in bringing a program to completion.

Marketing, General and Administrative Expenses. Our marketing, general and administrative expenses for the years ended December 31, 2003, 2002 and 2001 were approximately $17.6 million, $21.7 million and $15.2 million, respectively. These changes are primarily due to non-cash charges recorded in 2002 in connection with the acceleration of the vesting of certain stock options and compensation expenses recorded in 2002 in connection with payments to be made under separation agreements, as well as certain financial advisory and legal fees incurred in conjunction with the execution of the Glaxo agreement.

Other Income (Expense). Our other income decreased in 2003 as compared to 2002, and in 2002 as compared to 2001, due to a reduction in average investment balances and lower interest rates in the later years as compared to the prior years.

Net Loss Outlook

Our net loss for the years ended December 31, 2003, 2002 and 2001 was approximately $51.2 million, $60.5 million, and $42.4 million, respectively. We have not generated any product sales revenues and have not achieved profitable operations. Our deficit accumulated during the development stage through December 31, 2003 aggregated approximately $206.4 million, and we expect to continue to incur substantial losses in future periods. We are highly dependent on the success of our research, development and licensing efforts and, ultimately, upon regulatory approval and market acceptance of our products under development. We may never become profitable and even if we become profitable, we may not be able to sustain profitability on a continuing basis.

Income Taxes

As of December 31, 2003, we had approximately $60,716,000 of Federal and $61,003,000 of state net operating loss carryforwards potentially available to offset future taxable income. The Federal and state net operating loss carryforwards will begin expiring in 2009 and 2005, respectively, if not utilized. In addition, the utilization of the state net operating loss carryforwards is subject to a $2.0 million annual limitation. At December 31, 2003, we also had approximately $4,421,000 of Federal and $716,000 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 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 income tax purposes.

Recently Issued Accounting Pronouncements

In April 2003, the Financial Accounting Standards Board ("FASB") issued Statement of Financial Accounting Standards ("SFAS") No. 149, *Amendment of Statement 133 on Derivative Instruments and Hedging Activities.* This statement amends and clarifies accounting for derivative instruments, including certain derivative instruments embedded in other contracts, and for hedging activities under SFAS No. 133. SFAS No. 149 was effective for contracts entered into or modified after June 30, 2003, for hedging relationships designated after June 30, 2003, and to certain preexisting contracts. The adoption of SFAS No. 149 did not have a material impact on our financial statements.

In May 2003, the FASB issued SFAS No. 150, *Accounting for Certain Financial Instruments with Characteristics of Both Liabilities and Equity*. The Statement requires issuers to classify as liabilities (or assets in some circumstances) three classes of freestanding financial instruments that embody obligations for the issuer. Generally, the Statement is effective for financial instruments entered into or modified after May 31, 2003 and is otherwise effective at the beginning of the first interim period beginning after June 15, 2003. The Company did not enter into any financial instruments within the scope of the Statement during June 2003. As a result of adopting the Statement in July 2003 for existing financial instruments entered into on or before May 31, 2003 there was no impact on the consolidated financial statements.

In December 2003, the FASB issued FASB Interpretation No. 46 (revised December 2003), *Consolidation of Variable Interest Entities"* (FIN 46R), which addresses how a business enterprise should evaluate whether it has a controlling interest in an entity through means other than voting rights and accordingly should consolidate the entity. FIN 46R replaces FASB interpretation No. 46, *Consolidation of Variable Interest Entities,* which was issued in January 2003. We do not have any variable interests in variable interest entities.

Certain Risks Related to Our Business

As further described herein, our performance and financial results are subject to risks and uncertainties including, but not limited to, the following specific risks:

We are highly dependent on achieving success in the clinical testing, regulatory approval and commercialization of our lead product candidate, Entereg™, which may never be approved for commercial use.

We have invested a significant portion of our time and financial resources since our inception in the development of Entereg™, and our potential to achieve revenues from product sales in the foreseeable future is dependent upon successfully commercializing Entereg™. Prior to commercialization of Entereg™ in the United States, we will have to submit, and the FDA will have to approve, an NDA for Entereg™. Drug development is a highly uncertain process. We or Glaxo, with whom we are collaborating to develop Entereg™, may suffer significant setbacks in advanced clinical trials of Entereg™, even after achieving potentially promising results in earlier clinical trials.

Our Entereg™ POI Phase III program consists of four studies, POI 14CL302, POI 14CL313, POI 14CL308 and POI 14CL306. While we have reported top-line results from these studies, the results of these studies have not been submitted to or reviewed by the FDA or any other regulatory agency in an application for regulatory approval for Entereg™. We are targeting submission of an NDA for Entereg™ for the management of postoperative ileus late in the first half of 2004. We may not meet our submission target. Even if we submit this NDA we may not receive FDA approval for Entereg™ for the management of postoperative ileus.

Adverse safety findings from one or more of our clinical trials will adversely affect our ability to obtain regulatory approval for Entereg™. Additional clinical trials of Entereg™, conducted by us or our collaborator, Glaxo, could produce undesirable or unintended side effects that have not been evident in our clinical trials conducted to date. In addition, in patients who take multiple medication, drug interactions with Entereg™ could occur that can be difficult to predict. These events, among others, may make it more difficult for us to obtain regulatory approval for Entereg™. The most frequent adverse events in both the placebo and treatment groups in study POI 14CL302 were nausea, vomiting and abdominal dystension. The most frequent adverse events in both the placebo and treatment groups in study POI 14CL313 were nausea, vomiting and hypotension. The most frequent adverse events in both the placebo and treatment groups in study POI 14CL306 were nausea, vomiting and constipation. The most frequent adverse events in both the placebo and treatment groups in study POI 14CL308 were nausea, vomiting and pruritis.

Our Entereg™ clinical trials are testing whether Entereg™ is able to selectively block the effects of narcotic analgesics in the gastrointestinal tract. As combination clinical trials, they are subject to the risk that the use of Entereg™ with narcotic analgesics may result in unexpected toxicity, or increase the side effects associated with the individual products to an unacceptable level, or interfere with the efficacy of the narcotic analgesic. In addition, assessing clinical trial results of Entereg™ in combination with narcotic analgesics may add to the complexity of interpreting the study results.

Even if we conclude that the results from our preclinical studies and clinical trials of Entereg™ are positive, the FDA may not agree with us.

While we believe the results of studies POI 14CL302, POI 14CL313, POI 14CL306 and POI 14CL308, support our goal of submitting an NDA for Entereg™, there can be no assurance that the FDA will concur with that assessment. The FDA may evaluate the results by different methods or conclude that the clinical trial results are not statistically significant or clinically meaningful, or that there were human errors in the conduct of the clinical trials or otherwise. Even if we believe we have met the FDA guidelines for submission of data and information to the NDA, there is a risk that the FDA will require additional data and information that we are unable to provide.

While the FDA has designated Entereg™ as a Fast Track product, there is no assurance that such designation will expedite the review of our NDA by FDA, and such designation does not increase the likelihood of approval of our NDA. There can also be no assurance that Entereg™ will be granted priority review status by FDA.

If we are unable to commercialize Entereg™, our ability to generate revenues will be impaired and our business will be harmed.

We have not yet commercialized any products or technologies, and we may never be able to do so. If our NDA for Entereg™ is not approved by the FDA, or if approval is delayed, our ability to achieve revenues from product sales will be impaired and our stock price will be materially and adversely affected. FDA approval is contingent on many factors, including clinical trial results and the evaluation of those results. Even if Entereg™ is approved by the FDA for marketing, we will not be successful unless Entereg™ gains market acceptance. The degree of market acceptance of Entereg™ will depend on a number of factors, including:

- the establishment and demonstration in the medical community of the safety and clinical efficacy of Entereg™ and its potential advantages over competitive products; and
- pricing and reimbursement policies of government and third-party payors, such as insurance companies, health maintenance organizations and other plan administrators.

Physicians, patients, payors or the medical community in general may be unwilling to accept, utilize or recommend Entereg™.

Certain results from our clinical trials show that the differences between our product candidates and placebos are not statistically significant.

In study POI 14CL302, the 12 mg Entereg™ treatment group's difference from placebo was not statistically significant. In study POI 14CL308, neither the 6 mg nor the 12 mg treatment groups difference from placebo was statistically significant. Even though the P-value for the 12mg dose group of study POI 14CL308 was below 0.05, it was not considered formally statistically significant because of the multiple dose comparison. In studies involving multiple comparisons, statisticians control the overall study error rate (i.e. the likelihood that the drug response occurred by chance) by requiring that each of the multiple dose comparisons meet a P-value of $P < 0.05$ to show statistical significance. In the event that one of the dose comparisons in any of these POI Phase III studies does not reach a significance level of $P < 0.05$, the other dose comparison in that study needs to reach a significance level of $P < 0.025$ to be considered statistically significant.

These results may make it more difficult to achieve regulatory approval of Entereg™.

Patients may discontinue their participation in our clinical studies, which may negatively impact the results of these studies, and extend the timeline for completion of our development programs.

The time required to complete clinical trails is dependent upon, among other factors, the rate of patient enrollment. Patient enrollment is a function of many factors, including:

- the size of the patient population;
- the nature of the clinical protocol requirements;
- the diversion of patients to other trials or marketed therapies;
- our ability to recruit and manage clinical centers and associated trials;
- the proximity of patients to clinical sites; and
- the patient eligibility criteria for the study.

We are subject to the risk that patients enrolled in our clinical studies may discontinue their participation at any time during the study as a result of a number of factors, including, withdrawing their consent or experiencing adverse clinical events which may or may not be related to our product candidates under evaluation. We are subject to the risk that if a large number of patients in any one of our studies discontinue their participation in the study, the results from that study may not be positive or may not support an NDA for regulatory approval of our product candidates.

In clinical study POI 14CL302, discontinuation rates were 21%, 16%, and 27% in the placebo group, 6 mg dose group and 12 mg dose group, respectively. This resulted in fewer efficacy evaluable patients in the placebo and 12 mg treatment groups compared to the 6 mg treatment group. Following the analysis of study POI 14CL302, we increased enrollment in studies POI 14CL313 and POI 14CL308, with the objective of potentially increasing the number of efficacy evaluable patients in each dose group in our ongoing studies. In study POI 14CL313 discontinuation rates were 30%, 23% and 19% in the placebo, 6 mg and 12 mg dose groups, respectively. In study POI 14CL308 discontinuation rates were 13%, 14% and 14% in the placebo, 6 mg and 12 mg treatment groups, respectively.

We may not be able to successfully develop Entereg™ for use in treating chronic opioid bowel dysfunction ("OBD").

We have completed several Phase II trials and one Phase III clinical trial studying the use of Entereg™ for the reversal of the severe constipating effects associated with chronic use of opioids. The overall responsibility for the development of Entereg™ in chronic indications is now carried on by Glaxo. Additional long-term animal toxicity studies are necessary to support further development of Entereg™ in OBD. Adverse safety findings in these long-term animal toxicity studies could adversely affect our prospects for Entereg™, including its prospects for use in POI. Results from the clinical studies conducted to date in OBD are not necessarily indicative of the results that may be obtained in further OBD studies, or in the on-going clinical studies in the POI indication. Additional studies for chronic OBD investigating longer duration of patient exposure and different dosing strategies, as well as preclinical toxicology studies, will be required prior to initiating the confirming clinical studies required to be successfully completed before any NDA could be filed for use of Entereg™ in OBD.

Our stock price may be volatile, and your investment in our stock could decline in value. We may become involved in securities class action litigation.

The market price for our common stock has been highly volatile and may continue to be highly volatile in the future. For example, in the calendar year ended December 31, 2003, the closing price of our common stock reached a low of $9.55 per share in March 2003 and a high of $21.75 per share in December 2003.

The market price for our common stock is highly dependent on the success of our product development efforts, and in particular, clinical trial results, and regulatory review results.

The following additional factors may have a significant impact on the market price of our common stock:

- developments concerning our collaborations, including our collaboration with Glaxo;
- announcements of technological innovations or new commercial products by our competitors or us;
- developments concerning proprietary rights, including patents;
- publicity regarding actual or potential medical results relating to products under development by our competitors or us;
- regulatory developments in the United States and foreign countries;
- litigation;
- economic and other external factors or other disasters or crises;
- period-to-period fluctuations in our financial results; and
- the general performance of the equity markets and in particular, the biopharmaceutical sector of the equity markets.

Following periods of volatility and decline in the market price of a particular company's securities, securities class action litigation has often been brought against that company. We may become involved in this type of litigation in the future. Litigation of this type is often extremely expensive and diverts management's attention and resources.

If we continue to incur operating losses for a period longer than anticipated, we may be unable to continue our operations.

We believe our existing cash, cash equivalents and short-term investments as of December 31, 2003 of approximately $210.2 million will be sufficient to meet our currently estimated operating and investing requirements into 2007. We have generated operating losses since we began operations in November 1994. We expect to continue to generate such losses and will need additional funds that may not be available in the future. We have no products that have generated any revenue, and as of December 31, 2003, we have incurred a cumulative net loss of approximately $206.4 million. During the calendar years ended December 31, 2003 and 2002, we incurred operating losses of approximately $53.6 million and $65.0 million, respectively, and net losses of approximately $51.2 million and $60.5 million, respectively. Even if we succeed in developing a commercial product, we expect to incur substantial losses for at least the next several years and expect that these losses will increase as we expand our research and development and sales and marketing activities. If we fail to obtain the capital necessary to fund our operations, we will be forced to curtail our operations and we will be unable to develop products successfully. We do not know whether additional financing will be available when needed, or that, if available, we will obtain financing on terms favorable to our stockholders or to us. If adequate funds are not available on acceptable terms, our ability to fund our operations, products or technologies or otherwise respond to competitive pressures could be significantly delayed or limited, and we may have to reduce or cease our operations. If additional funds become available there can be no assurance that we can predict the time and costs required to complete development programs or that we will not substantially exceed our budgets.

We are dependent on our collaborators to perform their obligations under our collaboration agreements.

In April 2002, we and Glaxo entered into a collaboration agreement for the exclusive worldwide development and commercialization of Entereg™ for certain indications. We and Glaxo agreed to develop Entereg™ for a number of indications, both acute and chronic, which would potentially involve the use of Entereg™ in in-patient and out-patient settings. In the United States, we have the right to co-develop and

co-promote Entereg™ with Glaxo, and share development expenses and commercial returns, if any, pursuant to contractually agreed percentages. We have overall responsibility for the development of acute care indications such as POI, and Glaxo has overall responsibility for the development of chronic-care indications such as OBD. We and Glaxo are required to use commercially reasonable efforts to develop the indications for which we and they are respectively responsible. We and Glaxo have established numerous joint committees to collaborate in the development of Entereg™. These committees meet at regularly scheduled intervals. We depend on Glaxo to provide us with substantial assistance and expertise in the development of Entereg™. Any failure of Glaxo to perform its obligations under our agreement could negatively impact our product candidate, Entereg™, and could lead to our loss of potential revenues from product sales and milestones that may otherwise become due under our collaboration agreement and would delay our achievement, if any, of profitability. Glaxo has extensive experience in the successful commercialization of product candidates which it would be difficult for us to replace if the collaboration agreement was not in place. In the near term, our success will largely depend upon the success of our collaboration with Glaxo to further develop Entereg™ and our success in obtaining regulatory approval to commercialize Entereg™.

The term of the collaboration agreement varies depending on the indication and the territory. 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, if any. Generally the term for the OBD indication in the United States is fifteen years from the first commercial sale of Entereg™ in that indication, if any. In the rest of the world, the term is generally fifteen years from the first commercial sale of Entereg™, if any, on a country-by-country and indication-by-indication basis.

Glaxo has certain rights to terminate the collaboration agreement. Glaxo also has the right to terminate its rights and obligations with respect to the acute-care indications, or its rights and obligations for the chronic-care indications. Glaxo 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. Glaxo's rights to terminate the acute-care indications or the chronic-care indications are generally triggered by failure to achieve certain milestones within certain timeframes, adverse product developments or adverse regulatory events. If Glaxo terminates the collaboration agreement, we may not be able to find a new collaborator to replace Glaxo, and our business will be adversely affected.

Our corporate collaborators, including Glaxo, may determine not to proceed with one or more of our drug discovery and development programs. If one or more of our corporate collaborators reduces or terminates funding, we will have to devote additional internal resources to product development or scale back or terminate some development programs or seek alternative corporate collaborators.

Our ability to enter into new collaborations and to achieve success under existing collaborations is uncertain.

We have entered into, and may in the future enter into, collaborative arrangements, including our arrangement with Glaxo, for the marketing, sales and distribution of our product candidates, which require, or may require, us to share profits or revenues. 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 and 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 cannot be certain that any of these parties, including Glaxo, will fulfill their obligations in a manner consistent with our best interests. Collaborators may also pursue alternative technologies or drug candidates, either on their own or in collaboration with others, that are in direct competition with us.

Our quarterly operating results may fluctuate significantly depending on the initiation of new corporate collaboration agreements, the activities under current corporate collaboration agreements or the termination of existing corporate collaboration agreements.

We may not be able to successfully develop in-licensed product candidates, which could prevent us from commercializing any such candidates.

We intend to explore opportunities to expand our product portfolio by acquiring or in-licensing products and/or product development candidates. In July 2003, we entered into an agreement with EpiCept, under which we obtained exclusive rights to develop and commercialize in North America a sterile lidocaine patch which is being developed for the management of postoperative incisional pain. Although we conduct extensive evaluations of product candidate opportunities as part of our due diligence efforts, there can be no assurance that our product 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 development efforts. Additionally, while we have built certain capabilities as an organization in executing the development plan for Entereg™, in-licensed products such as this sterile patch product will require capabilities and expertise which we do not currently possess, and there is no assurance that we will be able to develop or acquire these capabilities. If we do not develop or acquire these capabilities, we may not be able to commercialize our in-licensed products and technologies.

Because our product candidates are in development, there is a high risk that further development and testing will demonstrate that our product candidates are not suitable for commercialization.

We have no products that have received regulatory approval for commercial sale. All of our product candidates, including Entereg™, are in development, and 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. To satisfy these standards, we will need to conduct significant additional research, animal testing, or preclinical testing, and human testing, or 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.

We may suffer significant setbacks in advanced clinical trials, even after promising results in earlier 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 disease 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.

We have limited commercial manufacturing capability and expertise. If we are unable to contract with third parties to manufacture our products in sufficient quantities, at an acceptable cost and in compliance with regulatory requirements, we may be unable to obtain regulatory approvals, or to meet demand for our products.

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. It is difficult and expensive to change contract manufacturers for pharmaceutical products, particularly when the products are under regulatory review in an NDA process. We currently do not have long-term supply agreements with our third party manufacturers. 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 pre-clinical or clinical development. Our dependence upon others for the manufacture of our products may adversely affect our future profit margin and our ability to commercialize products, if any are approved, on a timely and competitive basis.

To receive regulatory approval for Entereg™, our contract manufacturers will be required to obtain approval for their manufacturing facilities to manufacture Entereg™, and there is a risk that such approval may not be obtained. We will be required to submit, in an NDA, information and data regarding chemistry, manufacturing and controls which satisfies the FDA that our contract manufacturers are able to make Entereg™ in accordance with cGMPs. Under cGMPs, our manufacturers 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 Entereg™. 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 delays in manufacture if outside contractors give other products greater priority than our products.

We maintain a relationship with Torcan Chemical Ltd. for the supply of the active pharmaceutical ingredient ("API") in Entereg™. We also maintain a relationship with Girindus AG as an additional supplier of API for Entereg™. We maintain a relationship with Pharmaceutics International Inc. for the supply of Entereg™ finished capsules, and a relationship with Sharp Corporation for the packaging of Entereg™ finished capsules. We have no formal commercial supply arrangement as yet with any of these parties. We also rely upon these parties for the performance of scale-up and other development activities, and for the maintenance and testing of product pursuant to applicable stability programs.

Clinical trials in our Phase III Entereg™ program use drug product incorporating active pharmaceutical ingredient manufactured by two different contract manufacturing facilities, one of which is no longer in business. Our efforts to obtain regulatory approval for Entereg™ may be impaired as a result of using material from two different contract manufacturing facilities.

We also expect to depend on third parties to manufacture product candidates we may acquire or in-license, including the sterile patch product we in-licensed from EpiCept. We have no experience in manufacturing sterile patch products and will need to develop our own internal capabilities and external relationships in that regard, as well as assess the capabilities of third party manufacturers that have been involved in the manufacture of this product candidate to date.

If we are unable to develop sales, marketing and distribution capabilities or enter into agreements with third parties to perform these functions, we will not be able to commercialize products.

We currently have no sales or distribution capability and limited marketing capabilities. In order to commercialize products, if any are approved, we must internally develop sales, marketing and distribution

capabilities or make arrangements with third parties to perform these services. If we obtain regulatory approval, we intend to sell some products directly in certain markets and rely on relationships with established pharmaceutical companies to sell products in certain markets. To sell any of our products directly, we must develop a marketing and sales force with technical expertise and with supporting distribution capabilities. We may not be able to establish in-house sales and distribution capabilities or relationships with third parties. To the extent that we enter into co-promotion or other licensing arrangements, our product revenues may be lower than if we directly marketed and sold our products, and any revenues we receive will depend upon the efforts of third parties, which efforts may not be successful.

We have limited experience in conducting and managing the clinical trials necessary to obtain regulatory approval and depend on third parties to conduct our clinical trials.

We have limited experience in managing clinical trials, and delays or terminations of clinical trials we are conducting or may undertake in the future could impair our development of product candidates. Delay or termination of any clinical trials could result from a number of factors, including adverse events, stringent enrollment requirements, slow rate of enrollment, competition with other clinical trials for eligible patients and other factors. We are subject to the risk that subjects enrolled in our clinical studies may discontinue their participation at anytime during the study as a result of a number of factors, including, withdrawing their consent or experiencing adverse clinical events which may or may not be judged related to our product candidates under evaluation.

We 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. The failure of any third party to comply with any governmental regulations would substantially harm our development efforts and delay or prevent regulatory approval of our product candidates.

The concept of developing peripherally acting opioid antagonist drugs is relatively new and may not lead to commercially successful drugs.

Peripherally acting compounds given to patients as potential drugs are designed to exert their effects outside the brain and spinal cord, in contrast to centrally acting compounds which are designed to exert their effects on the brain or spinal cord. We are developing Entereg™ as a peripherally acting opioid antagonist. An opioid antagonist is designed to block the effects of the opioid at the receptor level; in the case of Entereg™, it is designed to block the unwanted effects of opioid analgesics on the gastrointestinal tract. Since there are no products on the market comparable to our product candidates, we do not have any historical or comparative sales data to rely upon to indicate that peripherally acting opioid antagonist drugs will achieve commercial success in the marketplace. Market acceptance of our product candidates will depend on a number of factors, including:

- perceptions by members of the health care community, including physicians, of the safety and efficacy of our product candidates;
- cost-effectiveness of our product candidates relative to competing products;
- the availability of government or third-party payor reimbursement for our product candidates; and
- the effectiveness of marketing and distribution efforts by us, our collaborators and our licensees and distributors.

Other products that are currently sold for pain management are already recognized as safe and effective and have a history of successful sales in the United States and elsewhere. Our new products in this area, if any, will be competing with drugs that have been approved by the FDA and have demonstrated commercial success in the United States and elsewhere.

Our product candidate Entereg™ is under investigation for use in patients taking opioid analgesics and reduction in the use of opioid analgesics would therefore reduce the potential market for Entereg™.

If the use of drugs or techniques which reduce the requirement for *mu*-opioids increases, the demand for Entereg™ would be decreased. Various techniques to reduce the use of opioids are used 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 post-operative period can reduce or eliminate the use of opioids. Non-steroidal inflammatory agents may also 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 which act at non-*mu*-opioid receptors 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™.

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 ultimately treat and they may develop effective and commercially successful products. Our competitors may succeed in developing products either that are more effective than those that we may develop, or that they market before we market any products we may develop.

We believe that Progenics Pharmaceuticals, Inc. is developing methylnaltrexone for the treatment of opioid bowel dysfunction and POI. We also believe a European specialist pharmaceutical company with a focus on the gastrointestinal market, is in preclinical development in the area of peripherally acting opioid antagonists for use in opioid induced constipation. There are products already on the market for use in treating irritable bowel syndrome which may be evaluated for utility in opioid induced bowel dysfunction. There may be additional competitive products about which we are not aware. If our competitors are able to reach the commercial market before we are, this could have a material adverse effect on our ability to reach the commercial 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.

Our business could suffer if we cannot 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, including our president and chief executive officer, Bruce A. Peacock. 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.

Companies and universities that have licensed technology and product candidates to us are sophisticated entities that could develop similar products to compete with products we hope to develop.

Licensing product candidates from other companies, universities, or individuals does not prevent such parties from developing competitive products for their own commercial purposes, nor from pursuing patent protection in areas that are competitive with us. The individuals who created these technologies are sophisticated scientists and business people who may continue to do research and development and seek patent protection in the same areas that led to the discovery of the product candidates that they licensed to us. The development and commercialization by us of successful products is also likely to attract additional research by our licensors and by other investigators who have experience in developing products for the pain management market. By virtue of their previous research activities these companies, universities, or individuals may be able to develop and market competitive products in less time than might be required to develop a product with which they have no prior experience.

If we breach our licensing agreements, we will lose significant benefits and may be exposed to liability for damages.

We may breach our license agreements and may thereby lose rights that are important. We are subject to various obligations with respect to license agreements, including development responsibilities, royalty and other payments and regulatory obligations. If we fail to comply with these requirements or otherwise breach a license agreement or contract, the licensor or other contracting party may have the right to terminate the license or contract in whole or in part or change the exclusive nature of the arrangement. In such event we would not only lose all or part of the benefit of the arrangement but also may be exposed to potential liabilities for breach in the form of damages or other penalties.

Because we are not certain we will obtain necessary regulatory approvals to market our products in the United States and foreign jurisdictions, we cannot predict whether or when we will be permitted to commercialize any of our products.

The pharmaceutical industry is subject to stringent regulation by a wide range of authorities. We cannot predict whether we will obtain regulatory clearance for any product candidate we develop. We cannot market a pharmaceutical product in the United States until it has completed rigorous preclinical testing and clinical trials and the FDA's extensive regulatory clearance process. Satisfaction of regulatory requirements typically takes many years, is dependent upon the type, complexity and novelty of the product and requires the expenditure of substantial resources for research and development, testing, manufacturing, quality control, labeling and promotion of drugs for human use. Since neither the FDA nor international regulatory authorities have approved peripherally restricted narcotic antagonist drugs for marketing, there is additional uncertainty as to whether our research and clinical approaches to developing new products for the pain management market will lead to drugs that the FDA will consider safe and effective for indicated uses. Before receiving FDA approval to market a product, we must demonstrate that the product candidate is safe and effective in the patient population that will be treated. Outside the United States, our ability to market a product is also contingent upon receiving a marketing authorization from the appropriate regulatory authorities, and is subject to similar risks and uncertainties.

We do not know whether our current or future preclinical and clinical studies will demonstrate sufficient safety and efficacy necessary to obtain the requisite regulatory approvals, or will result in marketable products. Any failure to adequately demonstrate the safety and efficacy of our product candidates will prevent receipt of

FDA and foreign regulatory approvals and, ultimately, commercialization of our product candidates. Regulatory authorities may refuse or delay approval as a result of many other factors, including changes in regulatory policy during the period of product development and regulatory interpretations of clinical benefit and clinical risk. Regulatory clearance that we may receive for a product candidate will be limited to those diseases and conditions for which we have demonstrated in clinical trials that the product candidate is safe and efficacious. Even if we receive regulatory approval for our product candidates we must comply with applicable FDA post marketing regulations and other regulatory requirements. Failure to comply with applicable regulatory requirements could subject us to criminal prosecution, civil penalties, recall or seizure of products, total or partial suspension of production or injunction, as well as other regulatory actions against our product or us.

If we market our products in a manner that violates health care fraud and abuse 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 health care fraud and abuse laws have been applied to restrict certain marketing practices in the pharmaceutical industry in recent years. These laws include antikickback statutes and false claims statutes.

The federal health care program antikickback 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 health care 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 one hand and prescribers, purchasers, and formulary managers on the other. Although there are a number of 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, purchases, or recommendations 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 antikickback 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 health care companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. The majority of states also have statutes or regulations similar to the federal antikickback 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.

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 such laws. Such a challenge could have a material adverse effect on our business, financial condition and results of operations.

The federal Controlled Substances Act might impose significant restrictions, licensing and regulatory requirements on the manufacturing, distribution and dispensing of certain of our product candidates.

The federal Controlled Substances Act imposes significant licensing, recordkeeping, reporting, prescribing, and other regulatory requirements on the manufacturing, distribution and dispensing of controlled substances. Therefore, we must determine whether the Drug Enforcement Administration ("DEA") would consider any of our product candidates to be a controlled substance. We believe that it is unlikely that any of our product candidates other than those which may act on the central nervous system may be subject to regulation as controlled substances.

Facilities that conduct research, manufacture or distribute controlled substances must be registered with DEA to perform these activities and have the security, control and accounting systems required by the DEA to prevent loss and diversion. Failure to maintain compliance, particularly as manifested in loss or diversion, can result in significant regulatory action. In addition, individual state laws may also impose separate regulatory restrictions and requirements, including licenses, recordkeeping and reporting.

We may not obtain FDA approval to conduct clinical trials that are necessary to satisfy regulatory requirements.

Clinical trials are subject to oversight by institutional review boards and the FDA and:

- must conform with the FDA's good clinical practice regulations;
- must meet requirements for institutional review board oversight;
- must meet requirements for informed consent;
- are subject to continuing FDA oversight; and
- may require large numbers of test subjects.

Before commencing clinical trials in humans, we must submit and receive approval from the FDA of an Investigational New Drug Application, or IND. We, or the FDA, may suspend clinical trials at any time if the subjects participating in the trials are exposed to unacceptable health risks, or if the FDA finds deficiencies in the IND application or the conduct of the trials.

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 rights.

Our commercial success will depend in part on obtaining patent protection on our products and successfully defending these patents against third party challenges. The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions. Accordingly, we cannot predict the breadth of claims allowed in our patents or those of our collaborators.

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 the United States Patent and Trademark Office.

Although no third party has asserted a claim of infringement against us, others may hold proprietary rights that will 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 we or our collaborators would prevail in any of these 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. If we become involved in litigation, it could consume substantial managerial and financial resources.

We 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 and consultants to enter into confidentiality agreements, we may not be able to protect adequately 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 collaborations, our ability to receive patent protection or protect our proprietary information may be imperiled.

Others may hold proprietary rights that will prevent our product candidates from being marketed unless we are able to obtain a license to those proprietary rights. 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, and accordingly are unable to exercise the same degree of control over this intellectual property as we exercise over our internally developed technology.

Our ability to generate revenues will be diminished if we fail to obtain acceptable prices or an adequate level of reimbursement for our products from third-party payors.

Our ability to commercialize pharmaceutical products, alone or with collaborators, may depend in part on the extent to which reimbursement for the products will be 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 health care 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 health care programs such as Medicare and Medicaid. For example, federal legislation was enacted on December 8, 2003, which provides a new Medicare prescription drug benefit beginning in 2006 and mandates other reforms. Although we cannot predict the full effects on our business of the implementation of this new legislation, it is possible that the new Medicare benefit, which will be managed by private health insurers, pharmacy benefit managers, and other managed care organizations, will result in decreased reimbursement for prescription drugs, which may further exacerbate industry-wide pressure to reduce the prices charged for prescription drugs. This could have an adverse effect on our business. In addition, increasing emphasis on managed care in the United States will continue to put pressure on the pricing of pharmaceutical products. Significant uncertainty exists as to the reimbursement status of newly approved health care products. Cost control initiatives could decrease the price that any of our collaborators or we would receive for any products in the future and may impede patients' ability to obtain reimbursement under their insurance program for our products. Further, cost control initiatives could adversely affect our collaborators' ability to commercialize our products, and our ability to realize royalties from such commercialization.

If we engage in an acquisition 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.

If product liability lawsuits are successfully brought against us, we may incur substantial liabilities and may have to limit or cease commercialization of our products.

The testing and marketing of medical products entail an inherent risk of product liability. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit or cease commercialization of our products. We currently carry clinical trial insurance at a level we believe is commercially reasonable but do not carry product liability insurance. Our corporate collaborators or we may not be able to obtain insurance at a reasonable cost, if at all. There is no assurance that our clinical trial insurance will be adequate to cover claims that may arise. We enter into indemnification agreements where we indemnify third parties such as investigators for certain product liability claims related to our products under investigation. These indemnification obligations may cause us to pay significant sums of money for claims that are covered by these indemnifications.

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.

Certain provisions of our charter documents and under Delaware law 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 by-laws, 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.

We have shares of our common stock and preferred stock 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.

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.

In addition, we adopted a shareholder rights plan, the effect of which may be to make an acquisition of the company more difficult.

Under our collaboration agreement with Glaxo, there are certain limitations on Glaxo's ability to acquire our securities. These limitations make it more difficult for Glaxo to acquire us, even if such an acquisition would benefit our stockholders.

During and for one year after the term of the collaboration agreement, Glaxo and its affiliates will not, alone or with others, except as permitted under limited circumstances:

- acquire or agree to acquire, directly or indirectly, any direct or indirect beneficial ownership or interest in any of our securities or securities convertible into or exchangeable for any of our securities;
- make or participate in any solicitation of proxies to vote in connection with us;
- form, join or in any way participate in a group with respect to our voting securities;
- acquire or agree to acquire, directly or indirectly, any of our assets or rights to acquire our assets, unless we are selling those assets at that time; or
- otherwise seek to change the control of us or propose any matter to be voted on by our stockholders or nominate any person as a director of us who is not nominated by the then incumbent directors.

The limitations on Glaxo do not prevent Glaxo, 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 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

A substantial portion of our assets are investment grade fixed income securities including U.S. Treasury obligations, U.S. government sponsored obligations and corporate securities. 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 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, 2003 was $204.8 million and the weighted-average interest rate was approximately 1.57% with maturities of up to 23 months.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. A list of the financial statements filed herewith can be found at "Item 15. Exhibits, Financial Statement Schedules and Reports on Form 8-K."

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

None.

ITEM 9A. CONTROLS AND PROCEDURES

Within the ninety days prior to the date of this Annual Report, we carried out an evaluation, under the supervision and with the participation of our management, including our President and Chief Executive Officer and our Senior Vice President and Chief Financial Officer (the principal finance and accounting officer), of the effectiveness of the design and operation of our disclosure controls and procedures pursuant to Rules 13a-15 and 15d-15 under the Exchange Act. Based upon this evaluation, our President and Chief Executive Officer and our Senior Vice President and Chief Financial Officer concluded that, as of December 31, 2003, our disclosure controls and procedures have been designed and are being operated in a manner that provides reasonable assurance that the information required to be disclosed by the Company in reports filed under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the rules and forms of the Commission. A control system, no matter how well designed and operated, cannot provide 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.

Additionally, our President and Chief Executive Officer and Senior Vice President and Chief Financial Officer determined, as of December 31, 2003, that there were no significant changes in our internal controls or in other factors that could significantly affect our internal controls subsequent to the date of their evaluation.

PART III

ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT

We incorporate by reference the information contained under the captions "Election of Directors, Item 1 on Proxy Card", "Executive Officers of the Registrant" and "Section 16(a) Beneficial Ownership Reporting Compliance" in our Definitive Proxy Statement related to our annual meeting of stockholders, to be filed within 120 days after the end of the year covered by this Report pursuant to Section 14(a) of the Securities Exchange Act of 1934, as amended (the Exchange Act).

ITEM 11. EXECUTIVE COMPENSATION

We incorporate by reference the information contained under the caption "Compensation Tables" in our Definitive Proxy Statement related to our annual meeting of stockholders, to be filed within 120 days after the end of the year covered by this Report pursuant to Section 14(a) of the Exchange Act.

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

We incorporate by reference the information contained under the captions "Security Ownership of Certain Beneficial Owners and Directors and Officers" and "Other Forms of Compensation" in our Definitive Proxy Statement related to our annual meeting of stockholders, to be filed within 120 days after the end of the year covered by this Report pursuant to Section 14(a) the Exchange Act.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

We incorporate by reference the information contained under the caption "Certain Relationships and Related Transactions" in our Definitive Proxy Statement related to our annual meeting of stockholders, to be filed within 120 days after the end of the year covered by this Report pursuant to Section 14(a) of the Securities Exchange Act.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

We incorporate by reference the information contained under the caption "Ratification of Appointment of Independent Accountants—Report of the Audit Committee—Audit Fees; Audit-Related Fees; Tax Fees; All Other Fees" in our Definitive Proxy Statement related to our annual meeting of stockholders, to be filed within 120 days after the end of the year covered by this Report pursuant to Section 14(a) of the Securities Exchange Act.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES AND REPORTS ON FORM 8-K

(a) 1. Financial Statements

Reference is made to the Index to Consolidated Financial Statements on page F-1 of this Report.

2. Financial Statement Schedules

None

(b) We filed the following Current Reports on Form 8-K during the quarter ended December 31, 2003:

1. We filed a Current Report on Form 8-K on October 10, 2003 to amend the report on Form 8-K/A that we filed on August 20, 2003 to file our collaboration agreement with Glaxo Group Limited entered into on April 22, 2002.

2. We filed a Current Report on Form 8-K on October 22, 2003 to report, pursuant to Item 12, our financial results for the quarter ended September 30, 2003.

3. We filed a Current Report on Form 8-K on October 23, 2003 to report, pursuant to Item 5, the top-line results of our Phase III clinical safety study POI 14CL306 of our product candidate Entereg™.

4. We filed a Current Report on Form 8-K on November 4, 2003 to report, pursuant to Item 5, our plan to publicly offer up to 6,900,000 shares of our Common Stock under a registration statement declared effective by the SEC on October 27, 2003.

5. We filed a Current Report on Form 8-K on November 7, 2003 to report, pursuant to Item 5, that we entered into a Purchase Agreement with Merrill Lynch & Co., as lead underwriter, for the sale of up to 6,900,000 shares of our Common Stock in a public offering.

6. We filed a Current Report on Form 8-K on November 13, 2003 to report, pursuant to Item 5, completion of the sale of 6,900,000 shares of our Common Stock at a public offering price per share of $17.25.

7. We filed a Current Report on Form 8-K on December 3, 2003 to report, pursuant to Item 9, that on December 3, 2003, GlaxoSmithKline presented an update on the alvimopan development program.

(c) Exhibits

Reference is made to the Exhibit Index on page 41 of this Report for a list of exhibits required by Item 601 of Regulation S-K to be filed as part of this Report.

SIGNATURES

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

Date: March 4, 2004

ADOLOR CORPORATION

By: /s/ BRUCE A. PEACOCK
Name: Bruce A. Peacock
Title: *President, Chief Executive Officer and Director*

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

Signature	Title	Date
/s/ BRUCE A. PEACOCK Bruce A. Peacock	President, Chief Executive Officer and Director (Principal Executive Officer)	March 4, 2004
/s/ MICHAEL R. DOUGHERTY Michael R. Dougherty	Senior Vice President, Chief Financial Officer (Principal Financial Officer)	March 4, 2004
/s/ ARMANDO ANIDO Armando Anido	Director	March 4, 2004
/s/ PAUL GODDARD Paul Goddard	Director	March 4, 2004
/s/ GEORGE V. HAGER, JR. George V. Hager, Jr.	Director	March 4, 2004
/s/ DAVID M. MADDEN David M. Madden	Director	March 4, 2004
/s/ CLAUDE H. NASH Claude H. Nash	Director	March 4, 2004
/s/ ROBERT T. NELSEN Robert T. Nelsen	Director	March 4, 2004
/s/ DONALD E. NICKELSON Donald E. Nickelson	Director	March 4, 2004

EXHIBIT INDEX

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation of Adolor (incorporated by reference to Exhibit 3.1 to the Report on Form 10-Q filed by the Company on August 14, 2001).
3.2	Restated Bylaws of Adolor. [1]
4.1	Series A Convertible Preferred Stock Purchase Agreement among Opian Pharmaceuticals, Inc. and the parties set forth therein, dated November 7, 1994 (incorporated by reference to Exhibit 4.1 to the Registration Statement filed by the Company on February 8, 2000 (Registration No. 333-96333)).
4.2	Series B Convertible Preferred Stock Purchase Agreement among Adolor and the parties set forth therein, dated March 1, 1996 (incorporated by reference to Exhibit 4.2 to the Registration Statement filed by the Company on February 8, 2000).
4.3	Series C Convertible Preferred Stock Purchase Agreement among Adolor and the parties set forth therein, dated March 1, 1997 (incorporated by reference to Exhibit 4.3 to the Registration Statement filed by the Company on February 8, 2000).
4.4	Stock Purchase Agreement between Adolor and Kwang Dong Pharmaceutical Company, dated November 5, 1997 (incorporated by reference to Exhibit 4.4 to the Registration Statement filed by the Company on February 8, 2000).
4.5	Series E Convertible Preferred Stock Purchase Agreement among Adolor and the parties set forth therein, dated December 8, 1998 (incorporated by reference to Exhibit 4.5 to the Registration Statement filed by the Company on February 8, 2000).
4.6	Series F Convertible Preferred Stock Purchase Agreement among Adolor and the parties set forth therein, dated July 26, 1999 (incorporated by reference to Exhibit 4.6 to the Registration Statement filed by the Company on February 8, 2000).
4.7	Series G Convertible Preferred Stock Purchase Agreement among Adolor and the parties set forth therein, dated January 10, 2000 (incorporated by reference to Exhibit 4.7 to the Registration Statement filed by the Company on February 8, 2000).
4.8	Registration Rights Agreement among Opian Pharmaceuticals, Inc. and the parties set forth therein, dated November 4, 1994 (incorporated by reference to Exhibit 4.8 to the Registration Statement filed by the Company on February 8, 2000).
4.9	Amendment No. 1 to Registration Rights Agreement among Adolor and the parties set forth therein, dated February 27, 1996 (incorporated by reference to Exhibit 4.9 to the Registration Statement filed by the Company on February 8, 2000).
4.10	Amendment No. 2 to Registration Rights Agreement among Adolor and the parties set forth therein, dated May 1, 1997 (incorporated by reference to Exhibit 4.10 to the Registration Statement filed by the Company on February 8, 2000).
4.11	Amendment No. 3 to Registration Rights Agreement among Adolor and the parties set forth therein, dated December 8, 1998 (incorporated by reference to Exhibit 4.11 to the Registration Statement filed by the Company on February 8, 2000).
4.12	Amendment No. 4 to Registration Rights Agreement among Adolor and the parties set forth therein, dated July 26, 1999 (incorporated by reference to Exhibit 4.12 to the Registration Statement filed by the Company on February 8, 2000).
4.13	Amendment No. 5 to Registration Rights Agreement among Adolor and the parties set forth therein, dated January 10, 2000 (incorporated by reference to Exhibit 4.13 to the Registration Statement filed by the Company on February 8, 2000).

Exhibit Number	Description
4.14	Form of Common Stock Certificate (incorporated by reference to Exhibit 4.14 to Amendment No. 3 to the Registration Statement filed by the Company on March 21, 2000).
4.15	Series H Convertible Preferred Stock Purchase Agreement among Adolor and the parties set forth therein, dated July 6, 2000 (incorporated by reference to Exhibit 4.15 to Amendment No. 8 to the Registration Statement filed by the Company on October 23, 2000).
4.16	Amendment No. 6 to Registration Rights Agreement among Adolor and the parties set forth therein, dated June 29, 2000 (incorporated by reference to Exhibit 4.16 to Amendment No. 8 to the Registration Statement filed by the Company on October 23, 2000).
4.17	Rights Agreement, dated as of February 20, 2001, between Adolor and StockTrans, Inc., as Rights Agent (incorporated by reference to Exhibit 4.1 to Form 8-K filed by the Company on February 23, 2001), which included as Exhibit B thereto the Form of Rights Certificate, incorporated by reference to Exhibit 1.1 to the Company's Registration Statement on Form 8-A, dated February 22, 2001.
10.1	Amended and Restated 1994 Equity Compensation Plan (incorporated by reference to Exhibit 10.1 on Form 10-Q filed by the Company on August 7, 2003). [4]
10.2	Option and License Agreement between Adolor and Roberts Laboratories, Inc., dated June 10, 1998 (incorporated by reference to Exhibit 10.2 to Amendment No. 1 to the Registration Statement filed by the Company on February 18, 2000). [2]
10.3	License Agreement between Adolor and Kwang Dong Pharmaceutical Company, Ltd., dated November 5, 1997 (incorporated by reference to Exhibit 10.2 to Amendment No. 1 to the Registration Statement filed by the Company on February 18, 2000). [2]
10.4	Amended and Restated Build to Suit Lease between the Company and 700 Pennsylvania Drive Associates, dated February 27, 2003 (incorporated by reference to Exhibit 10.4 to Form 10-K filed by the Company on March 18, 2003).
10.5	License Agreement between Adolor Corporation and Eli Lilly and Company, dated August 8, 2002 (incorporated by reference to Exhibit 10.1 to Form 10-Q filed by the Company on November 1, 2002). [2]
10.6	Amendment dated January 26, 2004 to Letter Agreement between the Company and Michael R. Dougherty, dated October 24, 2002. [1] [4]
10.7	Letter Agreement between the Company and John J. Farrar, dated as of April 3, 2002 (incorporated by reference to Exhibit 10.2 to Form 8-K filed by the Company on April 25, 2002). [4]
10.8	Letter Agreement between the Company and John J. Farrar, effective September 30, 2002 (incorporated by reference to Exhibit 10.1 to Form 8-K filed by the Company on September 30, 2002). [4]
10.9	Retirement Agreement between Adolor and Peter J. Schied dated April 11, 2003 (incorporated by reference to Exhibit 10.1 to Form 8-K filed by the Company on April 11, 2003). [4]
10.10	Adolor Corporation 2003 Stock-based Incentive Compensation Plan. [1] [4]
10.11	Consulting Agreement between the Company and Paul Goddard dated as of July 28, 2003 (incorporated by reference to Exhibit 10.3 to Form 10-Q filed by the Company on August 7, 2003). [4]
10.12	Adolor Corporation Executive Severance Pay Program (incorporated by reference to Exhibit 10.2 to Form 10-Q filed by the Company on November 1, 2002). [4]
10.13	Letter Agreement between the Company and Bruce A. Peacock, dated April 22, 2002 (incorporated by reference to Exhibit 10.1 to Form 8-K filed by the Company on April 25, 2002). [4]

Exhibit Number	Description
10.14	Letter Agreement between the Company and Martha E. Manning, dated June 30, 2002 (incorporated by reference to Exhibit 10.1 to Form 10-Q filed by the Company on August 13, 2002).[4]
10.15	Letter Agreement between the Company and Michael R. Dougherty, dated October 24, 2002 (incorporated by reference to Exhibit 10.15 to Form 10-K filed by the Company on March 18, 2003).[4]
10.16	Letter Agreement between the Company and David Jackson, dated January 10, 2001 (incorporated by reference to Exhibit 10.16 to Form 10-K filed by the Company on March 18, 2003).[4]
10.17	Collaboration Agreement dated as of April 14, 2002, by and between the Company and Glaxo Group Limited (incorporated by reference to Exhibit 10.1 to Form 8-K/A filed by the Company on October 10, 2003).[2]
10.18	Agreement by and between the Company and Toray Industries, Inc., dated March 5, 2002 (incorporated by reference to Exhibit 10.1 to Form 10-Q filed by the Company on May 15, 2002).[2]
10.19	Option Agreement between the Company and Bruce A. Peacock, dated as of April 22, 2002 (incorporated by reference to Exhibit 10.19 to Form 10-K filed by the Company on March 18, 2003).[4]
10.20	Option Agreement between the Company and Bruce A. Peacock, dated as of April 22, 2002 (incorporated by reference to Exhibit 10.20 to Form 10-K filed by the Company on March 18, 2003).[4]
10.21	Agreement dated May 6, 2002 between the Company and Bruce A. Peacock (incorporated by reference to Exhibit 10.21 to Form 10-K filed by the Company on March 18, 2003)[4]
21.1	Adolor Finance LLC as Subsidiary[1]
23.1	Consent of KPMG LLP.[1]
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.[1]
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.[1]
32.1	Certification Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to section 906 of the Sarbanes-Oxley Act of 2002.[1]
32.2	Certification Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to section 906 of the Sarbanes-Oxley Act of 2002.[1]

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1 Filed herewith.

2 Confidential treatment granted.

3 Confidential treatment has been requested with respect to portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission.

4 Compensation plan or arrangement in which directors and executive officers are eligible to participate.

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INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

The following Consolidated Financial Statements, and the related Notes thereto, of Adolor Corporation and subsidiary and the Report of Independent Auditors are filed as a part of this annual report on Form 10-K.

Independent Auditors' Report

The Board of Directors and Stockholders
Adolor Corporation:

We have audited the accompanying consolidated balance sheets of Adolor Corporation (a development-stage company) and subsidiary as of December 31, 2003 and 2002, and the related consolidated statements of operations, comprehensive loss, stockholders' equity and cash flows for each of the years in the three-year period ended December 31, 2003 and for the period from August 9, 1993 (inception) to December 31, 2003. These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits.

We conducted our audits in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the consolidated financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of Adolor Corporation (a development-stage company) and subsidiary as of December 31, 2003 and 2002, and the results of their operations and their cash flows for each of the years in the three-year period ended December 31, 2003, and for the period from August 9, 1993 (inception) to December 31, 2003, in conformity with accounting principles generally accepted in the United States of America.

/s/ KPMG LLP

Philadelphia, Pennsylvania
February 13, 2004

ADOLOR CORPORATION AND SUBSIDIARY
(A Development Stage Company)

CONSOLIDATED BALANCE SHEETS

	December 31, 2003	December 31, 2002
Assets		
Current assets:		
Cash and cash equivalents	$ 5,339,202	$ 36,667,369
Short-term investments (Note 3)	204,835,289	117,317,240
Accounts receivable from collaboration agreement (Note 4)	3,079,757	7,502,379
Prepaid expenses and other current assets	2,946,254	3,061,170
Total current assets	216,200,502	164,548,158
Equipment and leasehold improvements, net (Note 5)	8,293,324	3,546,558
Other assets	169,915	176,565
Total assets	$ 224,663,741	$ 168,271,281
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,542,699	$ 1,605,765
Accrued expenses (Note 6)	14,960,176	18,459,369
Deferred licensing fees—current (Note 4)	4,166,676	4,192,980
Total current liabilities	20,669,551	24,258,114
Deferred licensing fees – non-current (Note 4)	38,715,256	43,285,451
Total liabilities	59,384,807	67,543,565
Commitments and Contingencies (Note 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, par value $.0001 per share; 99,000,000 shares authorized; 38,793,122 and 31,494,237 shares issued and outstanding at December 31, 2003 and 2002, respectively (Note 7)	3,879	3,149
Additional paid-in capital	372,245,584	259,854,489
Notes receivable for stock options	(54,149)	(593,034)
Deferred compensation	(757,588)	(3,707,038)
Unrealized gains on available for sale securities	221,224	343,947
Deficit accumulated during the development stage	(206,380,016)	(155,173,797)
Total stockholders' equity	165,278,934	100,727,716
Total liabilities and stockholders' equity	$ 224,663,741	$ 168,271,281

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

ADOLOR CORPORATION AND SUBSIDIARY
(A Development Stage Company)

CONSOLIDATED STATEMENTS OF OPERATIONS

Years ended December 31, 2003, 2002 and 2001, and for the period from August 9, 1993 (inception) to December 31, 2003

	Year ended December 31,			Period from August 9, 1993 (inception) to December 31, 2003
	2003	2002	2001	
Contract revenues (Note 4)	$ 20,726,637	$ 28,409,417	$ 1,386,803	$ 50,727,665
Operating expenses incurred during the development stage:				
Research and development	56,653,827	71,705,449	36,005,044	204,326,362
Marketing, general and administrative	17,648,178	21,693,270	15,229,041	70,804,427
Total operating expenses	74,302,005	93,398,719	51,234,085	275,130,789
Other income (expense):				
Interest income	2,421,312	4,484,040	7,480,587	18,377,425
Other expense	(52,163)	(19,208)	(40,535)	(354,317)
	2,369,149	4,464,832	7,440,052	18,023,108
Net loss	(51,206,219)	(60,524,470)	(42,407,230)	(206,380,016)
Undeclared dividends attributable to mandatorily redeemable convertible preferred stock	—	—	—	10,546,314
Beneficial conversion feature on mandatorily redeemable convertible preferred stock	—	—	—	48,905,779
Net loss allocable to common stockholders	$(51,206,219)	$(60,524,470)	$(42,407,230)	$(265,832,109)
Basic and diluted net loss per share allocable to common stockholders	$ (1.57)	$ (1.94)	$ (1.42)	
Shares used in computing basic and diluted net loss per share allocable to common stockholders	32,585,928	31,252,004	29,801,136	

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

ADOLOR CORPORATION AND SUBSIDIARY
(A Development Stage Company)

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

Years ended December 31, 2003, 2002 and 2001,
and the period August 9, 1993 (inception) to December 31, 2003

	Years ended December 31,			Period from August 9, 1993 (inception) to December 31, 2003
	2003	2002	2001	
Net loss	$(51,206,219)	$(60,524,470)	$(42,407,230)	$(206,380,016)
Other comprehensive income (loss):				
Unrealized gains (losses) on available for sale securities	(122,723)	(386,281)	604,647	221,224
Realized (gain)/loss on available for sale securities	29,348	—	(119,862)	(90,514)
Comprehensive loss	$(51,299,594)	$(60,910,751)	$(41,922,445)	$(206,249,306)

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

ADOLOR CORPORATION AND SUBSIDIARY
(A Development Stage Company)

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

For the period from August 9, 1993 (inception) to December 31, 2000, for the years ended December 31, 2001, 2002, and 2003

	Common stock		Additional paid-in capital	Notes receivable	Deferred compensation	Unrealized gain on available for sale securities	Deficit Accumulated during the development stage	Total stockholders' equity
	Number of shares	Amount						
Inception, August 9, 1993	—	$ —	$ —	$ —	$ —	$ —	$ —	$ —
Issuance of common stock to founder in November 1994 at $.001 per share	100,000	10	12,490	—	(12,400)	—	—	100
Issuance of restricted stock in November 1994 and May 1996	565,411	57	72,355	—	(66,767)	—	—	5,645
Issuance of common stock for technology license agreements in December 1995 at $.125 per share	50,000	5	6,245	—	—	—	—	6,250
Issuance of common stock for services in April 1999 at $3.736 per share	3,570	—	13,339	—	—	—	—	13,339
Value attributed to issuance of warrants	—	—	60,000	—	—	—	—	60,000
Notes issued to employees for stock options exercised	—	—	—	(1,056,488)	—	—	—	(1,056,488)
Accretion of Series H preferred stock issuance costs	—	—	(281,794)	—	—	—	—	(281,794)
Exercise of stock options	1,507,450	150	1,461,508	—	—	—	—	1,461,658
Unrealized gain on investments	—	—	—	—	—	125,581	—	125,581
Conversion of preferred shares	18,818,421	1,882	80,381,821	—	—	—	—	80,383,703
Net proceeds from initial public offering	6,900,000	690	95,375,779	—	—	—	—	95,376,469
Deferred compensation resulting from grant of stock options	—	—	23,234,032	—	(23,234,032)	—	—	—
Amortization of deferred compensation	—	—	—	—	5,187,238	—	—	5,187,238
Net loss	—	—	—	—	—	—	(52,242,097)	(52,242,097)
Balance, December 31, 2000	27,944,852	2,794	200,335,775	(1,056,488)	(18,125,961)	125,581	(52,242,097)	129,039,604
Payments on notes granted to employees for stock options	—	—	—	156,839	—	—	—	156,839
Interest receivable converted to principal on employee notes	—	—	—	(69,339)	—	—	—	(69,339)
Forfeiture of stock options	(67,303)	(7)	(1,124,660)	150,942	973,725	—	—	—
Exercise of stock options	226,755	23	307,313	—	—	—	—	307,336
Unrealized gain on investments	—	—	—	—	—	604,647	—	604,647
Net proceeds from issuance of newly registered shares of common stock	3,000,000	300	58,962,347	—	—	—	—	58,962,647
Deferred compensation resulting from grant of stock options	—	—	562,242	—	(562,242)	—	—	—
Amortization of deferred compensation	—	—	—	—	6,186,781	—	—	6,186,781
Net loss	—	—	—	—	—	—	(42,407,230)	(42,407,230)
Balance, December 31, 2001	31,104,304	3,110	259,043,017	(818,046)	(11,527,697)	730,228	(94,649,327)	152,781,285

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

ADOLOR CORPORATION AND SUBSIDIARY
(A Development Stage Company)

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY—Continued

For the period from August 9, 1993 (inception) to December 31, 2000, for the years ended December 31, 2001, 2002 and 2003

	Common stock		Additional paid-in capital	Notes receivable	Deferred compensation	Unrealized gain on available for sale securities	Deficit Accumulated during the development stage	Total stockholders' equity
	Number of shares	Amount						
Payments on notes granted to employees for stock options	—	—	—	267,677	—	—	—	267,677
Interest receivable converted to principal on employee notes	—	—	—	(49,534)	—	—	—	(49,534)
Forfeiture of stock and stock options	(2,943)	—	(739,447)	6,869	732,578	—	—	—
Reduction of estimated offering costs	—	—	400,000	—	—	—	—	400,000
Exercise of stock options	385,526	39	889,437	—	—	—	—	889,476
Issuance of common stock for bonus awards and under an employment agreement	7,350	—	320,307	—	(2,172)	—	—	318,135
Unrealized loss on investments	—	—	—	—	—	(386,281)	—	(386,281)
Deferred compensation resulting from grant of stock options adjustment	—	—	(30,270)	—	30,270	—	—	—
Accelerated amortization and cancellation of deferred compensation resulting from the acceleration of vesting of stock options	—	—	(28,555)	—	2,884,232	—	—	2,855,677
Amortization of deferred compensation	—	—	—	—	4,175,751	—	—	4,175,751
Net loss	—	—	—	—	—	—	(60,524,470)	(60,524,470)
Balance, December 31, 2002	31,494,237	3,149	259,854,489	(593,034)	(3,707,038)	343,947	(155,173,797)	100,727,716
Payments on notes granted to employees for stock options	—	—	—	546,681	—	—	—	546,681
Interest receivable converted to principal on employee notes	—	—	—	(10,051)	—	—	—	(10,051)
Forfeiture of stock and stock options	(1,001)	—	(2,255)	2,255	—	—	—	—
Exercise of stock options	396,057	40	932,785	—	—	—	—	932,825
Issuance of common stock for technology license agreements	3,829	—	50,006	—	—	—	—	50,006
Unrealized loss on investments	—	—	—	—	—	(122,723)	—	(122,723)
Net proceeds from issuance of newly registered shares of common stock	6,900,000	690	111,584,379		—	—	—	111,585,069
Deferred compensation resulting from grant of stock options to non-employees	—	—	145,007	—	(145,007)	—	—	—
Cancellations and accelerated amortization of deferred compensation resulting from the acceleration of vesting of stock options	—	—	(318,827)	—	567,482	—	—	248,655
Amortization of deferred compensation	—	—	—	—	2,526,975	—	—	2,526,975
Net loss	—	—	—	—	—	—	(51,206,219)	(51,206,219)
Balance, December 31, 2003	38,793,122	$3,879	$372,245,584	$ (54,149)	$ (757,588)	$ 221,224	$(206,380,016)	$165,278,934

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

ADOLOR CORPORATION AND SUBSIDIARY
(A Development Stage Company)

CONSOLIDATED STATEMENTS OF CASH FLOWS

Years ended December 31, 2003, 2002 and 2001, and for the period from August 9, 1993 (inception) to December 31, 2003

	Year ended December 31,			Period from August 9, 1993 (inception) to December 31, 2003
	2003	2002	2001	
Net cash flows from operating activities:				
Net loss	$ (51,206,219)	$ (60,524,470)	$ (42,407,230)	$(206,380,016)
Adjustments to reconcile net loss to net cash used in operating activities:				
Non-cash compensation expense	2,679,095	7,349,563	6,186,781	21,402,677
Non-cash warrant value	—	—	—	60,000
Depreciation and amortization expense	1,854,195	1,395,582	873,691	5,214,453
Non-cash benefit from the trade of equipment	—	120,000	—	120,000
(Gain)/loss on the sale of equipment	41,412	(61,639)	—	(20,227)
Issuance of common stock for technology license agreements	50,006	—	—	56,256
Changes in assets and liabilities:				
Accounts receivable from collaboration agreements	4,422,622	(7,502,379)	—	(3,079,757)
Prepaid expenses and other current assets	114,916	1,173,339	(1,731,261)	(2,946,254)
Other assets	6,650	(94,530)	3,972	(169,915)
Accounts payable	(63,066)	(724,336)	597,570	1,542,699
Accrued expenses	(3,463,637)	10,024,622	5,242,214	14,960,176
Deferred licensing fees	(4,596,499)	47,022,291	(489,035)	42,881,932
Net cash used in operating activities	(50,160,525)	(1,821,957)	(31,723,298)	(126,357,976)
Net cash flows from investing activities:				
Purchases of equipment and leasehold improvements	(6,642,373)	(1,724,198)	(2,903,817)	(13,738,483)
Proceeds from the sale of equipment	—	144,273	—	144,273
Purchases of short-term investments	(260,410,834)	(101,681,763)	(115,569,886)	(574,004,391)
Maturities of short-term investments	172,770,061	90,405,159	73,985,221	369,390,325
Net cash used in investing activities	(94,283,146)	(12,856,529)	(44,488,482)	(218,208,276)
Net cash flows from financing activities:				
Net proceeds from issuance of mandatorily redeemable convertible preferred stock and Series B warrants	—	—	—	78,501,909
Proceeds from Series D mandatorily redeemable convertible preferred stock Subscription	—	—	—	600,000
Net proceeds from exercise of common stock options and issuance of restricted common stock	1,029,361	889,476	307,336	2,637,087
Proceeds from notes payable—related parties	—	—	—	1,000,000
Proceeds from notes payable	93,824	248,506	88,033	1,832,474
Payment of notes payable	(129,380)	(427,769)	(609,086)	(1,832,474)
Proceeds received on notes receivable	546,681	267,677	156,839	971,197
Interest receivable converted to principal on notes	(10,051)	(49,534)	(69,339)	(128,924)
Net proceeds from issuance of common stock	111,585,069	400,000	58,962,647	266,324,185
Net cash provided by financing activities	113,115,504	1,328,356	58,836,430	349,905,454
Net increase (decrease) in cash and cash equivalents	(31,328,167)	(13,350,130)	(17,375,350)	5,339,202
Cash and cash equivalents at beginning of year	36,667,369	50,017,499	67,392,849	—
Cash and cash equivalents at end of year	$ 5,339,202	$ 36,667,369	$ 50,017,499	$ 5,339,202
Supplemental disclosure of cash flow information:				
Cash paid for interest	$ 10,751	$ 19,208	$ 40,535	$ 223,030
Supplemental disclosure of non-cash financing activities:				
Unrealized gains (losses) on available for sale securities	$ (122,723)	$ (386,281)	$ 604,647	$ 221,224
Deferred compensation from issuance of common stock, restricted common stock and common stock options	145,007	118,326	562,242	24,138,774
Issuance of common stock for technology license agreements or for services	—	—	—	19,589
Conversion of Series A through H (excluding D) preferred stock for common stock	—	—	—	80,383,703
Conversion of stock subscription to Series D mandatorily redeemable preferred stock	—	—	—	600,000
Conversion of bridge financing, including accrued interest, to Series B mandatorily redeemable preferred stock	—	—	—	1,019,787

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

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. ORGANIZATION AND BUSINESS ACTIVITIES

Adolor Corporation (together with its subsidiary, "Adolor" or the "Company") is a development stage biopharmaceutical corporation that was formed in 1993. The Company specializes in the discovery, development and commercialization of prescription pain management products. The Company has a number of small molecule product candidates that are in various stages of development ranging from preclinical studies to Phase III clinical trials. The Company's lead product candidate, Entereg™ (alvimopan), is designed to selectively block the unwanted effects of opioid analgesics in the gastrointestinal tract. Our other product candidates are being designed as analgesics to treat moderate-to-severe pain conditions.

The Company has not generated any product sales revenues and has not achieved profitable operations. The Company's deficit accumulated during the development stage through December 31, 2003 aggregated approximately $206.4 million, and the Company expects to continue to incur substantial losses in future periods. A significant portion of the Company's revenue recognized in 2002 and 2003 has been from reimbursement of expenses from Glaxo Group Limited ("Glaxo") under the Company's collaboration agreement and it is expected that such revenues will be reduced in future periods as the related reimbursable expenses are expected to decrease. The Company is highly dependent on the success of the Company's research, development and licensing efforts and, ultimately, upon regulatory approval and market acceptance of its products under development, particularly its lead product candidate, Entereg™. There is no assurance that the Company will ever generate product sales or achieve profitable operations, or that profitable operations, if achieved, could be sustained on a continuing basis.

The Company does not expect to generate a positive cash flow from operations for the next several years, if ever. The Company will need to raise additional funds to finance its operating activities prior to exhausting its current cash, cash equivalents and short-term investments. There are no assurances that the Company will be successful in obtaining an adequate level of financing for the long-term development and commercialization of its product candidates.

2. BASIS OF ACCOUNTING AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Principles of Consolidation

The consolidated financial statements include the accounts of Adolor Corporation and its wholly owned subsidiary. All significant intercompany accounts and transactions have been eliminated in consolidation.

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of three months or less when purchased to be cash equivalents. Cash equivalents are held in investment grade fixed income securities including U.S. Treasury obligations, U.S. Government sponsored obligations and corporate securities. The carrying amount of cash and cash equivalents approximates its fair value due to its short-term nature.

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. All short-term investments, including securities with

maturities in excess of one year, are classified as current, as management can sell these at any time at their option. 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.

Concentration of Credit Risk

The Company invests its excess cash in accordance with a policy objective that seeks to ensure 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.

Equipment and Leasehold Improvements

Purchases of equipment (consisting of computer, office and laboratory equipment, and furniture and fixtures) and leasehold improvements are recorded at cost. Depreciation and amortization is provided using the straight-line method over the estimated useful lives of the assets or lease term, whichever is shorter, generally three to seven years. Expenditures for repairs and maintenance are expensed as incurred.

Revenue Recognition

The Company records a liability for deferred revenue for amounts received as upfront payments under collaboration agreements in which the Company has continuing involvement. The Company recognizes such deferred amounts as revenue ratably over the estimated contract performance period. Such revenue recognition may be accelerated in the event of contract termination prior to completion of the expected performance period. Milestone amounts are recorded as revenue when the milestone event is achieved. Amounts reimbursable for costs incurred pursuant to the terms of collaboration agreements are recorded as revenue in the period in which the reimbursable cost is incurred. Such revenues are estimated based on estimates of the reimbursable amount and are subject to verification by the collaborators.

Research and Development Expenses

Research and product development costs are expensed as incurred. Costs incurred under agreements with third parties are expensed as incurred in accordance with the specific contractual performance terms of such agreements. 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, laboratory supplies costs and facility related costs.

Accounting for Income Taxes

Deferred income tax assets and liabilities are determined based on differences between the financial statement reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences 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 managed and operated as one business. The Company 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 Share

Net loss per share is computed by dividing the net loss allocable to common stockholders by the weighted average number of shares of common stock outstanding. Net loss allocable to common stockholders is calculated as the net loss plus preferred dividends accrued for the respective period, whether or not declared, plus the beneficial conversion feature on mandatorily redeemable convertible preferred stock. In computing the basic and diluted net loss per share allocable to common stockholders the weighted average number of shares remains the same for both calculations due to the fact that when a net loss exists, dilutive shares are not included in the calculation.

Use of Estimates

The preparation of the Company's consolidated financial statements in conformity with accounting principles generally accepted in the United States requires management to adopt critical accounting policies and to make estimates and assumptions that affect the amounts reported in its financial statements and accompanying notes. The estimates we make are principally in the areas of contract revenue recognition and research and development expense accrual. Actual results could differ materially from those estimates.

Reclassifications

Certain prior year amounts have been reclassified to conform with the current year presentation.

Stock-Based Compensation

The Company accounts for stock option issuances to employees and members of the Board of Directors in accordance with the provisions of APB No. 25, "Accounting for Stock Issued to Employees," and related interpretations. The Company does not record compensation expense on options granted to employees with exercise prices equal to fair market value at date of grant. Deferred compensation is recorded only to the extent that the current estimated fair value of the underlying stock exceeds the exercise price of the options on the date of grant. Such deferred compensation is amortized on a straight-line basis over the respective vesting periods of such option grants.

In December 2002, the FASB issued SFAS No. 148, "Accounting for Stock-Based Compensation – Transition and Disclosure". This statement amends SFAS No. 123, "Accounting for Stock-Based Compensation", to provide alternative methods of transition for a voluntary change to the fair value based method of accounting for stock-based employee compensation. In addition, this statement amended the disclosure requirements of SFAS No. 123 to require prominent disclosures in both annual and interim financial statements about the method of accounting for stock-based employee compensation and the effect of the method used on reported results. The disclosure requirements of SFAS No. 148, which were effective for financial statements issued after December 15, 2002, have been incorporated herein.

Had the Company determined compensation cost for options granted during the years ended December 31, 2003, 2002 and 2001 based on the fair value method at the grant date under SFAS No. 123, the Company's net loss and net loss per share would have been increased to the pro forma amounts indicated below:

	Years Ended December 31,		
	2003	2002	2001
Net loss, as reported	$(51,206,219)	$(60,524,470)	$(42,407,230)
Add: Stock-based employee compensation expense included in reported net loss	2,461,017	6,884,428	6,039,781
Deduct: Total stock-based employee compensation expense determined under fair value based method of all awards	(7,740,796)	(9,031,775)	(7,029,598)
Pro forma net loss	$(56,485,998)	$(62,671,817)	$(43,397,047)
Loss per share:			
Basic and diluted—as reported	$ (1.57)	$ (1.94)	$ (1.42)
Basic and diluted– pro forma	$ (1.73)	$ (2.01)	$ (1.46)

The weighted average fair value of the options granted during 2003, 2002 and 2001, is estimated at $5.60, $6.07, and $10.17 per share, respectively, using Black-Scholes option pricing model with the following assumptions: dividend yield of zero; volatility of 50 percent, 47 percent, and 48 percent, respectively; weighted average risk-free interest rate of between 2.10 and 3.52 percent, between 2.67 and 4.76 percent, and between 3.73 and 5.01 percent, respectively; and an expected life of 4.0, 4.0, and 6.0 years, respectively.

3. SHORT-TERM INVESTMENTS

Short-term investments consist of investment grade fixed income securities with original maturities of greater than three months and include U.S. Treasury obligations, U.S. government sponsored obligations ("agencies") and corporate securities. All short-term investments are carried as "available for sale" investments.

The following summarizes the short-term investments at December 31, 2003 and 2002:

	Cost	Gross Unrealized gains	Gross Unrealized losses	Fair value
Corporate bonds	$ 32,067,478	$106,799	$ (8,090)	$ 32,166,187
US Government obligations & agencies	172,546,587	130,514	(7,999)	172,669,102
December 31, 2003	$204,614,065	$237,313	$(16,089)	$204,835,289
Corporate bonds	$112,953,120	$381,409	$(45,119)	$113,289,410
US Government obligations & agencies	4,020,173	7,657	—	4,027,830
December 31, 2002	$116,973,293	$389,066	$(45,119)	$117,317,240

At December 31, 2003, maturities of investments were as follows:

	Cost	Gross Unrealized gains	Gross Unrealized losses	Fair value
Less than 1 year	$138,080,814	$ 37,652	$(15,887)	$138,102,579
Due in 1-2 years	66,533,251	199,661	(202)	66,732,710
December 31, 2003	$204,614,065	$237,313	$(16,089)	$204,835,289

4. CONTRACT REVENUES

The following summarizes revenues for the year ended December 31, 2003, 2002 and 2001:

	December 31,		
	2003	2002	2001
Collaborative agreement cost reimbursement	$16,141,916	$24,246,332	$ —
Amortization of up-front license fees	4,584,721	2,977,710	556,732
Grant revenue	—	735,375	80,071
License and milestone payments	—	450,000	750,000
Total revenue	$20,726,637	$28,409,417	$1,386,803

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 during the quarter ended June 30, 2002. The $50.0 million signing fee is reflected in deferred licensing fees and is expected to be recognized as revenue on a straight-line basis through April 2014, the estimated performance period under the collaboration agreement. Revenue of $4,166,675 and $2,951,394, respectively, was recognized in the years ended December 31, 2003 and 2002, related thereto. The Company may receive milestone payments of up to $220.0 million over the term of the agreement, upon the successful achievement, if any, of certain clinical and regulatory objectives. The milestone payments relate to substantive achievements in the development lifecycle and will be recognized as revenue if and when the milestones are achieved.

The Company and Glaxo agreed to develop Entereg™ for a number of acute and chronic indications which would potentially involve the use of Entereg™ in in-patient and out-patient settings. In the United States, the Company and Glaxo intend to co-develop and intend to co-promote Entereg™ and share development expenses and commercial returns, if any, pursuant to contractually agreed percentages. The Company has overall responsibility for development activities for acute care indications, such as POI, and Glaxo has overall responsibility for development activities for chronic care indications, such as OBD. Outside the United States, Glaxo will be responsible for the development and commercialization of Entereg™ for all indications, and the Company will receive royalties on sales revenues, if any. Glaxo has certain rights to terminate the collaboration agreement, as well as certain rights to terminate its rights and obligations with respect to the acute-care indications and/or chronic-care indications.

External expenses for research and development and marketing activities incurred by each company in the United States are reimbursed by the other party pursuant to contractually agreed percentages. Contract reimbursement amounts owed to the Company by Glaxo are recorded gross on its consolidated statements of operations as contract reimbursement revenue. Amounts reimbursable to Glaxo by the Company are recorded as research and development expense or marketing expense, as appropriate, on the Company's consolidated

statements of operations. The Company recorded contract reimbursement revenues of $16,141,916 and $24,246,332, respectively, in the years ended December 31, 2003 and 2002 under this arrangement. As of December 31, 2003 and 2002, $3,079,757 and $7,502,379, respectively, were receivable from Glaxo for reimbursement of expenses incurred by the Company pursuant to the collaboration agreement.

In September 2001, the National Institutes of Health awarded the Company three Small Business Innovation Research ("SBIR") grants to fund research into novel compounds for pain relief. These grants have been completed.

In July 1999, the Company entered into a license agreement with an affiliate of GlaxoSmithKline, SB Pharmco ("SB"), granting SB an exclusive license to ADL 2-1294 for certain indications in all countries in the world other than North and South Korea. Upon signing the agreement, the Company received a non-refundable licensing fee of $500,000. This licensing fee had been deferred and was being recognized over the remaining life of the patents. In December 2001, SB discontinued this license agreement. Upon termination of this agreement, the remaining balance of $438,596 of deferred revenue was recognized as revenue based on the fact that the balance was non-refundable and there would be no further continuing involvement.

In April 2000, the Company entered into a license agreement with Santen Pharmaceutical Co., Ltd. granting Santen an exclusive royalty bearing license to develop and sell products in the field of ophthalmic pain in all countries other than South Korea and North Korea. A $500,000 non-refundable payment has been paid to the Company upon execution of the agreement. Such amount was recorded as deferred revenue and was being recognized over the remaining patent life. In 2003 Santen terminated this agreement, and as a result, the remaining balance of $418,046 of deferred revenue was recognized as revenue in 2003.

5. EQUIPMENT AND LEASEHOLD IMPROVEMENTS

Equipment and leasehold improvements consist of the following:

	December 31, 2003	December 31, 2002
Laboratory, computer and office equipment	$ 7,511,064	$ 5,783,897
Furniture, fixtures and leasehold improvements	5,041,250	1,033,157
	12,552,314	6,817,054
Less accumulated depreciation and amortization	(4,258,990)	(3,270,496)
	$ 8,293,324	$ 3,546,558

6. ACCRUED EXPENSES

Accrued expenses consist of the following:

	December 31, 2003	December 31, 2002
Clinical development costs	$ 2,995,095	$ 8,802,441
Manufacturing costs	4,522,001	4,300,964
Consulting and other costs	2,744,098	2,743,524
Collaboration agreement expenses	1,479,474	80,000
Professional fees	288,214	790,907
Personnel related costs	2,931,294	1,741,533
	$14,960,176	$18,459,369

7. COMMON STOCK AND COMMON STOCK OPTIONS

In November 2000, the Company sold 6 million shares of common stock in its initial public offering. Upon the exercise of the underwriter's over-allotment option, the Company sold an additional 900,000 shares of common stock. The price to the public of the 6.9 million shares of common stock sold was $15.00 per share. The proceeds of the offering were approximately $95,376,000, net of offering costs.

In May 2001, the Company sold 3 million shares of common stock to certain institutional investors at $20.00 per share. The proceeds of the offering were approximately $58,962,000, net of offering costs.

In November 2003, the Company sold 6,000,000 shares of our common stock. Upon the exercise of the underwriter's over-allotment option, we sold an additional 900,000 shares of common stock. The price to the public of the 6.9 million shares of common stock sold was $17.25 per share. The proceeds of the offering were approximately $111,585,000, net of offering costs.

On September 13, 2000, the Board of Directors approved a reverse stock split of its common stock on a 1-for-5 basis, changed the number of authorized shares of common stock to 99,000,000 and authorized 1,000,000 shares of undesignated preferred stock, which action became effective on March 22, 2001. All common stock, option, and per share amounts in the accompanying financial statements have been retroactively adjusted to reflect the reverse stock split for all periods presented.

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 Arrangement

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.

Stock Options

The Company's 1994 Amended and Restated Equity Compensation Plan, as amended (the "1994 Plan") and 2003 Stock-Based Incentive Compensation Plan (the "2003 Plan"), together known as the Plans, allow the granting of incentive and nonqualified stock options to employees, directors, consultants and contractors to purchase an aggregate of 8,850,000 shares of the Company's common stock. The options are exercisable generally for a period of seven to ten years from the date of grant and vest over terms ranging from immediately to four years. Additionally, in 2002, the Company granted its Chief Executive Officer options to purchase 540,000 shares of common stock outside of the Plans.

A summary of option activity from January 1, 2001 to December 31, 2003, is as follows:

	Number of options	Exercise Price per share
Balance, January 1, 2001	1,683,183	$
Granted	556,782	11.32-27.99
Exercised	(226,755)	.13-19.50
Cancelled	(86,989)	.21-21.81
Balance, December 31, 2001	1,926,221	
Granted	1,599,754	9.85-17.33
Exercised	(385,526)	.21-16.11
Cancelled	(207,060)	.13-21.30
Balance, December 31, 2002	2,933,389	
Granted	1,021,790	11.26-20.14
Exercised	(386,798)	.21-17.59
Cancelled	(140,583)	.21-27.99
Balance, December 31, 2003	3,427,798	

A summary of options outstanding and exercisable by price range at December 31, 2003 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)
$0.00—2.79	144,091	5.9	$ 1.99	128,020	$ 1.91
$2.80—5.59	371,723	6.6	3.50	309,230	3.50
$5.60—8.39	—	—	—	—	—
$8.40—11.19	132,250	8.5	10.09	48,335	10.09
$11.20—13.99	908,239	8.6	13.05	276,458	13.31
$14.00—16.79	1,302,690	8.1	15.17	453,530	15.40
$16.80—19.59	302,069	9.2	18.49	56,440	18.00
$19.60—22.39	256,736	7.1	21.09	226,494	21.12
$22.40—25.19	—	—	—	—	—
$25.20—27.99	10,000	7.4	27.99	6,249	27.99
	3,427,798		$13.36	1,504,756	$12.26

During the year ended December 31, 2000, the Company granted options to certain employees to acquire 1,657,035 shares of the Company's common stock at exercise prices ranging from $2.25 to $3.50 per share for which deferred compensation, based on a fair value of $14.40 per share on the grant date, amounting to $18.7 million was recorded and is being amortized to compensation expense over the respective vesting periods of the options.

During the years ended December 31, 2003 and 2001, the Company granted options to non-employees to acquire 4,000 and 20,000 shares of common stock, respectively, for which deferred compensation of $24,627 and $294,000 was recorded in 2003 and 2001, respectively, based on fair value as determined using a Black-Scholes option pricing model and is being amortized to expense over the vesting periods of the options. The amount of amortization for option grants to non-employees is subject to change each reporting period based upon changes in the fair value of the Company's common stock, estimated volatility and the risk free interest rate until the non-employee completes his or her performance under the option agreement.

Compensation expense, during the years ended December 31, 2003 and 2002, relating to option grants was approximately $2.8 million and $7.0 million, respectively, of which approximately $0.3 million and $2.6 million was in connection with the acceleration of the vesting of certain stock options under an employment agreement and separation agreements. Future compensation expense relating to such option grants is expected to be approximately $0.8 million for the year ending December 31, 2004. The expense amortization of deferred compensation may change subject to termination or acceleration of vesting of the related stock options.

During March 2000, certain officers and employees exercised options to purchase 472,067 shares of common stock and delivered promissory notes to the Company in the aggregate amount of approximately $1,056,500 as consideration for the exercise price. The underlying shares of these exercised options were scheduled to vest monthly over four years, during which time the Company had the right to repurchase any unvested shares. The promissory notes were full recourse and were secured by shares of the Company's common stock. The promissory notes accrued interest at an annual rate of 6.80% and are payable in March 2007. As the makers of the promissory notes sell the shares of the Company's common stock that secure the notes, the makers are required to repay the principal amounts due under the notes secured by the sold shares. As of December 31, 2003 notes receivable of $54,149 were outstanding and 6,282 shares were subject to repurchase at the purchase price paid by the employee. Such amounts are reflected as a reduction of stockholders' equity.

8. LICENSE AND RESEARCH AGREEMENTS

In November 1996 Roberts Laboratories Inc. ("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 licensed from Roberts the rights Roberts had licensed from Eli Lilly for Entereg™. As of December 31, 2003, the Company has paid $600,000 to Roberts. Under the Option and License Agreement the Company is obligated to pay milestone payments to Roberts and Eli Lilly upon the achievement of certain clinical and regulatory milestones that in the aggregate may total up to $1.9 million. The Company is also responsible for the costs to develop Entereg™. In addition, if Entereg™ receives regulatory approval, the Company is obligated to pay royalties to Roberts and Eli Lilly on commercial sales of Entereg™. Under the terms of the arrangements, the license to Entereg™ expires on the later of either the life of the last to expire of the licensed Eli Lilly patents or fifteen years from November 5, 1996, following which the Company will have a fully paid up license.

In August 2002, the Company entered into an exclusive license agreement with Eli Lilly under which the Company obtained an exclusive license to six issued U.S. patents, related foreign equivalents and know-how relating to peripherally selective opioid antagonists. The Company paid Eli Lilly $4.0 million upon signing the

agreement. The Company 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 agreed to pay Eli Lilly a $4.0 million dollar payment upon acceptance by a regulatory authority of the first application for marketing authorization for Entereg™.

In July 2003, the Company entered into an agreement with EpiCept Corporation ("EpiCept") under which we licensed exclusive rights to develop and commercialize in North America a sterile lidocaine patch which is being developed for the management of postoperative incisional pain. We made a $2.5 million payment to EpiCept upon execution of the agreement and may make up to $20.0 million in additional development milestone payments if certain clinical and regulatory achievements are reached. The $2.5 million payment was recorded as research and development expense in 2003 as the underlying technology licensed has not reached technological feasibility and has no alternative uses.

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

9. INCOME TAXES

No federal and state taxes are payable as of December 31, 2003 and 2002. As of December 31, 2003, the Company had approximately $60,716,000 of Federal and $61,003,000 of state net operating loss carryforwards potentially available to offset future taxable income. The Federal and Pennsylvania net operating loss carryforwards will expire as follows:

	State	Federal
2005	$ 450,000	$ —
2006	1,232,000	—
2007	2,063,000	—
2008	3,519,000	—
2009	3,938,000	33,000
2010	6,780,000	482,000
2011	12,151,000	1,078,000
2012	20,032,000	1,867,000
Thereafter	10,838,000	57,256,000
	$61,003,000	$60,716,000

The utilization of the state net operating loss carryforwards is subject to a $2.0 million annual limitation. At December 31, 2003, the Company also has approximately $4,421,000 of Federal and $716,000 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 the Company's ability to utilize these carryforwards. The Company may have experienced various ownership changes, as defined by the Act, as a result of past financings and the initial public offering. Accordingly, the Company's ability to utilize the aforementioned carryforwards may be limited. Additionally, U.S. tax laws limit the time during which these carryforwards may be applied against future taxes; therefore the Company may not be able to take full advantage of these carryforwards for Federal income tax purposes.

Significant components of the Company's deferred tax assets and liabilities are shown below. At December 31, 2003, a valuation allowance of $84,408,000 has been recognized to fully offset the deferred tax asset balance. A valuation allowance to reduce the deferred tax assets is required if, based on 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 assets is dependent upon generating future taxable income and given the uncertainty of future profitability, management has determined that a valuation allowance is necessary to reduce net deferred tax assets to zero. The change in the deferred tax asset account before application of the valuation allowance in 2003 and 2002 were increases of $21,730,000 and $25,362,000, respectively, related primarily to additional net operating losses and capitalized research and development costs incurred by the Company.

	2003	2002
Deferred tax assets:		
Net operating losses	$ 25,159,000	$ 17,374,000
Capitalized research and development costs	36,711,000	18,332,000
Tax credit carryforwards	4,886,000	4,112,000
Deferred revenue	17,793,000	19,700,000
Accrued expenses and other	169,000	3,340,000
Total deferred tax assets	84,718,000	62,858,000
Less valuation allowance	(84,408,000)	(62,678,000)
Net deferred tax assets	310,000	180,000
Deferred tax liability	(310,000)	(180,000)
Net deferred tax	$ —	$ —

10. COMMITMENTS AND CONTINGENCIES

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

Year ending December 31,	
2004	$ 1,365,000
2005	1,268,000
2006	1,218,000
2007	1,215,000
2008	1,215,000
2009 & beyond	4,861,000
	$11,142,000

Rent expense was $1,603,304, $976,680, and $843,854 for the years ended December 31, 2003, 2002 and 2001, respectively. In December 2002, the Company signed a new ten-year lease agreement for office and laboratory space with minimum rental payments of approximately $1,110,000 for 2004 through 2008, and $1,170,000 for 2009 through 2013.

Glaxo Collaboration Agreement

Under the terms of the Glaxo agreement, the Company will 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 expects to incur 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 expects to record these expenses as incurred.

Other Service Agreements

The Company has entered into various agreements for services with third party vendors, including agreements to conduct clinical trials, to manufacture product candidates, and for consulting and other contracted services. The Company accrues the costs of these agreements based on estimates of work completed to date. The Company estimates that approximately $15.0 million will be payable in future periods under arrangements in place at December 31, 2003. Of this amount, approximately $10.3 million has been accrued for work estimated to have been completed as of December 31, 2003 and approximately $4.7 million relates to future performance under these arrangements.

11. 401(k) PROFIT SHARING PLAN

In 1995, the Company adopted 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 20% of their salary, not to exceed the limits established by the Internal Revenue Code. All contributions made by participants vest immediately into the participant's account. The Company was not required to make and did not make any contributions to the 401(k) Plan in 2000 and 2001. In 2003 and 2002, the Company made contributions to the 401(k) Plan of approximately $174,000 and $143,000, respectively. The Company's common stock is not and never has been an investment option for 401(k) Plan participants.

12. QUARTERLY INFORMATION (UNAUDITED)

This table summarizes the unaudited results of operations for each quarter of 2003 and 2002:

	Quarter Ended			
	March 31	June 30	September 30	December 31
	(In thousands, except per share amounts)			
Fiscal 2003				
Revenue	$ 6,637	$ 5,120	$ 4,848	$ 4,122
Net loss	(11,329)	(11,491)	(13,838)	(14,548)
Basic and diluted loss per share	(0.36)	(0.36)	(0.44)	(0.41)
Fiscal 2002				
Revenue	$ 317	$ 10,458	$ 9,068	$ 8,566
Net loss	(19,592)	(8,726)	(20,159)	(12,047)
Basic and diluted loss per share	(0.63)	(0.28)	(0.65)	(0.38)

Although the collaboration agreement with Glaxo was executed in April 2002, the cost sharing arrangement was retroactive to January 1, 2002. The second quarter of 2002 includes $3,427,102 of reimbursement revenue for first quarter reimbursable expenses.

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